KONFERENCJA

DIAGNOSTYKA I LECZENIE CHORÓB PRZYSADKI

VII ZJAZD POLSKIEGO TOWARZYSTWA NEUROENDOKRYNOLOGII

17–18 października 2025, Kraków

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PTNE

KONFERENCJA Diagnostyka i Leczenie Chorób Przysadki 17.10.2025

PIĄTEK 17.10.2025

09.00 – Otwarcie konferencji

09.05–09.40 – I. Sesja międzynarodowa
Przewodniczący sesji: Prof. Aleksandra Gilis-Januszewska,
Prof. Alicja Hubalewska-Dydejczyk, Prof. Beata Kos-Kudła, Prof. Marek Ruchała

09.05–09.25 Different clinical presentation and follow-up of Cushing syndrom. Do sex and age matter? – Prof. Elena Valassi (20 min.)

09.25–09.40 Dyskusja (15 min.)

09.40–11.05 – II. Diagnostyka i leczenie akromegalii, prolactinoma, zespoły wielogruczołowe – nowe standardy diagnostyki, i monitorowania skuteczności leczenia
Przewodniczący sesji: Prof. Alicja Hubalewska-Dydejczyk, Prof. Beata Kos-Kudła,
Prof. Marek Bolanowski, Prof. Grzegorz Zieliński, Prof. Marek Ruchała

09:40–09.55 Oznaczanie i interpretacja wyników badań IGF-1, HGH, kortyzolu i ACTH oraz prolaktyny – jak unikać pułapek interpretacyjnych – Prof. Krystyna Sztefko (15 min.)

09.55–10.10 Skuteczne leczenie akromegalii w 2025 r.
– Prof. Alicja Hubalewska-Dydejczyk (15 min.)
– wykład pod patronatem firmy Ipsen

10.10–10.40 Kiedy kierować pacjenta z prolactionoma do zabiegu neurochirurgicznego – punkt widzenia endokrynologa i chirurga
– Prof. Marek Bolanowski / Prof. Grzegorz Zieliński (30 min.)

10.40–10.55 Nowotwory neuroendokrynne w zespołach wielogruczołowych: wyzwania terapeutyczne i miejsce leczenia radioizotopowego
– Prof. Beata Kos-Kudła (15 min.)
– wykład pod patronatem firmy Novartis

10.55–11.05 Dyskusja (10 min.)

11.05–11.20 Przerwa kawowa

11.20–12.15 III. Diagnostyka i leczenie Zespołu Cushinga – sesja pod patronatem firmy Recordati
Przewodniczący sesji: Prof. Aleksandra Gilis-Januszewska,
Prof. Renata Świątkowska-Stodulska,
Dr Jacek Kunicki, Prof. Dariusz Kajdaniuk

11.20–11.35 Leczenie hiperkortyzolemii – indywidualizacja postępowania w zależności od sytuacji klinicznej
– Prof. Aleksandra Gilis-Januszewska (15 min.)

11.35–11.50 Diagnostyka różnicowa Zespołu Cushinga, interpretacja testów dynamicznych – Prof. Renata Świątkowska-Stodulska (15 min.)

11.50–12.05 Postępowanie w agresywnych guzach kortykotropowych z perspektywy neurochirurga/neuropatologa
– Dr Jacek Kunicki (15 min.)

12.05–12.15 Dyskusja (10 min.)

12.15–12.50 Lunch

12.50–14.20 IV. Akromegalia, Prolactinoma, kortykotropinoma, NFPA, zapalenia przysadki – standardy postępowania vs real life – forum dyskusyjne

Przewodniczący sesji: Dr Izabela Czajka-Oraniec, Dr Renata Orłowska-Florek, Dr hab. Maria Stelmachowska-Banaś, Prof. Przemysław Witek, Dr Dorota Filipowicz, Prof. Anna Wędrychowicz

12.50–13.05 Pacjentka z agresywnym, opornym na leczenie zapaleniem przysadki - Dr Izabela Czajka Oraniec (10 min. wykład + 5 min. dyskusja)

13.05–13.20 Makrogruczolak przysadki wydzielający GH i ACTH – Dr Renata Orłowska-Florek (10 min. wykład + 5 min. dyskusja)

13.20–13.35 Czy stosowanie testosteronu u mężczyzny może stymulować progresję prolaktynoma? – Dr hab. Maria Stelmachowska-Banaś (10 min. wykład + 5 min. dyskusja)

13.35–13.50 Pacjent z agresywnym przebiegiem akromegalii - postępowanie – Prof. Przemysław Witek (10 min. wykład + 5 min. dyskusja)

13:50–14.05 Różne oblicza jednej choroby – heterogenność kliniczna NFPA – Dr Dorota Filipowicz (10 min. wykład + 5 min. dyskusja)

14.05–14.20 Cykliczny przebieg choroby Cushinga o początku w okresie dziecięcym – Prof. Anna Wędrychowicz (10 min. wykład + 5 min. dyskusja)

14.20–15.15 V. Leczenie niedoczynności osi somatotropowej u dorosłych w okresie tranzycji. Leczenie niedoczynności osi nadnerczowej – indywidualizacja wyboru preparatów HC

Przewodniczący sesji: Prof. Marek Ruchała, Prof. Roman Junik, Prof. Urszula Ambroziak

14.20–14.35 Leczenie niedoczynności osi somatotropowej u osób dorosłych (AGHD) – Prof. Marek Ruchała (15 min.) wykład pod patronatem firmy Sandoz

14.35–14.50 Leczenie niedoczynności osi nadnerczowej – indywidualizacja wyboru preparatów HC – Prof. Urszula Ambroziak (15 min.)

14.50–15.05 Leczenie niedoczynności osi somatotropowej u dorosłych i w okresie tranzycji

15.05–15.15 Dyskusja (10 min.)

15.15–16.10 VI. Diagnostyka i leczenie otyłości

Przewodniczący sesji: Prof. Aleksandra Gilis-Januszewska, Prof. Beata Matyjaszek-Matuszek, Prof. Bogdan Marek, Prof. Wojciech Bik

15.15–15.30 Otyłość wtórna do zaburzeń okolicy podwzgórzowo przysadkowej – Prof. Beata Matyjaszek-Matuszek (15 min.) – wykład pod patronatem firmy Eli Lilly

15.30–15.45 MASLD a zaburzenia endokrynne i neuroendokrynne – diagnostyka i leczenie – Prof. Bogdan Marek (15 min.)

15.45–16.00 Nowoczesne leczenie otyłości – Prof. Wojciech Bik (15 min.)

16.00–16.10 Dyskusja (10 min.)

16.10 Zakończenie konferencji

VII Zjazd PTNE 17-18.10.2025

PIĄTEK 17.10.2025

16.00–16.30 Kawa powitalna

16.30–18.00 Uroczyste otwarcie Zjazdu, 25 lecie PTNE, Walne Zebranie Zarządu PTNE
Dwadzieścia pięć lat PTNE

Przewodniczący sesji: Prof. Jolanta Kunert-Radek, Prof. Marek Pawlikowski,
Prof. Krystyna Pierzchała-Koziec, Prof. Aleksandra Gilis-Januszewska,
Prof. Wojciech Bik, Prof. John Russell, Prof. Alina Gajewska

Wykład inauguracyjny: Dwadzieścia pięć lat PTNE na tle rozwoju neuroendokrynologii na świecie – Prof. Marek Pawlikowski, Prof. Jolanta Kunert-Radek (20 min.)

Neuroendokrynologia stresu – historia, teraźniejszość i przyszłość
– Prof. Krystyna Pierzchała-Koziec (15 min.)

18.00–19.30 Walne zgromadzenie PTNE

20.00–22.00 Uroczysta Kolacja z okazji 25-lecia PTNE

SOBOTA 18.10.2025

09.00–09.40 I. Sesja międzynarodowa

Przewodniczący sesji: Prof. Aleksandra Gilis-Januszewska, Prof. Wojciech Bik,
Prof. Alicja Hubalewska-Dydejczyk, Prof. Jolanta Kunert-Radek

09.00–09.30 Paraneoplastic autoimmune hypophysitis – Prof. Yutaka Takahashi

09.30–09.40 Discussion

09.40–10.35 II. Psychoneuroendokrynologia

Przewodniczący sesji: Prof. Krystyna Pierzchała-Koziec,
Prof. Marta Dziedzicka-Wasylewska, Prof. Stanisław Okrasa, Prof. Dariusz Kajdaniuk,
Dr hab. Barbara Bętkowska-Korpała, Prof. UJ

09.40–09.55 Hiperprolaktynemia – przyczyna czy skutek leczenia zaburzeń neuropsychia-trycznych – Dr hab. Agata Faron-Górecka, Prof. IF PAN (15 min.)

09.55–10.10 Zaburzenia neuropsychiatryczne w chorobach tarczycy – Prof. Dariusz Kajdaniuk (15 min.)

10:10–10.25 Neuroimmunoendokrynna interakcja osi mózgowo-żołądkowo-jelitowej – Dr hab. Marek Wieczorek, Prof. UŁ (15 min.)

10.25–10.35 Dyskusja

10.35–11.00 Przerwa kawowa

11.00–12.25 III. Neurohormony – Otyłość i zaburzenia łaknienia – problem interdyscyplinarny

Przewodniczący sesji: Prof. Alina Gajewska, Dr hab. Krzysztof Gil, Prof UJ,
Prof. Wojciech Bik, Dr hab. Agnieszka Baranowska-Bik, Prof. CMKP

11.00–11.15 Rola kisspeptyny w patogenezie jadłowstrętu psychicznego z perspektywy osi jelitowo-mózgowej – Dr Kamil Skowron (15 min.)

11.15–11.30 Aktywność układu GNRH – gonadotropiny w okresie okołopubertalnym – Prof. Alina Gajewska (15 min.)

11.30–11.45 Melatonina-neurohormon, który wykazuje również działanie antyoksydacyjne
– Prof. Małgorzata Karbownik-Lewińska (15 min.)
11.45–12.00 Otyłość a neurozapalenia – Dr Anna Litwiniuk (15 min.)
12.00–12.15 Zaburzenia łaknienia i płodność
– Dr hab. Agnieszka Baranowska-Bik, Prof. CMKP (15 min.)
12.15–12.25 Dyskusja

12.25–13.05 IV. Diagnostyka i leczenie agresywnych guzów przysadki i zmian nowotworowych w przebiegu zespołów wielogruczołowych
Przewodniczący sesji: Prof. dr hab. n. med Marek Bolanowski,
Dr hab. Aleksandra Jawiarczyk-Przybyłowska, Prof. Dariusz Kajdaniuk,
Prof. Bogdan Marek
12.25–12.40 Zastosowanie metod biologii molekularnej w prognozowaniu leczenia agresywnych guzów przysadki
– Dr hab. Mateusz Bujko, Prof. NIO
12.40–12:55 Diagnostyka i leczenie zmian nowotworowych w OUN w przebiegu zespołów wielogruczołowych VHL, NF-1 ,NF-2 – Dr Borys Kwinta
12.55–13.05 Dyskusja

13.05–14.05 V. Sesja prezentacji plakatowych / Lunch
Neuroedokrynologia doświadczalna
Przewodniczący sesji: Prof. Krystyna Pierzchała-Koziec, Prof. Alina Gajewska,
Dr hab. Marek Wieczorek, Prof. UŁ, Prof. Stanisław Okrasa,
Dr hab. Agata Faron-Górecka, Prof. IF PAN, Dr hab. Krzysztof Gil, Prof. UJ
Neuroendokrynologia kliniczna
Przewodniczący sesji: Prof. Aleksandra Gilis-Januszewska, Prof. Bogdan Marek,
Prof. Dariusz Kajdaniuk, Prof. Wojciech Bik, Prof. Marek Bolanowski,
Dr Maria Stelmachowska-Banaś, Dr hab. Aleksandra Jawiarczyk-Przybyłowska,
Prof. Roman Junik, Dr Dorota Filipowicz, Dr Anna Bogusławska, Dr Mari Minasyan

14.05–15.35 VI. Sesja krótkich doniesień ustnych
14.05–14.50 Neuroedokrynologia doświadczalna
Przewodniczący sesji: Prof. Krystyna Pierzchała-Koziec, Prof. Alina Gajewska,
Dr hab. Marek Wieczorek, Prof. UŁ, Prof. Stanisław Okrasa,
Dr hab. Agata Faron-Górecka, Prof. IF PAN, Dr hab. Krzysztof Gil, Prof. UJ,
Prof. Roman Junik, Dr Dorota Filipowicz, Dr Anna Bogusławska, Dr Mari Minasyan
14.50–15.35 Neuroendokrynologia kliniczna
Przewodniczący sesji: Prof. Aleksandra Gilis-Januszewska, Prof. Bogdan Marek,
Prof. Dariusz Kajdaniuk, Prof. Wojciech Bik, Prof. Marek Bolanowski,
Dr hab. Maria Stelmachowska-Banaś, Dr hab. Aleksandra Jawiarczyk-Przybyłowska,
Prof. Roman Junik, Dr Dorota Filipowicz, Dr Anna Bogusławska, Dr Mari Minasyan

15.35 Zakończenie Zjazdu

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Prof. dr hab. n. med. Marek Pawlikowski
Prof. dr hab. n. med. Wojciech Bik
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Lek. Martyna Więcławek
Maria Borysowicz

KOMITET NAUKOWY KONFERENCJI

Diagnostyka i leczenie chorób przysadki

Prof. dr hab. Aleksandra Gilis-Januszewska
Prof. dr hab. Bogdan Marek
Prof. dr hab. Alicja Hubalewska-Dydejczyk
Dr n. med. Renata Orłowska-Florek

Drogie Koleżanki i Koledzy
Szanowni Członkowie PTNE

Jubileusz 25-lecia Polskiego Towarzystwa Neuroendokrynologii pozwala niewątpliwie na poczucie dumy z osiągnięć naukowych Członków Towarzystwa. PTNE powstało w 2000 roku z inicjatywy Profesorów Kazimierza Kochmana i Marka Pawlikowskiego. Ideą przewodnią powołania Towarzystwa była integracja naukowców z różnych dziedzin nauk podstawowych oraz lekarzy. PTNE stworzyło forum współpracy naukowo-dydaktycznej Członków Towarzystwa. Potwierdziło to VI kolejnych Zjazdów PTNE organizowanych w Łodzi, Krakowie i Warszawie, V cyklicznych Łódzkich Spotkań Przysadkowych, liczne sympozja i konferencje naukowe. Udział wielu znamienitych gości zagranicznych, w większości już Członków Honorowych PTNE jest dowodem ożywionej współpracy międzynarodowej Towarzystwa. Interdyscyplinarna szeroka współpraca, nawiązywanie kontaktów i wymiana doświadczeń świadczą o naszej sile.

Badania realizowane przez Członków PTNE i ich Ośrodki dotyczą neuropeptydów, analogów i leków ingerujących w układy receptorowe. Ukazują ich rolę w regulacji metabolizmu, rozrodczości, a także szerokie zastosowanie w leczeniu chorób metabolicznych, co zrewolucjonizowało terapię cukrzycy 2 typu i otyłości, w leczeniu chorób neurodegeneracyjnych, nowotworowych, a szczególnie w farmakoterapii guzów przysadki i guzów neuroendokrynnych.

Pozwolę sobie na osobistą dygresję. To guzy przysadki były moją największą pasją w pracy endokrynologa-klinicysty, a osobiście wykonywane hodowle organotypowe i komórkowe guzów przysadki indukowanych estrogenami u szczurów, jak też guzów uzyskanych z operacji neurochirurgicznych były spełnieniem w pracy eksperymentalnej. To w Łodzi, w wyniku współpracy Prof. Marka Pawlikowskiego z Prof. Jacqueline Trouillas z Uniwersytetu w Lyonie wprowadzono pierwsze w Polsce kompleksowe badania immunohistochemiczne wszystkich operowanych guzów przysadki. Ta diagnostyka stała się aktualnie niemal powszechnym standardem postępowania w guzach przysadki, jak również warunkiem koniecznym do publikacji naukowych. To w oparciu o immunohistochemię dokonano nowego podziału guzów przysadki.

Ogromny postęp dokonał się w zakresie leczenia guzów przysadki. Wszyscy pamiętamy początki farmakoterapii, zastosowanie agonistów dopaminy w guzach prolaktynowych, burzliwe dyskusje toczone początkowo z neurochirurgami o priorytety w leczeniu. Zastosowanie analogów somatostatyny I i aktualnie II generacji było przełomem w leczeniu nawrotowej akromegalii i jest obecnie powszechnie stosowane.

Miałam zaszczyt zorganizowania V cyklicznych Łódzkich Spotkań Przysadkowych integrujących badaczy z wielu dziedzin nauki, diagnostów i lekarzy zajmujących się chorobami przysadki. Z radością obserwuję świetną kontynuację naukowo-dydaktycznych spotkań przysadkowych w środowisku Krakowa, realizowanych przez Klinikę Endokrynologii UJ pod auspicjami PTE i PTNE.

Podziw budzi ożywiona aktywność dydaktyczna Członków PTNE i ich Ośrodków. Imponująca jest lista kursów i sympozjów cyklicznych Zakładu Neuroendokrynologii Klinicznej CMKP, Kliniki Endokrynologii CMKP, oddziałów lokalnych PTE z udziałem PTNE, szczególnie Oddziałów Śląska i Krakowa. Ten bogaty program dydaktyczny pozwala pewnie prognozować sukcesy naukowe w kolejnym ćwierćwieczu.

Dziękuję serdecznie Pani Prezes PTNE, Profesor Aleksandrze Gilis-Januszewskiej za zaproszenie do tego krótkiego historycznego wprowadzenia. W imieniu „starej gwardii" gratuluję aktualnemu Zarządowi świetnej pracy i gorąco życzę wybitnych sukcesów w kolejnych latach.

Przesłaniem dla młodych naukowców niech będzie hasło, aby polska neuroendokrynologia pozostała silna w kraju i widoczna na świecie.

Jolanta Kunert-Radek

Członek PTNE-Łódź
Honorowy Prezes PTNE

Wykład – *M. Pawlikowski, J. Kunert-Radek:*
25 lat Polskiego Towarzystwa Neuroendokrynologii na tle rozwoju neuroendokrynologii na świecie
jest zamieszczony na stronie PTNE (www.ptne.pl).

NEUROENDOCRINOLOGY OF STRESS – HISTORY, PRESENT AND FUTURE

Pierzchała-Koziec K.[1], G. Scanes C.[2]

[1]Department of Animal Physiology and Endocrinology, University of Agriculture in Kraków, Al. Mickiewicza 24/28, 30-059 Kraków, Poland

[2]Department of Biological Sciences, University of Wisconsin Milwaukee, 3209 N Maryland Ave, Milwaukee, WI 53211, USA

Background: Since Walter Cannon formulated in 1905 "fight-or-flight" concept, neurotransmitters adrenaline/noradrenaline were connected to the brain's ability to mobilize this so-called stress response in line with activation of corticotropin-releasing hormone (CRH) in several nuclei, including the hypothalamus, amygdala and locus ceruleus, and stimulation of the locus ceruleus norepinephrine (LC/NE) system in the brain stem. During the 1950s, Hans Selye hypothesis of stress was that these systems perpetuate one another, interact with several other transmitter systems in the brain and directly activate the hypothalamic-pituitary-adrenal (HPA) axis and the three components of the autonomic nervous system, namely the sympatho-adrenal, the cranio-sacral parasympathetic and the enteric nervous systems.
Purpose: The widespread body system responses to stress are discussed, and the implications of aberrant stress system activity on physical and mental health are outlined.
Methodology: The different methods and animal models were chosen to present the bidirectional route between brain neurotransmitters and peripheral hormones during stress responses.
Results: The evolution of the neuroendocrinology of stress concept depends on the modern methods, possibility of using the animal, organs and cells models and understanding the power of molecular biology.
Conclusion: The neuroendocrine response to stress is an excellent example of a plastic system that responds to homeostasis disorders and alters its output to meet current and expected future demands.
Keywords: neurotransmitters, HPA hormones, animal models, stressors
Financial support: The study was supported by the University of Agriculture in Kraków (Grant no. sub. 020002-D015).

INFLUENCE OF ULTRA-PROCESSED FOODS ON BODY MASS REGULATION IN RATS

Kurnik-Łucka M.[1], Korczyński M.[1], Sobocińska W.[1], Jurczyk M.[1], Baranowska A.[1], Gil K.[1]

[1] Department of Pathophysiology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland

Background: The rising consumption of ultra-processed foods (UPFs) has been associated with adverse health outcomes.
Purpose: This study aimed to investigate the preliminary effects of a UPF diet on body weight gain in female Wistar rats over a 6-week period to provide a relevant framework for further exploration of metabolic impacts of UPF consumption.
Methodology: Two groups of female Wistar rats (n=8, each) were fed either a standard laboratory diet (Zoolab, ZL-B1) or a customized UPF diet (Zoolab, Poland). The standard diet provided 3644.1 kcal/kg with 70.1% energy from carbohydrates, 10.1% from fat, and 19.8% from protein. The UPF diet delivered 4607.3 kcal/kg with 49% energy from carbohydrates (70% derived from sucrose and glucose-fructose syrup), 34% from fat (primarily butter and hydrogenated palm oil, >60% saturated fatty acids), and 17% from protein. This study was carried out following ethical, regulatory, and scientific principles (protocol number 963/2025). Food intake and body mass were recorded weekly over the period of 6 weeks. Feed efficiency ratio (FER) was calculated as total weight gain (g) over total feed consumption (kcal). Statistical analysis was performed using unpaired t-tests.
Results: Total feed consumption (g) was significantly lower in the UPF group compared to controls (715.2g ± 99.1 vs. 865.1g ± 160.6; $p = 0.041$), while caloric intake did not differ significantly between groups (3306.7 kcal ± 466.4 vs. 3152.6 kcal ± 585.4; $p = 0.569$). FER was similar between groups (52.8 ‰ ± 7.2 vs. 52.2 ‰ ± 5.5; $p = 0.852$) as well.
Conclusion: Although the specific combination of sucrose, glucose-fructose syrup, butter, and hydrogenated palm oil used in this study is not widely reported in existing rodent models, its individual components are commonly utilized to investigate the metabolic effects of ultra-processed diets. Our preliminary data indicate that a UPF diet can result in a caloric intake comparable to that of control diets. This results serve as a preliminary step to further investigations on the metabolic health of offspring born from UPF-exposed dams.
Financial support: The project was financed by the Ministry of Science SKN/SP/601218/2024 – „Studenckie koła naukowego tworzą innowacje"
Keywords: ultra-processed foods, female Wistar rats, body weight, feed efficiency

NEUROIMMUNOENDOCRINE ASPECTS OF CATECHOLAMINES ACTIVITY DURING STRESS RESPONSES

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[1] Department of Animal Physiology and Endocrinology, University of Agriculture in Krakow, Krakow, Poland

Background: Chronic stress, combined with positive energy balance, may be a contributor to the increased risk for obesity, especially upper body obesity, and other metabolic diseases. This association may be mediated by alterations in the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic system neurotransmitters, mainly catecholamines. Hormones produced by the adrenal glands and adipose tissues have important roles in physiology and are altered in many disease states. It is recognized that adipose tissue produces peptides, called adipokines, which influence the local function and affect the metabolic and immune pathways through the bloodstream.
Purpose: The aim of the study was to estimate the impact of metabolic disorders/inflammation on the catecholamines activity in piglets.

Methodology: Experiment was carried out on 10-weeks old piglets divided into 4 groups: I- control, II- with overweight (chronic inflammation), III- acute inflammation and IV- overweight with acute inflammation. Prolonged inflammation was induced in groups II and IV by developing overweight with high-calories diet. In order to induce acute inflammation animals received a single injection of streptozotocin. Plasma adrenaline and noradrenaline were determined using commercial RIA kits.
Results: Adrenaline concentration decreased significantly in the group of overweight piglets (by 29%) and after streptozotocin injection (by 19%), while the combination of both experimental factors significantly increased the adrenaline concentration to 0.58±0.11 ng/ml compared to the control group (0.32±0.06 ng/ml, $P<0.05$). In contrast, in all experimental groups there was a significant increase in noradrenaline concentration by 322%, 1370%, and 784%, respectively, ($P<0.05$).
Conclusion: Obtained results may suggest an important neuroimmunoendocrinal interaction of hormones and neurotransmitters under acute and prolonged stress responses.
Keywords: adrenaline, noradrenaline, stress, obesity, inflammation, piglets
Financial support: The study was supported by the University of Agriculture in Kraków (Grant NCN - NN 311 227 138 and sub. 020002-D015)

PHENETHYL ESTER OF ROSMARINIC ACID - A NOVEL POTENTIAL THERAPEUTIC AGENT FOR AUTOIMMUNE DISEASES

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Background: The cumulative incidence of thyroid disease is significant. Approximately 20% of the Polish population will develop a thyroid condition in their lifetime. The most common thyroid diseases are autoimmune disorders: hypothyroidism (Hashimoto's thyroiditis) and hyperthyroidism (Graves' disease, GD). GD is chronic disease caused by autoantibodies against the thyroid stimulating hormone receptor (TSHR), leading to overstimulation of the thyroid gland often associated with development of Graves' orbitopathy (GO). Therapeutic options for the treatment of GO/GD are very limited. Recent studies have shown that a novel derivative (phenethyl ester) of rosmaric acid (PERA) is a promising immunomodulatory agent that attenuates the development of type 1 diabetes and experimental autoimmune encephalomyelitis.
Aim: In the present study, we investigated for the first time the effect of PERA on the outcome of Graves' disease and Graves' orbitopathy in vivo.
Methodology: PERA was administered orally or intraperitoneally (alternately) during disease onset (preventively) or after disease onset (therapeutically). Serological and histological analyses of the thyroid and orbital tissue were performed to assess the degree of activity of the autoimmune hyperthyroidism and orbitopathy.
Results: Administration of PERA during the onset of the disease prevented formation of TSHR-specific autoantibodies and resulted in a slight decrease in the level of their stimulating subtype. Consequently, autoimmune hyperthyroidism, which is characterized by elevated serum thyroxin levels, hyperplastic thyroid morphology and gland size, as well as weight gain, showed milder manifestations both in preventively and therapeutically treated animals. Examination of orbital tissue showed a moderately normalized amount of brown adipose tissue in both treated groups; however, there was no significant effect on the fibrosis process.
Conclusion: Here, we demonstrate that PERA delays the development and progression of thyroid eye disease in an experimental murine model for Graves' disease, suggesting its immunomodulatory potential.
Keywords: Autoimmunity; Graves' disease; Graves' orbitopathy; thyroid eye disease; Rosmarinic acid; Preclinical mouse model
Funding: This research was supported by the Centre of Postgraduate Medical Education (No. 506-1-026-02-23/25) and the National Science Centre (No. 2023/51/B/NZ6/02376).

OPIOID AND GHRELIN GENES EXPRESSION AND NEUROPEPTIDE CONCENTRATIONS CHANGES IN SELECTED BRAIN STRUCTURES OF NEWLY HATCHED CHICKENS

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Background: The first hours of a chicken's life after hatching are a period of intense physiological and metabolic changes that require precise neurohormonal regulation. Brain structures such as the hypothalamus and pituitary are responsible for maintaining homeostasis and integrating neuroendocrine signals. Neuropeptides, including Met-enkephalin, ghrelin, somatostatin, and growth factors such as IGF-1, play a key role in the adaptation of newly hatched chicks to a new environment.
Purpose: The aim of the study was to evaluate changes in the expression of selected opioid and ghrelin genes and the concentrations of neuropeptides and hormones in the hypothalamus and pituitary gland of chicks during the first 24 hours after hatching (day 0 vs day 1).
Methodology: Hypothalamus and pituitary tissues were collected from chicks on day 0 (immediately after hatching) or 24 hours later (day 1). Genes expression (PENK, GHRL, GOAT, GHSR) was analyzed by real-time quantitative PCR (qPCR), and results

were expressed as relative quantity units (RQ). Met-enkephalin, ghrelin, IGF-1, and somatostatin concentrations were determined using RIA method. Data are presented as mean ± SEM, and differences were assessed for significance at P<0.05.
Results: During the first 24 hours of life in the chickens hypothalamus, expression of all genes was significantly decreased but opposingly in the pituitary the increases of these genes expression were observed. Interestingly, the concentrations of native Met-enkephalin and ghrelin were increased in hypothalamus as well as in the pituitary. In contrast, concentrations of IGF-1 and somatostatin were lowered in both tested structures.
Conclusion: The results indicate intense and opposing neuroendocrine changes occurring in the hypothalamus and pituitary gland of chicks during the first 24 hours of life. These changes may represent adaptive mechanisms regulating homeostasis and the development of the hypothalamic-pituitary axis during the crucial post-hatching period.
Keywords: Genes expression, Met-enkephalin, ghrelin, IGF-1, somatostatin, chickens
Financial support: The study was supported by the University of Agriculture in Kraków (Grant no. sub. 020002-D015).

THE ROLE OF THE AUTONOMIC NERVOUS SYSTEM AND ADIPOSE TISSUE IN ANOREXIA NERVOSA: EVIDENCE FROM ANIMAL STUDIES OF ACTIVITY-BASED ANOREXIA

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Background: Anorexia nervosa (AN) is a life-threatening eating disorder with complex and multifactorial etiology, including genetic, endocrinological, and metabolic disturbances. Increasing evidence suggests that the autonomic nervous system (ANS) may regulate adipose tissue metabolism and may serve as a critical link between neurological and metabolic mechanisms in AN.
Purpose: This study investigates the role of ANS modulation in rodent models of AN, focusing on β3-adrenergic signaling and its effects on adipose tissue activity, metabolism, and systemic homeostasis.
Methodology: Female rats (n=54) were divided into a control group (n=6) and two anorexia models: activity-based anorexia with feeding window (ABA-FW) and activity-based anorexia with food-controlled supplementation (ABA-FC). Animals received vehicle, propranolol, SR 59230A, or CL 316243 to modulate adipose tissue through ANS pathways. Serum, white (WAT), and brown adipose tissues (BAT) were collected.
Results: The ABA-FC showed a more abrupt course of weight loss in the CL 316234 group than in the vehicle group. In the same group, we also noticed higher activity than in any other groups. The WAT sample weight was significantly lower in the CL316234 group than in the propranolol and control groups. The WAT calculated for the total weight did not differ between the propanol and the control group.
The ABA- FW group showed different results.
Conclusion: β3-adrenergic modulation influenced weight dynamics, physical activity, and adipose tissue composition in anorexia models. The results were not fully consistent across groups, and the limited sample size restricts interpretation. Further research is warranted to better define the contribution of ANS–adipose tissue interactions to AN pathophysiology.
Keywords: anorexia nervosa, eating disorders, autonomic nervous system, adipose tissue

MOLECULAR MECHANISMS OF STRESS RESILIENCE – STUDIES USING ANIMAL MODELS

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Stress is most often defined as conditions that precipitate a state of equilibrium, and can be about both psychological and physiological balance. Preclinical studies using experimental animals highlight a variety of strategies for coping with stress, reflecting the situation found in the human population. Identifying markers to differentiate these different strategies can be helpful in understanding the mechanisms that regulate the stress response. An interesting animal model exhibiting a stress resilient phenotype is transgenic mice lacking the gene encoding the noradrenergic transporter, NET-KO. Additionally, inter-strain differences in responses to various stress stimuli have been demonstrated between C57Bl/6J and SWR/J mice - the former appeared more passive in their coping strategy, while the latter exhibited a more active strategy. Also rats subjected to chronic mild stress can be divided into stress-susceptible and stress-resilient group. One of recently appreciated levels which might help to identify differences between these groups is the level of micro-RNAs (miRNAs) in the peripheral blood (serum) and selected brain regions of the experimental animals. MiRNAs are short RNA sequences that are involved in the regulation of protein-coding transcripts. There are far fewer of them (about 2,000) than genes (e.g., 20,000-30,000) or transcripts - so by profiling miRNAs in screening, important proteins or signaling pathways can be more easily identified. Often a multidirectional research approach is used, from behavioral studies through advanced microRNA level assays and in vitro experiments to complex bioinformatics analyses, which allows to identify target sequences for selected miRNAs (whose expression was important in the reactivity of experimental animals to stress stimuli) and verify the results at the biochemical level in the form of expression measurements of selected genes and also verify the signaling pathways activated by these sequences. Intracerebral administration of selected miRNA sequences might be useful to reverse the phenotype from susceptible to resilient to stress and vice versa.

THE EFFECT OF ALL-TRANS RETINOIC ACID ON THE CYTOKINE PROFILE IN VISCERAL ADIPOSE TISSUE OF APO-E MICE

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Background: All-trans retinoic acid (ATRA), the biologically active metabolite of vitamin A, has been implicated in the prevention of cardiovascular diseases. Previous studies showed that ATRA attenuates the progression of atherosclerotic lesions; however , the precise mechanisms underlying its protective actions remain incompletely understood. Visceral adipose tissue (VAT) -a metabolically active tissue surrounding internal organs contributes to cardiovascular disease through its role in glucose and lipid metabolism and modulation of local immune responses.
Purpose: The aim of the study was to evaluate the effect of ATRA on the cytokine and chemokine profile of VAT in Apo-E mice, which spontaneously develop atherosclerotic lesions.
Methodology: The experiment was performed on four groups of mice fed either a standard or high-fat diet (HFD) and ATRA (5 mg/kg/day) or corn oil (vehicle) administration via intragastric gavage for 8 weeks. VAT was isolated and subsequently cultured for a 24 hours. The culture medium was analysed for the levels of secreted cytokines (IL-10, IL-12(p40), IL-12(p70), IL-13, IL-17, IL-4, and IL-9) and chemokines (EOTAXIN, GM-CSF, LIX, M-CSF, and MCP-1) using the MILLIPLEX® multiplex assay.
Results: ATRA administration significantly reduced atherosclerotic lesions, body weight, cholesterol, and insulin levels both on a standard and high-fat diet in Apo-E mice. ATRA increased MCP-1 and IL-9 concentrations and decreased IL-17 level in mice on standard diet. However, in mice on HFD administration of ATRA reduced IL-17 concentrations.
Conclusion: ATRA attenuates the progression of atherosclerosis, primarily through reductions in body weight, cholesterol, and insulin levels. ATRA influenced cytokine and chemokine profile of VAT in a diet-dependent manner. These results suggest that ATRA may play a potential beneficial role in atherosclerosis prevention through metabolic and immune regulation of VAT.
Keywords: all trans retinoic acid, atherosclerosis, cytokine, chemokine, Apo-E mice
Financial support: The study was funded by the National Science Centre (NCN), grant no. 2020/39/D/NZ5/02514.

TRANSCRIPTOMIC RESPONSE OF NEURON-LIKE SH-SY5Y CELLS TO SHORT-TERM EXPOSURE TO AMYLOID B1-42: ACTIVATION OF AUTOPHAGY AND REPRESSION OF NEUROPLASTICITY PATHWAYS

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Background: Amyloid β1-42 (Aβ1-42) is a key neurotoxic peptide implicated in the pathogenesis of Alzheimer's disease, where it induces cellular stress, inflammatory responses, and synaptic dysfunction.
Purpose: The aim of this study was to characterize transcriptomic changes in neuron-like SH-SY5Y cells after short-term exposure to Aβ1-42 in order to identify the mechanisms underlying early neurotoxicity
Methodology: SH-SY5Y cells were differentiated for six days toward a neuronal phenotype and then treated with Aβ1-42 for 24 hours. Total RNA was isolated from both treated and control cells. RNA quantity was measured spectrophotometrically, and RNA integrity was evaluated using an Agilent Bioanalyzer to ensure high-quality samples (RIN ≥8.0) for downstream analysis. Gene expression profiling was performed using GeneChip Human Gene 2.1.ST microarrays (Thermo Fisher) to compare transcriptomic changes between Aβ1-42–treated and control samples.
Results: Aβ1-42 exposure increased expression of genes associated with autophagy (ATG14, VPS4B), oxidative stress response (TP53INP1, DUSP10, WRN), and transcriptional regulation (SMAD1, CDK7, ZNF), indicating activation of protective pathways. Concurrently, decreased expression was observed for cytoskeletal and neuroplasticity-related genes (NEFM, LUM, DKK1, CRABP2), along with repression of multiple microRNAs (miR-127, miR-433, miR-136), suggesting disruptions in post-transcriptional mechanisms and synaptic plasticity.
Conclusion: Short-term, 24-hour exposure of neuron-like SH-SY5Y cells to Aβ1-42 triggers activation of defensive mechanisms (autophagy, stress response) while simultaneously repressing genes involved in neuroplasticity, cytoskeletal stability, and mRNA regulation. These findings indicate that even brief Aβ1-42 exposure can elicit a complex cellular response integrating neuroprotective and neurodegenerative processes. The data support the utility of differentiated SH-SY5Y cells as a model for studying early stages of amyloid neurotoxicity and potential neuroendocrine mechanisms in Alzheimer's disease.
Keywords: Alzheimer disease, neurodegeneration, autophagy, oxidative stress
Financial support: This study was supported by CMKP grants No 501-1-31-22-24, 501-1-31-22-25

THE EFFECTS OF PHARMACOLOGICALLY INDUCED STRESS ON RATS' BEHAVIOR AND ELECTROPHYSIOLOGICAL ACTIVITY OF THE POSTERIOR HYPOTHALAMIC AREA: STRESS, HYPOTHALAMUS, THETA RHYTHM

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Background: Stress is a common physiological response in-

volving complex interactions between neurobiological and endocrinological factors. Its impact on individuals depends on the nature and intensity of the stressful stimuli and individual susceptibility. Numerous studies show that stress has a major contribution to the pathogenesis of multiple central nervous system dysfunctions, such as post-traumatic disorder (PTSD), major depression disorder, and anxiety disorders. To provide better insight into the mechanisms underlying those diseases, rodent-based models are widely used in studying the stress response. During the past decades, rodent-based study models have evolved not only in the kinds of stress stimuli but also by combining them with the analysis of both animal behavior and bioelectric activity of specific brain regions related to organisms' stress response, among others, the hypothalamus.

Purpose: The present study examines the effect of exposing rats to pharmacological stress, induced by corticosterone on both animal behavior and bioelectrical activity of the posterior hypothalamic area.

Methodology: Ten male Wistar rats for 21 days were receiving constant doses of corticosterone and were exposed to the open field behavioral test (OF) nine times. While undergoing the OF test, both the behavior and bioelectrical activity of rats' posterior hypothalamic area were recorded continuously.

Results and conclusion: The combined model of monitoring both behavioral and bioelectrical activity in stressful conditions could be a possible tool in searching for the etiology and pharmacology of behaviors considered diagnostic criteria for PTSD, defined in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders.

Keywords: stress, hypothalamus, theta rhythm, behavioral analysis

EXOGENOUS MET-ENKEPHALIN MODULATES THE PROENKEPHALIN SYNTHESIS AND DELTA OPIOID RECEPTOR BINDING UNDER STRESS RESPONSE

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Background: Met-enkephalin is a neuropeptide whose release into the circulation is enhanced by stress. The main sources of this opioid are brain structures and peripheral nerves and organs like adrenals, gastrointestinal system, pancreas. Met-enkephalin is released as native, small pentapeptide and its precursor - proenkephalin (PENK). Opioid-like drugs are often prescribed for alleviating pain in human and animals, but unfortunately, some forms of them are overused by addicted patients.

Purpose: There have been studies on the effects of peripheral administered Met-enkephalin in animal model of mammals but not in birds. To remedy this, the effects of peripheral administration of Met-enkephalin per se and on stress response in bird model was determined.

Methodology: Fourteen-weeks-old female chickens were divided into 4 groups (n=6): control injected with saline (C), injected i.v. with 1 mg/kg b.w. of Met-enkephalin (MET), restrained for 30 min (RES), restrained and injected with opioid (MET+RES). Structures of hypothalamo-pituitary-adrenal axis were taken 30 min after terminating the stress. Proenkephalin expression (in situ hybridization) and delta opioid receptor binding (cell membrane method) were measured in hypothalamus, pituitary and adrenal.

Results: Administration of Met-enkephalin was followed by significant changes in proenkephalin (PENK) expression as well as in the hypothalamic, anterior pituitary and adrenal delta opioid binding.

Conclusion: The ability of Met-enkephalin to attenuate the stress response is novel and opens up several new lines of enquiry including its site of action and its source.

Keywords: Genes expression, Met-enkephalin, proenkephalin, stress, chickens

Financial support: The study was supported by the University of Agriculture in Kraków (Grant no. sub. 020002-D015).

THE EFFICACY OF PASIREOTIDE TREATMENT IN INVASIVE CROOKE'S CELL CORTICOTROPINOMA – CASE REPORT

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Background: Crooke's cell adenomas (CCA) are a rare type of pituitary neoplasm, associated with Cushing's disease. Due to their rarity, the management and treatment remain a challenge.
Clinical case: A 33-year-old male patient presented sudden visual impairment. The MRI revealed a 51.6x29.6x32.8 mm pituitary macroadenoma infiltrating surrounding structures with the optic chiasm compression. Two months after the initial diagnosis, the typical hypercortisolemia symptoms occurred. The laboratory results confirmed the ACTH-dependent Cushing syndrome. The patient underwent transsphenoidal surgery, the mass was partially (~50%) removed (diameters of mass 19x14x12 mm in MRI) without normalisation of ACTH and UFC. After the post operation period, gradual increases of cortisol hormones and tumour mass progression were observed. After analyzing the risk associated with reoperation or possible radiation therapy, the decision was made to start with long-acting pasireotide administered, with the initial dose of 10 mg i.m. with gradual titration to 30 mg. However, the normalisation of ACTH and UFC after 6 months of treatment was not achieved. For the next 6 months osilodrostat (1 mg twice a day) was added to the therapy simultaneous with pasireotide 30mg i.m. each month. In imaging data, a year after the pharmacology therapy, the slight progression in tumor size was detected (diameters of mass 22x15x20 mm in MRI). Another attempt at transnasal resection was made, but no complete resection was achieved. Postoperatively the normalisation of UFC was observed with persistent slight increase of ACTH concentration (150 pg/ml). Again, the therapy of pasireotide was restarted with stabilisation of the disease (normalization of UFC 54.6 ug/24 h and slight decrease of ACTH 135 pg/ml) after one year of observation. In the second year of therapy, asymptomatic bradycardia was observed.
Conclusion: Pasireotide could be considered as a second or third line treatment in CCA. However, further studies of the effectiveness of such treatment are required.
Keywords: Crooke's cell adenoma, Cushing disease, pasireotide

PARENTAL KNOWLEDGE OF ULTRA-PROCESSED FOODS AND THE IMPACT OF NUTRITION EDUCATION IN KINDERGARTEN SETTINGS

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Background: Healthy nutrition in early childhood is key to lifelong habits and the prevention of late-life obesity. Establishing lifelong healthy eating habits early in life requires a collaborative approach involving both educational institutions and families. Yet, parents' knowledge about ultra-processed foods (UPFs) and balanced diets most significantly influences children's dietary choices.
Purpose: This study aimed to assess parents' knowledge regarding UPFs and healthy eating in general, and to evaluate the impact of nutrition workshops conducted in kindergartens on children's awareness of healthy food choices.
Methodology: An anonymous, internet-based, proprietary questionnaire was administered to 112 parents (94 women, 18 men) of children aged 3-7, evaluating their self-assessed nutrition knowledge, sources of information, and awareness of the health effects of UPFs. The study was accepted by the Committee on Research Ethics of the Jagiellonian University Medical College. Following the survey, four educational workshops focusing on fruits, vegetables, and the use of spices as alternatives to salt were conducted, involving 38 children from two kindergartens in Krakow. Additionally, at the end of the workshops, parents received printed educational materials on nutrition to reinforce learning at home.
Results: Over 85% of parents rated their nutrition knowledge as good or very good. The primary sources of information were the internet (79.5%), books (60.7%), and social media (50.9%), while only 34.8% consulted specialists and 33% referred to scientific articles. Notably, 93.8% recognized the negative health impact of UPFs on children, and 100% acknowledged that a well-balanced diet can prevent lifestyle diseases such as obesity and diabetes later in life. The workshops were well received by children and parents, enhancing children's engagement with healthy eating habits.
Conclusion: Despite high self-reported nutrition knowledge and awareness of UPF risks, reliance on non-professional information sources suggests a need for continued education. Moreover, knowledge alone is insufficient to drive lasting behavior change and requires ongoing support, including involvement from governmental organizations and large-scale public health initiatives. In parallel, reducing the widespread availability of cheap, highly processed foods is essential. Kindergarten-based workshops, supplemented by printed materials for parents, present a valuable opportunity to promote healthy dietary behaviors early in life and to support family-centered nutritional education.
Financial support: The project was financed by the Ministry of Science SKN/SP/601218/2024 – „Studenckie koła naukowego tworzą innowacje"
Keywords: ultra-processed foods, parental knowledge, childhood nutrition, dietary workshops, healthy eating, early intervention

ENDOCRINE AND METABOLIC CONSEQUENCES OF A HYPOTHALAMIC TUMOR: A CASE REPORT OF GROWTH AND PUBERTAL ARREST WITH PROGRESSIVE OBESITY

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Central nervous system tumors are the second most common type of cancer in children. Approximately 10% of them are located in the suprasellar and infrasellar regions. Although rare, hypothalamic tumors are a major challenge due to their location, risk of complications and varied clinical symptoms.
Case presentation: An 8.5-year-old boy presented with a two-year history of weight gain and growth deceleration, accompanied by recent onset of retro-orbital headaches and decreased exercise tolerance. On admission, the patient's height was 122 cm (3rd-10th percentile, target height 25th-50th percentile based on parental heights), BMI was 20 kg/m^2 (94th percentile), and he was prepubertal. Tests revealed central hypothyroidism (TSH 5.8 mU/L [N:0.3–4], FT4 7.5 pmol/L [N:10–25]) and central adrenal insufficiency (maximum cortisol concentration after 1 µg of Synacthen was 125 ng/ml [N:>200], ACTH 20.6 pg/mL [N:10–60]). Magnetic resonance imaging of the brain revealed a 17×10×17 mm lesion with contrast enhancement and hyperintensity in T2/FLAIR sequences within the optic chiasm and optic tracts. Levothyroxine and hydrocortisone replacement therapy was initiated. Despite intensive dietary, exercise, and psychological interventions, progressive weight gain persisted (BMI 36 kg/m^2 – 99.5th percentile). Liraglutide was initiated, achieving temporary improvement (BMI 33 kg/m^2 – 99th percentile), but without sustained effect. Growth velocity was stable (4.3 cm/year), with height tracking the 3rd-10th percentile. At the age of 14, secondary hypogonadism was diagnosed (maximum LH and FSH concentrations after stimulation with a short-acting gonadotropin-releasing hormone analogue were 0.34 mIU/ mL and 1.7 mIU/mL, respectively). Testosterone therapy was initiated, resulting in the onset of pubertal signs (penile enlargement, pubic hair development) and modest acceleration of growth velocity.
Conclusion: In evaluating childhood obesity, assessment of growth and pubertal development is essential. Disorders in these areas, together with excessive weight gain, may indicate an organic cause, particularly dysfunction of the hypothalamus or pituitary gland leading to hormonal and metabolic disorders.
Keywords: multihormonal hypopituitarism, hypothalamic obesity, hypothalamic tumor;

"THE HOSPITAL CORRIDOR" DIAGNOSIS OF LONG LASTING ACROMEGALY WITH MULTIPLE, SEVERE COMPLICATIONS. A CASE REPORT.

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Introduction: Acromegaly is a rare endocrine disorder related to growth hormone hypersecretion. In the majority of cases it is caused by a pituitary adenoma. Clinical symptoms of the disease include progressive soft tissue hyperplasia and acral enlargement, as well as numerous metabolic disturbances. Early detection of acromegaly and implementation of the proper treatment is crucial for improving patient outcomes and preventing long-term complications.
Case presentation: We present the case of a 67-year-old female patient, who was waiting for a chest X-ray examination in the hospital corridor when she happened to encounter an endocrinologist. A strong suspicion of acromegaly was raised, prompting an immediate referral for further diagnostic evaluation.
Clinical presentation included severe headaches, coarse facial features and foot and hand enlargement. Over time, the patient developed multiple comorbidities secondary to acromegaly, such as hypertension, hyperlipidemia, nodular goiter, and osteoporosis. Based on the clinical symptoms, the delay in diagnosis of acromegaly could be estimated at over twenty years.
The initial diagnosis of acromegaly was confirmed by a significantly elevated IGF-1 level (3.5 times the upper limit of normal) and the lack of growth hormone suppression during the oral glucose tolerance test.
Additionally, magnetic resonance imaging revealed a tumor in the left lateral part of the anterior pituitary lobe, measuring approximately 5.9×8.8×10 mm, in contact with the left internal carotid artery.
The treatment with Somatostatin analogue Lanreotide LAR was initiated leading to a spectacular clinical improvement and a reduction in facial edema. Subsequently, the patient was qualified for surgical intervention.
Conclusions: Due to its rare incidence and relatively slow progression, acromegaly frequently remains undiagnosed for many years. According to current research, the average delay in diagnosis equals six years, however in up to 25% of cases the delay might exceed 10 years. Some of the comorbidities probably could have been prevented or minimized, had the typical symptoms been noticed at an earlier stage.
It seems crucially important to raise awareness of acromegaly, not only among the general population, but even more importantly among healthcare professionals. This would lead to an increase in early detection rates, ultimately resulting in improved therapeutic outcomes.

"IGG4-RELATED HYPOPHYSITIS MIMICKING A PITUITARY MACROADENOMA – A CASE OF PATIENT WITH ADRENAL AND THYROID AXIS INSUFFICIENCY AND SUBSEQUENT PRESENTATION OF ORBITAL TUMOR LEADING TO DIAGNOSIS"

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Background: Hypophysitis associated with IgG4-dependent disease (IgG4-RD) is a rare autoimmune disorder that can clinically and radiologically mimic pituitary tumors, leading to diagnostic and therapeutic challenges. IgG4-RD is a systemic chronic relapsing disease characterized by inflammatory-fibrosing infiltrates in various tissues and organs, leading to their dysfunction.
Purpose: In the presented case, we describe a patient with IgG4-RD disease presenting as a right orbital tumor and hypophysitis, which in imaging studies resembled a macroadenoma and led to adrenal and thyroid axis insufficiency.
Case report: A 64-year-old female patient reported to the Emergency Department with headaches, neck pain, weakness, increased sweating, vomiting and diarrhea for several days preceding admission. Laboratory tests revealed severe hyponatremia at a level of 110.6 mmol/l. Computed tomography of the head without contrast enhancement did not reveal any pathology. The patient was then transferred to the Internal Medicine and Endocrinology Department, where subsequent tests revealed low fasting morning cortisol levels (0.80 ug/dl), fT4 (4.9 pmol/l), ACTH at the lower limit of the norm (9.31 pg/ml) and hyperprolactinemia (50.71 ng/ml fasting). Contrast-enhanced magnetic resonance imaging revealed a pathological tissue mass measuring 10x24x16mm, with numerous calcifications, unclearly demarcated from the pituitary parenchyma, occupying the left part of the sella turcica with complete infiltration of the left cavernous sinus and a slightly thickened infundibulum displaced to the left side. Hormone replacement therapy was initiated due to adrenal and thyroid insufficiency, serum sodium levels were corrected, and the patient was discharged home in good general condition. Two years later, the patient reported to the ophthalmology department with symptoms of tearing, burning of the right eye, swelling and exophthalmos. MRI revealed a tumor in the right orbit measuring 24×27×35 mm, occupying a significant portion of the intraconal space and displacing the extraocular muscles, with suspected infiltration.
The patient was referred to the laryngology department, where she was qualified for a right orbitotomy with a sample of the lesion taken. Histopathological examination revealed the presence of fibrous and granulation tissue and fragments of the lacrimal gland, showing a dense chronic inflammatory infiltrate predominantly composed of IgG+ plasma cells, with a marked predominance of IgG4+ cells.
Extended laboratory diagnostics revealed elevated inflammatory parameters and an IgG4 level of 2.47 g/L (norm <2.01 g/L). The patient was referred to the rheumatology and immunology department, where the diagnosis of IgG4-RD was confirmed and treatment with steroid pulses and rituximab was initiated, achieving a good clinical response with significant improvement in ocular symptoms. Despite the improvement in the orbital lesions, the patient still has adrenal and thyroid insufficiency.
Conclusions: This case highlights the importance of thorough differential diagnosis in patients with pituitary lesions, especially in the context of rare diseases such as IgG4-related disease.
Keywords: hypophysitis, IgG4-RD, pituitary, macroadenoma

FIRST-GENERATION SOMATOSTATIN ANALOGUES IN THE TREATMENT OF INOPERABLE PARAGANGLIOMAS – A REPORT OF TWO CASES

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Paragangliomas may exhibit positive expression of somatostatin receptors (SSTRs). SSTR overexpression is particularly observed in tumors with confirmed mutations in the succinate dehydrogenase complex subunit B (SDHB), which is associated with an increased risk of aggressive disease progression.
We present two cases of patients treated with first-generation somatostatin analogues.
Case 1: The first patient, with a positive family history (father diagnosed with carotid body paraganglioma with SDHB mutation), demonstrated increasing levels of 3-methoxytyramine in serial measurements. At the age of 17, a [68Ga]Ga-SSTR PET/CT was performed, revealing an intrapericardial lesion measuring 26×39 mm, with markedly increased radiotracer uptake. Due to the tumour's location and high perioperative risk, surgical resection was not performed. The patient underwent two embolization procedures targeting the tumor's blood supply. The first embolization was complicated by an infarction of the inferoposterior wall of the left ventricle. A follow-up [68Ga]Ga-SSTR PET/CT showed tumor progression, with an increase in size to 41×34 mm and heterogeneously increased tracer uptake. Due to the lack of efficacy of embolization and further tumor growth, long-acting somatostatin analogue therapy was initiated, starting with octreotide 10 mg and escalated to 20 mg after three months, with good tolerability. Follow-up CT performed 8 months after treatment initiation showed a slight reduction in tumor size to 41×30 mm.
Case 2: The second patient, a 49-year-old woman, underwent a screening neck ultrasound which revealed a suspicious lesion in the right level III cervical region. Further diagnostic imaging, including MRI and MR angiography of the neck, revealed a highly contrast-enhancing mass located above the right common carotid artery bifurcation, suggestive of a paraganglioma measuring approximately 20×33×35 mm, along with several suspicious lymph nodes inferiorly. Due to the inoperable nature of the primary lesion, the patient underwent lymphadenectomy. Histopathological examination confirmed metastatic paraganglioma in the lymph nodes, with a Ki-67 index of approximately 24%. Follow-up imaging with [18F]FDG PET and [68Ga]Ga-SSTR PET/CT revealed pathological glucose metabolism (SUV max

15.1) and SSTR overexpression in the tumor area (Krenning score 4). Genetic testing ruled out the most common hereditary syndromes associated with paragangliomas. Given the aggressive disease course and inoperable nature of the tumor, the patient was qualified for proton therapy targeting the tumor and the involved cervical lymph nodes on the right side. Based on the positive SSTR expression, additional treatment with long-acting octreotide at a dose of 20 mg was initiated. The patient has received four doses so far, with good tolerability.
Due to their anatomical location, paragangliomas are frequently inoperable at diagnosis, necessitating a multimodal treatment approach to potentially inhibit tumor growth and reduce the risk of metastatic spread.
Keywords: paraganglioma, somatostatin analogues, inoperable, SDHB

FAMILIAL SDHB MUTATION AND 3P SYNDROME

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We present a case of a family with a confirmed SDHB gene mutation and a clinical history consistent with 3P syndrome (pituitary adenoma, pheochromocytoma, and paraganglioma).
The mother was diagnosed at the age of 29 with a macroadenoma of the pituitary gland secreting prolactin. Treatment with the dopamine agonist cabergoline was initiated; however, due to progressive tumor enlargement and poor tolerance of higher doses, surgical resection of the pituitary lesion was ultimately performed. Histopathological examination confirmed a prolactin-secreting pituitary adenoma.
Eighteen years later, her son underwent an abdominal ultrasound, which incidentallyrevealed a lesion in the right adrenal region. A subsequent CT scan confirmed the presence of an adrenal mass, and the patient was scheduled for adrenalectomy. He exhibited no clinical signs or symptoms of hormonal hypersecretion prior to surgery. Histopathological evaluation revealed a paraganglioma. Genetic testing identified a pathogenic missense mutation in the SDHB gene. In light of the positive family history, the mother underwent routine abdominal imaging,which suggested a lesion in the right adrenal gland. This finding was confirmed on CT imaging. Biochemical evaluation demonstrated significantly elevated levels of fractionated normetanephrines in a 24-hour urine collection. Preoperative alpha-adrenergic blockade was initiated, followed by successful adrenalectomy. Histopathological analysis confirmed the diagnosis of pheochromocytoma (Ki-67 index: 6%, PASS score: 7). The diagnosis of 3P syndrome was established, and genetic testing confirmed the presence of the familial SDHB mutation. Further detailed family history, obtained from the son, revealed an additional case of metastatic para-aortic paraganglioma in the patient's grandmother.
3P syndrome, characterized by the coexistence of pituitary adenoma, pheochromocytoma, and/or paraganglioma, represents a rare and heterogeneous clinical entity associated with mutations in genes such as SDHB. The causal relationship between pituitary adenomas and pheochromocytoma/paraganglioma remains an area of debate.
Keywords: paraganglioma, pituitary adenoma, SDHB, 3P syndrome

SERUM INFLAMMATION-BASED SCORES IN PREDICTION OF LIVER FIBROSIS AMONG CUSHING'S SYNDROME AND MACS PATIENTS: DATA FROM ERCUSYN KRAKOW DATABASE

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Background: Serum inflammation-based scores (SIBS) are evolving biomarkers of chronic liver diseases. Multiple SIBS can be simply calculated using complete blood count data. To the best of our knowledge, so far there are no studies investigating the role of SIBS in prediction of liver fibrosis (LF) in hypercortisolemia.
Purpose: To evaluate associations between selected SIBS and LF among newly diagnosed Cushing's syndrome (CS) and mild autonomous cortisol secretion (MACS).
Methodology: We retrospectively analyzed baseline data of adult patients from the ERCUSYN, Krakow database (N:184 - 51% pituitary CS, 26% adrenal CS, 23% ectopic CS), MACS patients (N:121), control group (N:177 for CS [CS-CG] and 121 for MACS [MACS-CG], non-secretory adrenal incidentalomas matched to age, gender, weight, presence of hypercholesterolemia and diabetes mellitus). FIB4 (Age×AST/PLT×ALT^1/2) was used as a LF predictor. The correlations between SIBS and FIB4 were assessed (RStudio version 4.2.2., $p<0.05$).
Results: Statistically significant SIBS correlations with FIB4:
CS (23% males, age 54 years [38-65]): NLR r=0.177, NPR r=0.331, PLR r= -0.17, SII r=-0,166
CS-CG (26% males, age 62 years [51-70]): NPR r=0.349, PLR r=-0.274, SII r=-0.3
MACS (29.8% males, age 68 years [60-72]): NPR r=0.343, PLR r=-0.44, SII r=-0.49
MACS-CG (29.8% males, age 67 years [60-71]): NPR r=0.281, LMR r=-0.224, SII r=-0.211
*Abbreviations for SIBS: NLR - Neutrophil-Lymphocyte ratio, NPR - Neutrophil-Platelet ratio, PLR - Platelet-Lymphocyte ratio, LMR - Lymphocyte-Monocyte ratio, SII - Systemic Inflammation Index
Conclusion: There may be an association between FIB4 and SIBS in the following pattern:
1) positive with NLR in CS;

2) positive with NPR and negative with PLR in: CS, MACS and normocortisolemic population;
3) negative with SII in CS, MACS and normocortisolemic population.
Further studies are needed to establish SIBS role in LF prediction.
Keywords: Cushing's syndrome, MACS, serum inflammation-based scores, liver fibrosis

HYPERGLYCAEMIA AND KETOACIDOSIS MIMICKING TYPE 1 DIABETES MELLITUS AS THE FIRST PRESENTATION OF HIGHLY AGGRESSIVE ACROMEGALY IN A YOUNG MALE: A CASE REPORT

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Introduction: Diabetes mellitus is one of the most common comorbidities secondary to acromegaly, primarily caused by the anabolic and insulin-antagonistic actions of growth hormone. [Esposito, 2024]. It is estimated that up to 56% of patients with acromegaly develop diabetes mellitus [Ferraù, 2018], however this is age-dependent and extremely rare in young patients [Bogusławska, 2022]. Moreover, it is exceptionally uncommon for advanced ketoacidosis to be the first clinical manifestation of the disease and the trigger for further diagnostics.
Case presentation: We present the case of a 32-year old male who was urgently admitted to the Department of Metabolic Diseases and Diabetology with severe hyperglycaemia (27,14 mmol/l) and ketoacidosis (pH 7.284). This, in correlation with a patient history of significant weight loss, polyuria and polydipsia led to a primary suspicion of decompensated type 1 diabetes mellitus.
Subsequent laboratory testing, including anti-GAD antibody assessment, led to the rejection of the initial diagnosis. The clinical symproms of acromegaly and significant elevation of plasma IGF-1 levels (3.5 times the upper limit of normal) and prolactin (3.4 times the upper limit of normal) prompted referral for pituitary magnetic resonance imaging.
Imaging revealed policyclic, T2 hyperintense pituitary macroadenoma (intrasellar part 25x31x27 mm, extrasellar part 19x15x10 mm) with a compression and displacement of the optic chiasm and a complete encasement of intracavernous left internal carotid artery (Knosp IV).
Due to anatomical limitations the patient was qualified for a non-radical transsphenoid resection of the adenoma. Moreover, combined treatment with cabergoline and lanreotide was introduced. Histopathology revealed a sparsely granulated somatotrophic adenoma, staining for GH and PRL. Ki-67 index -2%.
Owing to a lack of clinical and biochemical control of the disease, the patient was enrolled in a pegvisomant treatment combined with cabergoline. A spectacular improvement of metabolic parameters after introducing the growth hormone antagonist allowed for a complete discontinuation of treatment with insulin.
Conclusions: Given its diverse symptomatology, acromegaly can manifest in multiple ways. This case is particularly unusual because of the atypical presentation of secondary diabetes mellitus, mimicking type 1 of the disease. Immediate implementation of appropriate treatment and obtaining good control of the disease might lead to a significant alleviation of metabolic disorders. Therefore, it seems crucially important to consider acromegaly in the differential diagnosis of multiple endocrine diseases.

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DISORDERS OF NATURAL ANTICOAGULANTS IN PATIENTS WITH CUSHING'S SYNDROME

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Background: Patients with Cushing syndrome (CS) are at increased risk of venous thromboembolism. Mechanisms are only partly understood.
Purpose: We aimed to assess the abnormalities of natural anticoagulants in patients with Cushing's syndrome.
Methodology: In 7 patients with active CS, 5 confirmed Cushing disease and 2 awaiting bilateral inferior petrosal sinus sampling (BIPSS), aged 35-71 years (median 59), 6 women, with median urine free cortisol (UFC) of 1,17 upper limit of normal (ULN), we assessed: antithrombin activity, protein C (PC) activity, free protein S (PS) concentration, along with fibrinogen concentration and factor VIII activity (FVIII:C). The results were compared to age- and sex-matched control group. The patients with PC were also screened for activated PC resistance (APCR).
Results: Patients with CS did not differ regarding the antithrombin activity, PC activity, and concentration of PS as compared with control subjects, while had +41.5% higher FVIII:C (p=0.013). The correlation coefficient between the UFC and antithrombin activity was 0.72 (p=0.067), between UFC and PC activity, 0.64 (p=0.12). After exclusion of 2 patients with UFC within normal range, the PC activity almost reached statistical significance (149.5 [1337-151.0] vs. 122.4 [107.2-126.5], p=0.082). Patient with most elevated UFC (6.64 × ULN) had also the most elevated antithrom-

bin (158%, ULN: 120%) and PC activity (229.4%; ULN: 140%). This patient presented poor anticoagulant response to activated PC (APCR), i.e. reduced ability to cleave factors Va and VIIIa, thus creating the prothrombotic state. The possible explanation could be increased FVIII:C (in this patient 191.5%), but other patients with CS who had increased FVIII:C (6 out of remaining 6), were negative for APCR. The patient was negative towards the most common underlying hereditary defects, factor V Leiden (G1961A) and prothrombin G20210A mutations. The results of PC function in a coagulometric assay and total PS concentration are pending.

Conclusion: We hypothesize that in exacerbated CS, despite the increased activity of PC, the function of PC pathway may be disturbed.

Keywords: Cushing syndrome, urine free cortisol, venous thromboembolism, natural anticoagulants, antithrombin, protein C

HIPERPROLACTINEMIA AS DIAGNOSTIC FACTOR OF HYPOTHALAMIC DYSFUNCTION IN PATIENTS WITH ROHHAD SYNDROME- SINGLE CENTER STUDY.

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Background: ROHHAD syndrome is a rare disorder of symptomatic hypothalamic dysfunction. Hallmark criteria are strict and included in the acronym: Rapid-onset Obesity, Hypothalamic dysfunction, Hypoventilation, Autonomic Dysregulation. Etiology of the syndrome is unknown, morbidity and mortality is high.

Purpose: To analyze signs and symptoms of ROHHAD syndrome common in our patients diagnosed with this disorder in University Children Hospital in Cracow, especially signs and symptoms of hypothalamic dysfunction.

Methodology: Patients data analyze of 4 patients diagnosed and treated in our Center in years 2009-2024.

Results: All patients presented with with clinical and laboratory signs of hypothalamic dysfunction: hiperprolactinemia (mean:1328,5 ulU/ml, range 460- 3576) and hypernatremia (mean:152mmol/l, range 143-157). Other hypothalamic abnormalities included: hypothyroidism (n=3), hypodipsia (n=2) central precocious puberty (n=1). Two patients were diagnosed with short stature (height < -2,0 SD for sex, age according to Polish Growth Charts). One patient was diagnosed with growth hormone deficiency (height < -2,0 SD, delayed bone age, peak GH level on provocation was <1 ng/ml) and is being treated with somatotropin in Terapeutic Programme. One patient was diagnosed with hypogonadal hypogonadism.

All patients presented different degree of autonomic dysregulation: cold hands and feet (n=4), strabismus (n=2), thermal dysregulation (hypothermia n=3, hyperthermia: n=1), bradycardia (n=1) neurogenic bladder (n=2) excessive sweating (n=3)

We did not detect any structural anomaly of the pituitary in our patients, in two cases MRI of the brain revealed mild ventriculomegaly.

Conclusion: Hyperprolactinemia is a sign of hypothalamic dysfunction and should be investigated in all pediatric patients with obesity and lack of concomitant growth acceleration. Increased PRL in patients with obesity and respiratoty dysfunction could be an early symptom of potentially life-threatening ROHHAD syndrome

Keywords: hyperprolactinemia, ROHHAD, hipothalamic dysfunction

THE ROLE OF CORTISOL SECRETION IN PPGLS: CLINICAL AND PERIOPERATIVE IMPLICATIONS – A RETROSPECTIVE COHORT STUDY

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Background: Pheochromocytomas and paragangliomas (PPGLs) are tumors associated with considerable metabolic and cardiovascular risks. Recent evidence indicates that patients with pheochromocytomas exhibit elevated plasma glucocorticoid concentrations, which significantly decrease after adrenalectomy compared to individuals with primary hypertension.

Purpose: The aim of this study was to assess the prevalence, clinical significance, and perioperative outcomes of mild autonomous cortisol secretion in patients with PPGLs.

Methodology: This retrospective cohort study was conducted at two tertiary endocrinology centers and included patients with PPGLs who underwent surgical treatment. Patients were stratified into suppressive and non-suppressive groups according to the results of the 1 mg dexamethasone suppression test (DST). Clinical characteristics, biochemical markers, tumour features, perioperative outcomes, and follow-up data were analysed.

Results: Among 106 patients, 24.5% exhibited non-suppressive cortisol concentrations post-DST. These patients were older (median age: 66 vs. 56 years, P<0.001), predominantly female (84.6% vs. 48.8%, P=0.001), and presented with larger tumours (median: 5.2 vs. 4.0 cm, P<0.05). Diabetes was more common in the non-suppressive group both before adrenalectomy (50.0% vs. 26.8%, P<0.05) and after (33.3% vs. 12.7%, P<0.05). Non-suppressive patients had higher urinary and plasma metanephrine concentrations and more cardiovascular diseases. Perioperative complications, including blood loss, conversion to open surgery, and prolonged hospital stays, were more frequent in the non-suppressive group (P<0.05).

Conclusion: This study demonstrates that one-quarter of patients with PPGLs exhibit autonomous cortisol secretion, associated with larger tumours, higher diabetes prevalence, and increased perioperative risks. Routine DST-based hypercortisolaemia screening may improve preoperative management and offer insights into the impact of cortisol on PPGLs outcomes.
Keywords: pheochromocytoma, PPGLs, cortisol, MACS, DST

AIP VARIANTS AMONG ADULT PATIENTS WITH ACROMEGALY.

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Introduction: AIP variants are found in up to 40% of familial cases of acromegaly and gigantism, as well as in some sporadic cases, particularly those with early-onset disease. Patients with AIP variants often present with higher growth hormone (GH) levels. AIP variants are found in up to 40% of familial cases of acromegaly and gigantism, as well as in some sporadic cases, particularly those with early-onset disease. Patients with AIP variants often present with higher growth hormone (GH) levels with no difference in insulin growth factor 1 (IGF-1) level.
Objectives: We studied the prevalence of AIP variants in a cohort of unselected, consecutive adult patients with acromegaly from 2019 to 2024.
Materials and methods: A total of 134 patients (79 females, 55 males, age range 16-75
years) with somatotroph pituitary neuroendocrine tumor who were studied at the Jagiellonian
University (Krakow), a tertiary referral center, were enrolled in this study. Genetic testing (Sanger Sequencing) was performed in all patients with acromegaly.
Results: Germline AIP variants were identified in eight patients including five missense variants, one three-nucleotide deletion. The specific variants observed were c.47G>A (p.Arg16His) in three patients, c.911G>A (p.Arg304Gln) in one female patient, c.235A>C (p.Thr79Pro) in one male patient, c.941G>C (p.Arg-314Pro) in one male patient, c.811C>T (p.Arg271Trp) in one male patient, and c.742_744del (p.Tyr248del) in one female patient. The clinical significance of .47G>A and c.911G>A is still in debate.
The median age of symptom onset was 34 years (range: 14–71 years), while the median age at diagnosis was 39 years (range: 16–72 years). Most cases (7 out of 8) presented with macroadenomas, and six patients were not cured following surgery. Three patients harbored mix tumour (prolactin co-secretion). Additionally, 50% of AIP variant carriers met the criteria for familial isolated pituitary adenoma (FIPA).
Conclusions: This study show the prevalence of AIP variants among adult patients with acromegaly in Poland. Genetic testing in acromegaly should be considered to personalize and optimize the treatment of patients.
Keywords: acromegaly; AIP; gigantism, IGF-1, growth hormone

A RARE TUMOR IN AN UNUSUAL LOCALIZATION: SOLITARY FIBROUS TUMOR OF THE PITUITARY REGION – CASE REPORT

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Background: Solitary fibrous tumors rarely affect the central nervous system; cases arising in the sellar region are even more uncommon.
Results - case report: We present the case of a 42-year-old man with an unusual pituitary mass. The tumor was detected on a computed tomography performed in emergency department in July 2023 due to dizziness. The diagnostic workup was extended to include magnetic resonance imaging (MRI), which showed a neoplastic lesion in the pituitary gland measuring 12x19x17 mm. The sella turcica was widened. There was no evidence of infiltration of the sellar structures or compression of the optic chiasm. Hormonal assessment revealed hyperprolactinemia (>2x the upper limit of normal) and a decreased morning cortisol level, hydrocortisone supplementation was commenced. On November 8, 2023, the patient underwent transsphenoidal resection of the pituitary tumor. Histopatological examination confirmed the diagnosis of a solitary fibrous tumor SFT (CNS WHO G1, Ki-67 about 10%). The immunohistochemical evaluation showed: STAT6(+), CD34(-), MelanA(-), HMB-45(-), CKAE1/AE3 (-), EMA (-), GFAP(-), synaptophysin (-), chromogranin A(-). No hormonal disturbances were detected in a postoperative reassessment.
Additional imaging revealed an atypical focal lesion in the left femoral shaft, measuring 20×14 mm with no uptake on 18F-FDG PET scan. A biopsy was attempted, however based on radiological findings, the material was most likely collected from the periphery of the lesion. Following orthopedic assessment and the suggestion of benign nature of lesion, it remains under observation.
A follow-up MRI of pituitary gland, performed 10 months after the surgery, revealed a 9x8x9 mm lesion in the left part of the sella turcica, suspected of being a recurrence of the disease. The patient was consulted during a multidisciplinary meeting and qualified for radiotherapy, which was administered in December 2024 (total dose 25 Gy, Df 5 Gy). The latest MRI, scan showed a lesion measuring 12x9x6 mm (previously 12x10x11 mm). The patient currently has no symptoms of pituitary hormonal dysfunction. Due to the rare nature of the tumor and the high risk of recurrence, the patient requires close medical supervision.
Conclusion: Our case highlights that, despite its rarity, solitary fibrous tumor should be considered in the differential diagnosis of sellar masses.
Keywords: solitary fibrous tumor, pituitary gland

HYPERCORTISOLEMIA IN CUSHING SYNDROME AND MACS, PSYCHOLOGICAL AND COGNITIVE FUNCTIONING DURING ACTIVE ILLNESS AND IN REMISSION – PRELIMINARY RESULTS

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Background: hypercortisolemia in Cushing syndrome and MACS often causes widespread repercussions, manifesting in musculoskeletal, circulatory, reproductive and central nervous systems. In the central nervous system hypercortisolemia may contribute to the occurence of neuropsychiatric symptoms as worsening of memory efficiency, attention deficits, executive fuctions disorders or deterioration of linguistic communication. It also may mediate the occurence of depression symptoms, complaints from the spectrum of anxiety, and quasi-manic manifestations. In addiction to aforementioned, patients with hypercortisolemia often report sleep problems.
Purpose: assesment of relationship between hypercortisolemia and psychocognitive functioning during active illness and in remission
Methodology: 25 subjects (4 men and 21 women) diagnosed with hypercortisolemia underwent assesment of cognitive domains as memory, attention, verbal and non-verbal fluency, visuo-spatial processes and language communication. They also completed psychological tools designed to assess emotional/ psychological functioning including presence of depressive, manic, anxiety symptoms and sleep quality. Two years after the initial assessment, the subjects will be tested again to evaluate their cognitive and psychological/ emotional functioning in long-term observation.
Results: global cognitive functioning declined in 25% subjects, the same percentage experienced depressive symptoms, 56% faced spectrum of anxiety manifestation, 44% experienced range of sleep disorders. Subjects with the widest range of emotional disorders with concomitance of sleep problems experienced more pronounced cognitive impairment
Conclusion: hypercortisolemia may co-occur with cognitive decline, emotional disorders and sleep problems.
Keywords: Hypercortisolemia, cognitive decline, emotional functioning, sleeplessness

ECTOPIC CUSHING'S SYNDROME (ECS) IS COMMON AND DIFFICULT TO DIAGNOSE. DIFFERENCES BETWEEN ECS AND CUSHING'S DISEASE (CD) – DATA FROM THE EUROPEAN REGISTRY ON CUSHING'S SYNDROME (ERCUSYN), KRAKOW

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Background: Ectopic Cushing's syndrome (ECS) is a rare cause of endogenous hypercortisolism (9-18% of Cushing's syndrome,CS), resulting from ectopic ACTH secretion by various tumors. ECS prevalence, especially in small-cell lung cancer (SCLC), is likely underestimated. Its diverse clinical presentation hampers diagnosis, and due to severe hypercortisolism, rapid recognition and treatment are critical.
Purpose: To investigate the differences between patients with ECS and age- and sex-matched patients with pituitary-dependent ACTH secretion(CD).
Methodology: We retrospectively analyzed 200 CS patients (2000–2025) from the ERCUSYN registry (Krakow). We identified 106 CD and 42 ECS cases. After excluding 8 SCLC patients, ECS cases were matched by age and sex with CD controls. Clinical data and course of diagnosis were compared.
Results: ECS patients had a mean age of 58.7 years; 53% were female. Causes included gastrointestinal NETs(29%), pulmonary carcinoids(15%), medullary thyroid cancer(9%), pheochromocytoma(6%), thymic carcinoids(3%), rare tumors(6%), and other malignancies(18%). In 4 cases, the source remained unknown. ECS was diagnosed significantly faster than CD(median 2 vs 12 months,p<0.001). In compare to CD catabolic symptoms predominated in ECS: weight loss(median -4 vs +10 kg,p=0.001), bruising (71% vs 44%,p=0.027), tendency to infections(68% vs 35%,p=0.008), and muscle weakness(Lovett scale median 3 [IQR 2–3] vs 3 [IQR 3–4],p=0.003). Hypokalemia was the most common initial sign in ECS, with lower potassium levels(Me:3.3 vs 4.0 mmol/L, p<0.001) and higher supplementation needs(Me:80 vs 0 mEq/d, p<0.001). Classic Cushingoid features were less frequent in ECS than CD: striae(21% vs 62%,p<0.001), fat redistribution(18% vs 59%,p=0.03). ECS patients had higher cortisol (6AM: 26.2 vs 7.5 µg/dL; 12AM: 40.0 vs 18.7 µg/dL;both p<0.001) and ACTH (231.5 vs 104.0 pg/mL;p<0.001). Mortality was significantly higher in ECS (64.7% vs 8.8%;p<0.00001), with shorter follow-up (3 vs 30 months,p=0.001).
Conclusion: ECS differs clinically from CD, with prominent catabolic features and severe hypokalemia. Recognizing these patterns may improve diagnostic accuracy and outcomes.
Keywords: Ectopic Cushing's syndrome, hipercortisolemia, Cushing's disease

LIVER ASSESSMENT IN THE SHEAR WAVE ELASTOGRAPHY IN PATIENTS WITH CUSHING SYNDROME AND MACS: DATA FROM ERCUSYN KRAKOW DATABASE

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Introduction: Cushing syndrome (CS) and mild autonomous cortisol secretion (MACS) are associated with an increased prevalence of steatotic liver disease (SLD), which if not treated may lead to liver fibrosis (LF). The prevalence of SLD and LF in hypercortisolemia varies in different studies. To the best of our knowledge there are no studies assessing liver impairment in endogenous hypercortisolemia using Shear Wave Elastography (SWE).
Objectives: To assess LF and SLD among CS and MACS patients in (SWE).
Materials and Methods: 38 patients with endogenous hypercortisolemia(52+/-15year old; 82%women;26 pituitary[pCS],2adrenal[aCS],2 ectopic[eCS], 8 MACS).Liver stiffness (LF>8.27kPa) and steatosis (SLD>228db/m) values measured in SWE were compared with hypercortisolemia markers, liver enzymes and serum inflammation based scores (SIBS) calculated from complete blood count. Analysis:Statistica 13.3, p<0.05.
Results: LF: Mean stiffness value 6.6 +/- 1.16kPa (CS 6.4+/-1.15; MACS: 7.5+/-1.4). LF:2/30 CS and 3/8 MACS. Negative correlation with late night salivary cortisol (LNSC) and platelet/lyphocyte rate (PLR) (r= -0.36, r= -0.36, p<0.005). Positive correlation with ALT and AST (r=0.36, r=0.45, p<0.005).
SLD: Mean steatosis values 238+/-39.7db/m (CS 234.6+/-38.7; MACS: 254.2+/-39.4). SLD:16/30 CS (5mild,6moderate,5severe) and 5/8 MACS (3moderate,2severe). Positive correlation with ALT, AST and GGTP (r=0.5, r=0.44, r=0.56, p<0.005).
Conclusions: LF prevalence in CS was 6.7% and 37.5% in MACS. SLD prevalence in CS was 53% and 62.5% in MACS. LNSC and PLR may be potential candidates for non-invasive LF markers. We plan to extend the study group, add a control group and reassess the elastography after hypercortisolemia treatment.

INTERAETIOLOGICAL DIFFERENCES IN COMORBIDITIES' PREVALENCE AMONG CUSHING SYNDROME PATIENTS: DATA FROM ERCUSYN KRAKOW DATABASE

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Introduction: Cushing syndrome (CS) is a state of prolonged cortisol excess and is associated with multiple comorbidities.
Materials and methods: A retrospective analysis of baseline comorbidities prevalence among CS patients from the ERCUSYN Krakow database (N:214; 53% PIT-CS, 25% ADR-CS, 22% ECT-CS).
Median age: 54 (Q1:38,Q4:65). Women 77%. Statistica 13.0 was used to perform data analysis.
Results:

	Entire group	PIT-CS (pituitary CS)	ADR-CS (adrenal CS)	ECT-CS (ectopic CS)	p value for statistically significant differences
Age(years) Median(Q1-Q4)	54(38-65)	49,5(35-63)	55(41-66)	62(45-69)	*ECT-CS vs PIT-CS
BMI(kg/m2) Median(Q1-Q4)	29(25-33) N:189	28(25-33) N:107	30(26-33) N:51	29(24-33) N:31	–
Diabetes Mellitus	156/212 74%	84/112 75%	35/53 66%	37/47 79%	–
Hypertension	184/212 87%	90/112 80%	51/53 96%	43/47 91%	**PIT-CS vs ADR-CS
Ischemic heart disease	36/212 25%	12/112 11%	9/53 17%	15/47 32%	**PIT-CS vs ECT-CS
Atrial fibrillation	18/195 9%	7/107 7%	6/52 12%	5/36 14%	–
Dyslipidemia	164/211 78%	86/111 77%	44/53 83%	34/47 72%	–
Stroke	11/191 6%	4/107 4%	4/50 8%	3/34 9%	–
Chronic renal dysf	9/197 5%	2/108 2%	4/51 8%	3/38 8%	–
Heart failure	41/212 19%	14/112 13%	11/53 21%	16/47 34%	**PIT-CS vs ECT-CS
VTE	20/201 10%	9/112 8%	7/52 13%	4/37 11%	–
Fractures	41/201 20%	19/112 17%	11/52 21%	11/37 30%	–
Liver steatosis (LS)	49/211 23%	35/111 32%	12/53 23%	2/47 4%	**PIT-CS vs ECT-CS
Liver enzymes elevation (LE)	29/211 14%	13/111 12%	7/53 13%	9/47 19%	**PIT-CS vs ECT-CS
LS+LE	62/211 29%	27/111 24%	17/53 32%	18/47 38%	**PIT-CS vs ECT-CS
Psychiatric issues	120/197 61%	68/107 64%	26/50 52%	26/37 70%	–

*p<0.05 **p<0.01 ***p<0.001

Conclusions: Ischaemic heart disease,heart failure and liver steatosis were more prevalent among PIT-CS than in ECT-CS.Hypertension was more prevalent among PIT-CS than ADR-CS. Liver enzymes elevation was more prevalent among ECT-CS than PIT-CS.Other comorbidities didn't show interaetiological statistically significant differences.

MULTIPLE SPINAL FRACTURES AS THE FIRST MANIFESTATATION OF SEVERE CUSHING'S DISEASE

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Background: This case illustrates the challenges of diagnosing Cushing's Syndrome, especially when atypical symptoms such as muscle wasting and weight loss predominate rather than the usual weight gain. It underscores the importance of recognizing the full spectrum of symptoms, which may be overlooked.
Purpose: Key learning points include the complications of long-term hypercortisolemia, such as uncontrolled hypertension, diabetes, hyperlipidemia, vertebral fractures, and myopathy.
Methodology: A 63-year-old female with a complex medical history, including poorly controlled hypertension, diabetes, hyperlipidemia, liver steatosis, and a vertebral fracture, was referred for evaluation of a left adrenal incidentaloma. We collected a full medical history and performed thorough physical examination, followed by laboratory and imaging tests.
Results: Over the past five years, she experienced significant weight loss (30 kg), muscle weakness, sleep disturbances, hair loss, and worsening diabetes and hypertension. Physical examination revealed a cushingoid appearance with a round face, abdominal obesity, and proximal muscle wasting. Laboratory tests showed impaired circadian cortisol rhythm, elevated late-night salivary cortisol, urine free cortisol, and ACTH levels, indicating ACTH-dependent Cushing's syndrome. Imaging revealed a potential pituitary microadenoma, which was confirmed by bilateral inferior petrosal sinus sampling (BIPSS), supporting a diagnosis of Cushing's disease.
The patient was initially treated with metyrapone to control hypercortisolemia, which improved cortisol levels and facilitated surgical preparation. Transsphenoidal surgery was performed successfully, removing the pituitary microadenoma. Post-surgery, cortisol levels were monitored closely, but one month later, she developed glucocorticoid withdrawal syndrome and adrenal insufficiency, requiring hydrocortisone therapy.
Conclusion: Diagnostic strategies, including laboratory tests, imaging, and BIPSS, are crucial for identifying the cause of hypercortisolemia. Preoperative metyrapone treatment in patients with Cushing's disease improves metabolic stability, leading to faster recovery and reduced thromboembolic risks. Postoperative monitoring, including morning cortisol levels, helps assess surgical success. Differentiating between adrenal insufficiency and glucocorticoid withdrawal syndrome is vital for post-surgery management. Long-term follow-up with tests like late-night salivary cortisol, 1mg DST, and urine free cortisol is critical for detecting remission or recurrence.
Keywords: Cushing's disease, spinal fractures, unusual presentation, glucocorticoid withdrawal syndrome

PERSONALISED RADIOLIGAND THERAPY IN NEUROENDOCRINE TUMOURS – EXPERIENCE FROM THE DUONEN TRIAL

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Background: Radioligand therapy (RLT) with [^{177}Lu]Lu-DOTA-TATE improves survival in patients with advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs). However, fixed-activity dosing (4 × 7.4 GBq) may result in undertreatment for some or unnecessary toxicity for others. Individualized, dosimetry-guided approaches and tandem isotope therapy ([^{90}Y]/[^{177}Lu]) may optimize outcomes, but prospective randomized evidence has been limited.
Purpose: To evaluate the safety, feasibility, and dosimetric outcomes of individualized, dosimetry-guided RLT strategies versus standard fixed-activity [^{177}Lu]Lu-DOTA-TATE in patients with advanced GEP-NETs, aiming to optimize efficacy while maintaining safety thresholds.
Methods: DUONEN is a multicenter, randomized, phase 3 clinical trial (N=92 planned; 56 patients analyzed in this interim report). Patients were randomized into four arms:
• Arm A: standard fixed-activity RLT (4 × 7.4 GBq of [^{177}Lu]Lu-DOTA-TATE)
• Arm B: tandem RLT with [^{177}Lu]+[^{90}Y] (variable ^{90}Y activity)
• Arm C: tandem RLT with [^{177}Lu]+[^{90}Y] (variable ^{177}Lu activity)
• Arm D: individualized [^{177}Lu]Lu-DOTA-TATE monotherapy (variable activity)
Cycle-by-cycle dosimetry guided modifications to stay within 23 Gy (kidneys) and 2 Gy (bone marrow). Safety was assessed via hematologic, renal, and hepatic parameters.
Results: In this interim analysis 56 patients completed RLT, among them, activity reductions were common in Arms B and C, especially due to ^{90}Y use. Arm D frequently allowed safe dose escalation. The highest cumulative kidney and marrow doses were in Arm C (29.1 Gy, 0.79 Gy). Lymphocyte and platelet declines correlated with marrow dose but not with activity adjustments. Renal function remained stable; no relevant hepatotoxicity occurred.
Conclusion: Dosimetry-guided RLT—including tandem and individualized ^{177}Lu strategies—is feasible and safe. Individualized ^{177}Lu dosing (Arm D) allowed escalation without added toxicity. DUONEN provides the first randomized evidence for personalized RLT dosing. Long-term follow-up will determine efficacy impact.

Funding: The study is funded by the Polish Medical Research Agency (Project number 2019/ABM/01/00077-00).
Keywords: Neuroendocrine Tumors (NETs), Radioligand Therapy (RLT), Theranostics, Tandem Isotope Therapy, [^{177}Lu]Lu-DOTA-TATE, [^{90}Y]Y-DOTA-TATE

UNIQUE ANALGESIC EFFECT OF PASIREOTIDE IN AGGRESSIVE PITUITARY TUMORS (PITNETS). CORRELATION WITH SERUM INFLAMMATION BIOMARKERS (SIBS)

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Background: Aggressive PitNETs, defined as rapidly growing and refractory to standard treatment pituitary tumors, often present with severe headaches. Pasireotide has antitumour properties and unique analgesic effects.
Purpose: To assess the analgesic effect of pasoteotide and correlate headaches with serum inflammation biomarkers (SIBs) in aggressive PitNETs.
Methodology: We analyzed the data on headache severity (NRS) in 25 patients — 14 men and 11 women with different PitNETs: 15 somatotoph (60%), 6 corticotroph (24%) – 2 of them silent, 2 gonadotroph (8%), 1 prolactinoma (4%) and 1 NFPA (4%) treated with Pasireotide and correlated with SIBs: WBC, NEU, LYMPH, PLT. We performed subgroup analysis comparing patients with acromegaly (acro) and patients with other PitNETs (non-acro).
Results: Mean age at diagnosis was 43,4 years (range: 13–86). The maximum tumor diameter was 89 mm. Invasion of the cavernous sinuses was observed in 21/25 patients (84%).
Before pasireotide implementation, 20/25 (80%) patients were treated surgically, and surgical treatment was more frequent in patients with headaches (17/18(94%) vs 3/8(43%), p =0.012) 18/25 patients complained of headaches before Pasireotide implementation. The mean NRS score at baseline was 5.7 (range: 2-9), and after pasireotide administration, 0.6 (range:0-4). In 100% of patients, headaches were relieved or resolved (Wilcoxon test: Z = -3.632; p<0.001).
We found that a higher NEU count was correlated with a higher baseline NRS score (rho=0.530; p=0.009). In the acro-group, the PLT/LYMPH ratio positively correlated with NRS (rho=0.567; p=0.035). Moreover, the acro patients achieved a lower PLT/LYMPH ratio than patients with other PitNets (Me: 169.5 vs 116.09; p=0.003). In the non-acro-group, we found a strong positive correlation between baseline NRS and NEU/PLT (rho=0.752; p=0.012).
Conclusion: Baseline NRS is correlated with SIBs. Pasireotide LAR is effective in relieving headaches in patients with aggressive PitNETs.
Keywords: pasireotide, aggressive PitNETs, headaches, NRS

PERSISTENT SEVERE HYPOKALEMIA AS A CRITICAL MARKER OF DIAGNOSIS AND RESPONSE TO TREATMENT IN ECTOPIC CUSHING'S SYNDROME (ECS) CAUSED BY SMALL-CELL LUNG CANCER (SCLC)

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Background: Ectopic Cushing's syndrome(ECS) is a rare condition caused by excessive ACTH secretion from tumors, most often small-cell lung cancer(SCLC). While reported in 1–6% of SCLC, prevalence may reach 25% but remains underestimated, as many patients are not referred to endocrinologists. Severe hypercortisolism leads to complications such as hypokalemia, worsening prognosis.
Purpose: To compare the clinical presentation of SCLC-related ECS(ECS-SCLC) with other ECS etiologies and analyzes the diagnosis, treatment, and outcomes of ECS-SCLC.
Methodology: We retrospectively reviewed 39 ECS patients diagnosed between 2000–2025 at a tertiary endocrinology center. Seven cases(18%) were associated with SCLC. Diagnosis was based on clinical signs, biochemical testing, imaging, and histopathology, including ACTH immunostaining when available.
Results: Seven ECS-SCLC patients (five men, two women; age 55–74, median 61) presented with rapid-onset symptoms. Compared to other ECS, they had shorter time to diagnosis (median 1 vs. 2 months;p=0.03), worse performance status (ECOG 4 vs. 3; p=0.01), greater muscle weakness (Lovett scale 2[IQR 1–2] vs. 2[IQR 2–3];p=0.04), and more severe hypokalemia (mean 2.12 vs. 2.7 mmol/L;p=0.03). Potassium supplementation requirements were higher (200 vs. 120 mEq/day;p=0.001). Serum cortisol ranged from 22.7–192 µg/dL (mean 91.7). Cortisol-lowering therapy (metyrapone in 4, osilodrostat in 5) was initiated within 3.7 days on average, achieving 44–63% cortisol reduction and decreasing potassium needs, particularly with osilodrostat (>50% reduction). Oncological treatment (chemotherapy or radiotherapy) was possible in 5 patients after stabilization. Median follow-up was 3 months; 5 patients died (mean survival 2.5 months), but one survived >2 years with combined cortisol-lowering therapy and chemoimmunotherapy.
Conclusion: ECS-SCLC is characterized by rapid progression, severe hypokalemia, and muscle weakness. Early recognition and multidisciplinary management are essential. Cortisol-lowering therapy improves metabolic stability and facilitates oncological treatment. Persistent hypokalemia may serve as a key diagnostic marker in SCLC patients without typical Cushingoid features.
Keywords: Small-cell lung cancer (SCLC); ectopic Cushing's syndrome (ECS); hypercortisolemia; hypokalemia

TRANSFORMATION OF A SILENT CORTICOTROPH ADENOMA TO A FLORID CUSHING'S SYNDROME AND A FLORID CUSHING'S SYNDROME TO A SILENT CORTICOTROPH ADENOMA

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Background: Pituitary adenomas' transformation is a scarce and not sufficiently investigated phenomenon. Crooke's cell adenoma (CCA) is a potentially aggressive variant that can manifest as silent, "whispering," and finally, functional clinical hypercortisolemia.
Purpose and Methodology: Two cases of patients with transformation of the CCA.
Results – case reports: A 71-year-old man with a history of NFPA for 3 years was admitted to a hormonal reevaluation. On admission, he manifested very subtle symptoms of hypercortisolemia with elevated ACTH (96 pg/ml) and night serum cortisol (7.3 ug/dl). In MRI, the tumor consisted of suprasellar (14x13x16 mm) and sellar (23x15x21 mm) lesions. Non-radical transsphenoidal surgery (TSS) was performed. Histopathology revealed a CCA. Follow-up MRI showed residual macroadenoma. Moreover, the patient presented with typical symptoms of hypercortisolemia, elevated ACTH and cortisol and lack of suppression in the dexamethasone test. The therapy with pasireotide LAR was started along with stereotactic radiotherapy. Osilodrostat was indicated with the achievement of normocortisolemia. Owing to the aggressive behavior of the tumor, the implementation of temozolomide is planned.
A 22-year-old man presented with bilateral temporal vision loss and severe headaches. He complained of weight gain, redistribution of the fat mass, and myalgia. MRI showed a tumor (22x19x23mm) with infiltration of the optic chiasm. The hormonal assessment revealed elevated ACTH concentration (117 pg/ml) with a lack of cortisol suppression in a 1 mg dexamethasone test. The patient underwent TSS. The histopathologic result revealed CCA (Ki-67 15%). Gradual progression of the tumor mass has been observed with infiltration of RICA and LICA. The second TSS was performed (CCA with Ki-67 2% with ambiguous ATRX marking). Due to non-radical reoperation, the patient was qualified for proton therapy with significant improvement in the headaches and the visual deficits. In hormonal assessment, no signs of adrenal insufficiency were found with ACTH normalization (49 pg/ml).
Conclusion: Due to the possibility of aggressive behavior of CCA and hormonal transformation, it is essential to conduct a careful follow-up with reassessments of the cortisol and ACTH secretion and tumor growth.
Keywords: Crooke's cell adenoma, hypercortisolemia, Cushing syndrome, transformation, silent corticotroph adenoma

EFFICACY AND SAFETY OF CLONIDINE SUPPRESSION TEST IN DETERMINATION OF FALSE POSITIVE NORMETANEPHRINE RESULTS IN DIAGNOSTICS OF PHEOCHROMOCYTOMA-PARAGANGLIOMA

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Background: Determination of free plasma metanephrines by liquid chromatography–tandem mass spectrometry technique (LC–MS/MS) is the gold standard in the biochemical diagnosis of pheochromocytoma–paraganglioma (PPGL). However, despite optimal pre-analytical preparation, up to one fifth of patients present with false-positive results.
Purpose: To evaluate the efficacy and safety of the clonidine suppression test (CST) in distinguishing false-positive elevations of plasma normetanephrine.
Methodology: The study included 11 patients (median age 59 years, 8 females) with elevated plasma normetanephrine above age-adjusted cut-offs. Indications for diagnostic work-up included paroxysmal symptoms, suspicion of PPGL recurrence, adrenal incidentaloma with unenhanced CT density >10 Hounsfield Units, and suspected carotid paraganglioma.
All patients received oral clonidine 300 µg. Plasma normetanephrine (LC–MS/MS) was measured at baseline and 180 minutes post-dose. Patients were monitored throughout the procedure with vital signs assessed every 30 minutes, and adverse effects were recorded.
Results: Median decrease in plasma normetanephrine was 42 pg/mL. In all patients, concentrations fell below age-adjusted cut-offs; in 10 of 11 patients' levels also decreased to <80% of the cut-off. The most common adverse effects were somnolence, xerostomia, and fatigue. Median decreases in hemodynamic parameters were: systolic blood pressure –48 mmHg, diastolic blood pressure –31 mmHg, and heart rate –15 bpm.
Conclusion: The clonidine suppression test may be a safe and effective procedure for verifying isolated elevation in plasma normetanephrine concentrations in diagnostics of PPGL.
Keywords: pheochromocytoma, paraganglioma, clonidine suppression test, metanephrines, normetanephrine, liquid chromatography mass-spectrometry

DETERMINATION OF FREE PLASMA METANEPHRINES IN DIAGNOSTICS OF PHEOCHROMOCYTOMA AND CORRELATION OF THE RESULTS WITH CLINICAL PARAMETERS

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Background: Pheochromocytomas are neuroendocrine tumors derived from the neural crest that produce, metabolize, and release catecholamines and their metabolites. Metanephrines, released continuously, are the most clinically relevant metabolites, and their measurement is considered the biochemical gold standard for diagnosis.
Purpose: To assess the diagnostic performance of plasma free metanephrines measured by liquid chromatography–tandem mass spectrometry (LC–MS/MS), characterize biochemical phenotypes, and correlate the results with selected clinical parameters.
Methodology: We studied 28 patients with histologically confirmed pheochromocytoma (median age 60 years, 19 females, median tumor diameter 36 mm) and 31 patients with non-functional adrenal incidentaloma (NFAI) (median age 63 years, 22 females, median tumor diameter 17 mm). All patients underwent hormonal evaluation and imaging according to current guidelines. Plasma concentrations of free metanephrines were measured in all patients by LC–MS/MS.
Results: Metanephrine showed high diagnostic accuracy in distinguishing pheochromocytoma from NFAI group (sensitivity 92.9%, specificity 88.0%, AUC 0.913). Similar results were obtained for normetanephrine (sensitivity 89.3%, specificity 96.0%, AUC 0.966). Combined analysis of both metabolites further improved accuracy (sensitivity 89.3%, specificity 100%, AUC 0.99). Concentrations of metanephrine and normetanephrine correlated positively with tumor diameter (r = 0.656 and r = 0.635, respectively). Biochemical profiling identified an adrenergic phenotype in 22 patients and a noradrenergic phenotype in 8 patients. Lack of cortisol suppression in the 1 mg overnight dexamethasone test was observed in 25% (7/28) of pheochromocytoma patients (median cortisol 4.0 µg/dL, IQR 2.2–5.0).
Conclusions: Measurement of plasma free metanephrines by LC–MS/MS provides excellent diagnostic sensitivity and specificity for pheochromocytoma. Concurrent elevation of metanephrine and normetanephrine is particularly indicative of disease. Metabolite concentrations correlate with tumor size, and autonomous cortisol secretion may coexist in a significant proportion of cases.
Keywords: pheochromocytoma, neuroendocrine tumour, metanephrine, normetanephrine, liquid chromatography mass-spectrometry

EFFECTS OF ABNORMAL GROWTH HORMONE SECRETION TREATMENT ON BONE METABOLISM AND STRUCTURE IN ACROMEGALY AND ADULT GROWTH HORMONE DEFICIENCY-A PRELIMINARY REPORT

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Keywords: bone metabolism, bone turnover markers, acromegaly, growth hormone deficiency
Background: Both the excess of growth hormone in acromegaly (Acro) and its deficiency (GHD) may lead to impaired bone metabolism and bone mineral density (BMD) and fragility. However, the exact mechanism remains unclear.
Purpose: To evaluate the effects of Acro and GHD treatment on bone metabolism, including bone turnover markers, BMD and bone microarchitecture.
Methodology: In this single-center study 39 patients were recruited: 14 with Acro and 25 with GHD. Calcium, phosphorus (serum and urine), PTH, 25-hydroxy- and 1,25-dihydroxy-vitamin D and bone turnover markers: serum b-cross laps (Ct-x), procollagen type I N-terminal propeptide (P1NP), bone alkaline phosphatase (BALP), sclerostin (Scl) and Dikkopff-1 (Dkk-1), and BMD and TBS measured by dual-energy X-ray absorptiometry were assessed baseline, 6 months after (a6m) adequate treatment in both group.
Results: Median age was 48 (IQR:26.75) and 28.5 (IQR:16) in Acro and GHD group, respectively. Median baseline GH and IGF-1 levels in Acro were 12.5ug/L and 689ug/L (3.1xULN), respectively. In the GHD group median baseline IGF-1 was 74.9ug/L (0.86xLLN). In Acro a6m of treatment we observed a reduction in serum calcium (2.5 vs 2.42mmol/L; p=0.04) and phosphorus (1.42 vs 1.1mmol/L; p<0.001), urine calcium (5.53 vs 2.94mmol/24h; p<0.001) in 24-hour urine collection. We also observed an increase in PTH (29.85 vs 44.95pg/mL; p=0.023) and increase 25(OH)D (26.92 vs 35,6ng/ml; p=0.002). A6m of treatment we did not observe statistically significant changes in bone turnover markers.
In GHD there was increase in serum phosphorus (1.02 vs 1.19mmol/L; p=0.002), and increase in 24-hour urine calcium and phosphorus (3.95 vs 5.66mmol/L; p=0,004 and 17.71 vs 22.93mmol/L; p=0.02, respectively). A6m of treatment increase in BALP (70.5 vs 78.4U/L; p=0,034) and Scl (47.6 vs 64.6pg/ml; p=0.034) was observed. There were no notable changes in BMD a6m.
Conclusion: We present initial results of the study showing the impact of GH changes on bone turnover in both groups. However, most changes were not statistically significant, likely due to the small sample size and short follow-up.

DOES THE TREATMENT OF HYPERCORTISOLEMIA IMPROVE BONE METABOLISM AND STRUCTURE IN PATIENTS WITH ENDOGENOUS CUSHING'S SYNDROME?

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Background: Cushing's syndrome is a rare endocrine disorder. It is characterized by numerous clinical symptoms resulting from excess cortisol, which can lead to many comorbidities. Prospective studies in large groups of patients with endogenous hypercortisolemia evaluating bone morbidity are rare.
Purpose: To evaluate the effect of hypercortisolemia treatment on bone metabolism and structure in patients with endogenous Cushing's syndrome.
Patients and methods: This is a prospective, single-center study involving a total of 30 patients diagnosed with endogenous Cushing's syndrome. The patients' hormonal test results and calcium-phosphate homeostasis were evaluated at the time of diagnosis and after the implementation of treatment. Bone turnover markers such as sclerostin, Dkk-1, CTx, and PINP wereassessed before and 3, 6, and 12 months after achieving normocortisolemia.
Results: 10 patients with endogenous Cushing's syndrome have been included in the study to date, with males predominating (M:F=7:3). The mean age at diagnosis was 47.9 ± 16.6 years (27-64 years). Nine of the 10 patients were diagnosed with Cushing's disease. The mean cortisol concentration at the time of diagnosis was 22.17 ug/dL. Three months after achieving normocortisolemia, an increase in total serum calcium (2.46.....2.53 mmol/L), phosphorus (1.13.... 1.45 mmol/L) and a decrease in calciuria (4.78....3.64 mmol/24h) and phosphaturia (23.18.... 16.95 mmol/24h). There was an increase in alkaline phosphatase concentration (61.5..... 67.12 IU/l). The average sclerostin concentration at the time of diagnosis of hypercortisolemia was 62.94 ng/ml, and after 3 months it was 77.4 ng/ml.
There was a decrease in Dkk-1 concentration a fter achieving normocortisolemia (5078... 4621 ng/ml).
Conclusions: Preliminary results confirmed that normocortisolemia improved calcium and phosphate metabolism. Further conclusions regarding changes in calcium and phosphate homeostasis and bone turnover markers over time in patients with normocortisolemia will be possible after including a larger group of patients in the study.
Keywords: hypercortisolemia, Cushing's syndrome, bone metabolism, sclerostin

RECOMBINANT GROWTH HORMONE THERAPY AND FUNCTIONAL OUTCOMES IN ADULTS WITH SEVERE GROWTH HORMONE DEFICIENCY: PRELIMINARY RESULTS

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Background: Growth hormone (GH) regulates muscle development, body composition, and physical capacity. In adults with severe GH deficiency (GHD), reduced fitness and impaired quality of life are common. The role of recombinant human GH (rhGH) replacement in improving physical performance in this population remains insufficiently clarified.
Purpose: This study aimed to evaluate the effect of 12-month rhGH replacement therapy on physical fitness in adults with severe GHD. Preliminary results concern a 6-month period of rhGH administration.
Methodology: Seventeen adults with severe GHD (9 females, 8 males; mean age 40.4±12 years) participated. Physical performance was assessed at baseline and after 6 months of rhGH treatment using four validated tests: 6-minute walk test (exercise tolerance), 30-second chair stand test (lower body endurance), up-and-go test (agility and balance), and handgrip strength test (upper limb strength).
Results: All patients achieved normalization of IGF-1 levels after 6 months of rhGH treatment (156.45±58.29 ng/mL vs. 66.89±42.62 ng/mL at baseline). Significant improvements were observed in physical performance: 6-minute walk test (614.00±92.10 m vs. 539.65±43.10 m, $p<0.05$), chair stand test (18.32±5.60 vs. 13.06±2.70 repetitions, $p<0.05$), up-and-go test (5.21±0.77 s vs. 5.78±0.76 s, $p<0.05$), and handgrip strength (36.22±12.20 kg vs. 33.44±10.20 kg, $p<0.05$). Both men and women demonstrated improvements across all measures.
Conclusion: Six-month rhGH therapy in adults with severe GHD normalized IGF-1 levels and significantly enhanced physical fitness. These preliminary findings support rhGH replacement as a beneficial intervention for functional improvement in this population.
Keywords: growth hormone deficiency, recombinant human growth hormone, physical fitness, IGF-1, exercise tests, functional outcomes

AGGRESSIVE PITUITARY ADENOMAS AND PITUITARY CARCINOMAS – CASE SERIES FROM THE REFERRAL PITUITARY CENTER

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Background: Aggressive pituitary tumors (APTs) are rare neoplasms defined as invasive and refractory to treatment, with early recurrences. Pituitary carcinomas (PCs) besides their aggressive behavior are diagnosed by the presence of metastases.
Purpose: The aim of this study is to find clinical features characteristic for patients with APTs and PCs.
Methodology: The study is a retrospective analysis of a series of 45 patients (14 women and 31 men) treated from the 2006 to

2024 by the endoscopic transsphenoidal surgeries for pituitary adenomas presenting aggressive clinical behavior. The mean age of the patients was 48.4 years (20-70 years), and the mean follow-up period was 10.4 years (0-18 years).
Results: In this group 3 patients were diagnosed with PCs (6.7%) and the rest with APTs (93.3%). Six patients died during follow-up period (13.3%). There were 91.1% macroadenomas, the tumors were invasive in 75.5% and functioning in 33.3% of the patients. The patients had 3.3 resections for APTs or PCs on average. The Knosp scale grade assessed preoperatively was III in 9 patients (20.0%), and IV in 11 patients (24.4%). Twenty-nine patients (64.4%) had radiotherapy, and 13 patients had pharmacotherapy (28.9%) as additional treatment methods. According to Lyon's classification the most numerous groups were 2a (35.6%) and 2b (33.3%). The gross total resection was accomplished in 17 cases (37.8%), the subtotal resection - in 20 cases (44.4%), and the partial resection - in 6 cases (13.3%). Postoperatively 68.2% of the patients showed varying improvement in visual field defects and visual acuity. Transient diabetes insipidus (DI) was observed in 4 patients (8.8%), epistaxis in 4 patients (8.8%), and 2 patients (4.4%) had a postoperative oculomotor nerve paresis.
Conclusion: Surgical treatment of APTs and PCs is safe and associated with a low complication rate. The patients are younger and have more resections than in usual pituitary adenomas.
Keywords: Aggressive pituitary adenomas, pituitary carcinomas

CROOKE'S CELL ADENOMAS– CASE SERIES FROM THE REFERRAL PITUITARY CENTER

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Background: Crooke's cell adenoma (CCA) is a rare subtype of pituitary adenoma (<1%). CCAs are usually invasive, may exhibit aggressive behavior, and often recur. Thus, the treatment of CCAs is difficult and might not result in a complete remission.
Purpose: The aim of this study was to assess characteristics of a group of patients with CCAs treated with endoscopic endonasal resections.
Methodology: The study is a retrospective analysis of a series of 18 patients (6 women and 12 men) treated from the 2015 to 2024 by the endoscopic transsphenoidal surgeries for CCAs. The mean age of the patients was 48.3 years (18-77 years), and the mean follow-up period was 5.3 years (0-11 years).
Results: Preoperatively 8 patients had visual function deterioration (44.4%), 8 patients had Cushing's disease (44.4%), 6 patients had hypopituitarism (33.3%), 4 patients had headaches (22.2%). Gross total resections were achieved in 6 out of 8 patients with Cushing's disease (75%), and in 7 out of 10 patients with silent adenomas (70%). Most patients (88.9%) had macroadenomas. Postoperatively 75% of the patients showed varying improvement in visual field defects and visual acuity. The only complication was transient diabetes insipidus (DI) observed in 3 patients (16.7%). One patient progressed to pituitary carcinoma, had four subsequent resections, and eventually died. The remission of Cushing's disease was achieved in 6 patients after surgery (75%).
Conclusion: Endoscopic transsphenoidal treatment of patients with CCAs is safe and associated with a low complication rate. The patients are younger and have more resections than in usual pituitary adenomas.
Keywords: Crooke's cell adenoma, Cushing's disease

EXTENDED MEDIAL WALL RESECTION OF THE CAVERNOUS SINUS IN ENDOSCOPIC TREATMENT OF PITUITARY ADENOMAS CAUSING ACROMEGALY WITH CAVERNOUS SINUS INVASION (KNOSP I–III) – EARLY CLINICAL RESULTS

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Background: Currently, the first-line treatment for acromegaly is surgery—adenoma resection. In patients with invasive adenomas, standard transsphenoidal resection does not provide satisfactory results (remission of acromegaly in 30–50%). In cases of medial wall invasion of the cavernous sinus, its removal allows for improved treatment outcomes and higher remission rates.
Purpose: The aim of the study was to evaluate the outcomes of endoscopic transsphenoidal resections with removal of the medial wall of the cavernous sinus in the treatment of somatotropin-secreting pituitary adenomas with intermediate and high risk of invasive growth (Knosp I–III) causing acromegaly.
Methodology: This was a retrospective analysis of a series of 21 patients (15 women and 6 men) treated in 2024–2025 with endoscopic transsphenoidal resections for pituitary adenomas with possible invasive growth assessed by the Knosp scale (I–III) and causing acromegaly. The mean age at the beginning of treatment was 53 years (range 25–76 years), with a mean follow-up of 6 months (0–13 months).
Results: Most patients had macroadenomas prior to resection (n = 11; 52%). In 11 patients (52%), histopathological examination confirmed invasion of the medial wall of the cavernous sinus. In all patients, the medial wall of the cavernous sinus was removed and gross total resection was achieved. The mean intraoperative blood loss was 180 ml (range 50–450 ml). No neurological or vascular complications were observed postoperatively. Eighteen patients (86%) met the criteria for remission of acromegaly at early postoperative follow-up (2–5 months).
Conclusion: Endoscopic transsphenoidal resections of invasive somatotropin-secreting pituitary adenomas with removal of the medial wall of the cavernous sinus enable effective treatment of acromegaly. Although this method carries an additional risk, it is relatively safe and associated with a low rate of complications.
Keywords: Cavernous sinus, extended medial wall resection

CLINICAL CHARACTERISTICS AND OUTCOMES OF ENDOSCOPIC TREATMENT OF PITUITARY ADENOMAS WITH PIT-1 AND SF-1 COEXPRESSION

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Background: Pituitary adenomas arise from three lineages of cells expressing different transcription factors: Pit-1 (somatotroph, lactotroph, thyrotroph, mixed), TPIT (corticotroph), and SF-1 (gonadotroph). Typically, pituitary adenomas express only one of these transcription factors; however, in some cases, tumor cells show expression of several. Coexpression of Pit-1 and SF-1 is particularly common in densely granulated somatotroph adenomas.
Purpose: The aim of this study was to describe the outcomes of endoscopic treatment of pituitary adenomas with Pit-1 and SF-1 coexpression.
Methodology: This was a retrospective analysis of 26 patients (15 women and 11 men) treated between 2020 and 2024 with endoscopic transsphenoidal resections for pituitary adenomas showing Pit-1 and SF-1 coexpression. The mean age of patients was 53 years (range 26–79), and the mean follow-up was 2.4 years.
Results: The main clinical manifestation was acromegaly (n = 25; 96.2%). Five patients had visual disturbances (19.2%), and one patient presented with headaches (4.4%). Most patients had macroadenomas (n = 23; 88.5%), with an average size of 16 mm. According to the Knosp classification, 3 patients (11.5%) had grade 3 adenomas and 2 patients (7.7%) had grade 4 adenomas. Gross total resection was achieved in most cases (n = 24; 92.3%). Immunohistochemistry confirmed positive staining for growth hormone in all patients, for α-subunit in 23 patients, for prolactin in 16, for luteinizing hormone in 6, and for follicle-stimulating hormone in 1. Remission of acromegaly was achieved in 93.8% of patients.
Conclusion: The main clinical manifestation in patients with pituitary adenomas showing Pit-1 and SF-1 coexpression is acromegaly, which can be effectively treated with endoscopic transsphenoidal resection. This method is safe and associated with a low risk of complications.
Keywords: Pituitary adenomas, coexpression of Pit-1 and SF-1

PITUITARY METASTASES: A CASE SERIE

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Background: Pituitary metastases are rare lesions in this region; their exact incidence has not been clearly determined, although it is estimated at approximately 0.5%. However, given the increasing incidence of neoplastic diseases, a gradual rise in the number of diagnoses can be expected.
Purpose: The aim of this study is to present a series of cases of pituitary metastases, with particular emphasis on their clinical manifestations and their relevance in the differential diagnosis of lesions in the pituitary region.
Methodology: The presented case series includes three patients hospitalized at the University Clinical Center in Gdansk between 2010-2025. The inclusion criterion was histopathological confirmation of pituitary metastases in the tissue specimens.
Results: In this analysis, an attempt was made to identify patients hospitalized at the University Clinical Center in Gdansk with a diagnosis of pituitary metastases. Initially, seven patients were considered for inclusion. Upon detailed verification, only three female patients were confirmed to have pituitary metastases through histopathological examination. In the remaining four patients, the diagnosis was based on clinical and radiological findings, and radiotherapy targeting the pituitary and brain was administered, but without histopathological confirmation of the lesion.
The mean age at metastasis diagnosis was 58. The primary origin of pituitary metastases included breast cancer (n=1), lung cancer (n=1) and multiple myeloma (n=1). In one of the patients the pituitary metastasis was the only secondary lesion at the time of diagnosis. In two patients the pituitary metastasis was detected before the diagnosis of the primary tumor. The main clinical symptoms were headache (in all patients), nausea, dizziness, and vomiting. None of the patients presented symptoms of diabetes insipidus prior to neurosurgical intervention. Pituitary hormonal evaluation before metastasis resection was performed in two patients, as the one patient was referred for endocrinological care only after surgery.
Conclusion: Although pituitary metastases are rare, they should be considered in the differential diagnosis of lesions in this region, particularly in patients with a history of malignancy. Importantly, a pituitary metastasis are not a manifestation of end-stage disease – it may also be the first clinical presentation. The analyzed case series only suggest that diabetes insipidus is not an obligatory symptom, and nonspecific neurological complaints often predominate, while hormonal disturbances may remain undetected until surgical intervention. It should be emphasized that the actual incidence of pituitary metastases may be underestimated, as biopsies in this region are not routinely performed and therefore the definitive diagnosis is not always established.
Keywords: Metastasis, Pituitary gland, Pituitary metastases

THREE FACES OF MALE PROLACTINOMA: EFFECTIVE THERAPY, RESISTANCE, SURGERY

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Background: Prolactinomas account for about half of all pituitary adenomas and represent the most frequent hormonally active subtype. They are more common in women, while in men the peak incidence occurs after the age of 50. Compared with females, male prolactinomas are usually larger and more aggressive. Dopamine agonists remain the first-line therapy, regardless of sex, typically leading to normalization of prolactin levels and reduction of tumour size. Nevertheless, some patients respond inadequately to medical therapy, and in selected cases definitive treatment, such as surgery or radiotherapy, becomes necessary.
Purpose: This study aims to present three clinical scenarios illustrating diverse therapeutic pathways and outcomes in male patients with prolactinoma.
Methodology: Three clinical cases of male patients with prolactinoma are described: one with a microadenoma and hyperprolactinemia successfully treated with cabergoline; another with a macroprolactinoma resistant to high-dose dopamine agonists, ultimately managed with radiotherapy; and a third with a large tumour compressing the optic chiasm, requiring surgical intervention.
Results: The first case demonstrates a typical response to pharmacological therapy, with rapid prolactin reduction, tumour regression, and resolution of symptoms. The second highlights limited efficacy of dopamine agonists, necessitating high doses and, due to high surgical risk, subsequent radiotherapy, which achieved a favourable clinical outcome. The third emphasizes surgery as a life-saving intervention, resulting in visual improvement and partial biochemical remission, while requiring ongoing endocrinological follow-up.
Conclusion: Prolactinoma in men may present with a heterogeneous clinical course. Pharmacotherapy remains the standard of care, yet resistance or mass effect can require alternative approaches, including surgery or radiotherapy. The presented scenarios illustrate three distinct therapeutic pathways that can be encountered in patients with prolactinoma with the same diagnosis.
Keywords: male prolactinoma, dopamine agonists, resistance, pituitary surgery, radiotherapy

BODY IMAGE AND QUALITY OF LIFE IN GIRLS WITH TURNER SYNDROME

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Background: Turner syndrome (TS) affects women in multiple ways; however, research often focuses mainly on health-related aspects. Its impact on body image, linked to hormonal and reproductive issues, is less explored. Studying this area may enhance understanding of the experiences of women with Turner syndrome and contribute to the development more effective psychological and therapeutic support.
Purpose: The aim of the present study was to show the relationship between body image and quality of life (QoL) in girls with Turner syndrome and to test whether intergroup differences exist in body image, quality of life and their aspects.
Methodology: The study involved 56 girls aged 11 to 18 years (M = 14.39; SD = 2.095): 28 girls with TS (M = 14.39; SD = 2.114) and 28 healthy controls matched to them in pairs. Four questionnaires were used in the study: BES (Body Esteem Scale), SF-36 (Short Form Health Survey) and BESAA (Body-Esteem Scale for Adolescents and Adults) and KPJŻ (Quality of Life Questionnaire). In addition, an interview questionnaire was conducted with girls with TS and their parents.
Results: Turner syndrome significantly affected selected health-related quality of life dimensions and moderated the associations between body image and QoL, while karyotype variants influenced general health. No intergroup differences were observed in overall QoL and body image
Conclusion: The study revealed differences in quality of life between girls with Turner syndrome and their peers, correlations between QoL dimensions and body image, as well as the influence of karyotype. The results indicate the need for longitudinal research, larger sample size, and the development of targeted medical and psychological support programmes for girls with TS.
Keywords: Turner syndrome, body image, quality of life, adolescence, health-related quality of life

ANALYSIS OF MIR 16-5P, MIR 143-3P AND MIR 423-5P IN PATIENTS WITH INVASIVE NON-FUNCTIONING PITUITARY ADENOMAS AND PROLACTINOMAS

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Background: MicroRNAs (miRNAs) are small non-coding RNA molecules involved in the post-transcriptional regulation of gene expression. We aimed to analyze miR 16-5p, miR 143-3p and miR 423-5p expression in serum of patients with invasive non-functioning pituitary adenomas (NFPA) and prolactinomas, as candidates for non-invasive biomarkers.
Material and methods: That was a prospective study with consecutive enrollment. The study included 62 Patients with NFPA and 19 Patients with macroprolactinoma qualified for transsphenoidal surgical resection. The expression levels of hsa-miR-191-5p, hsa-miR-16-5p, hsa-miR-143-3p, and hsa-miR-423-3p were determined using TaqMan MicroRNA Assays (Thermo Fisher Scientific, Waltham, MA, USA). hsa-miR-191-5p served as a reference miRNA. The control group (CG) consisted of 26 healthy volunteers. The statistical analysis was performed with MedCalc, with significance level set as $p<0.05$.
Results: The total concentration of microRNA was significantly lower in NFPA than in the CG ($p=0.0419$). ROC curve analysis showed that the cutoff point of miRNA lower than 10.73 predicted the PA (sensitivity=70.0%; specificity=57.7%; AUC=0.629; $p=0.052$). We did not observe that for prolactinoma. No correlation between selected miRNAs and tumor type was found,

miR-143-3p (p=0.4610), miR-16-5p (p=0.8767), miR-423-5p (p=0.1459). The expression of miRNA also did not correlate with invasiveness (cavernous or sphenoid sinus invasion, compression of the optic chiasm). We observed significantly lower levels of FSH, LH, estardiol, testosterone and fT4 in NFPA and prolactinomas than in control group (p<0.05). IGF-1 and fT3 were significantly lower in NFPA than CG (p=0.024, p=0.0067, respectively).

Conclusions: Although the total expression of microRNA was significantly lower in NFPA, miR 16-5p, miR 143-3p and miR 423-5p are not useful as non-invasive biomarkers in patients with invasive non-functioning pituitary adenomas and prolactinomas.

Keywords: miRNA, pituitary tumor, invasive pituitary adenoma, prolactinoma

SEX RELATED DIFFERENCES IN NON-FUNCTIONING PITUITARY ADENOMAS – DATA FROM TWO EUROPEAN REFERRAL CENTERS

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Background: Sex- related differences have been described in functioning pituitary adenomas. Less is known about the differences between men and women in the clinical course of non-functioning pituitary adenomas.

Purpose: Assessment of sex related differences in non functioning pituitary adenomas (NFPAs) in patients qualified for transsphenoidal pituitary surgery in two European referral centers (Genoa, Italy and Szczecin, Poland)

Methodology: Clinical, histopathological, and biochemical data of patients undergoing first-time surgery for NFPAs (excluding silent corticotroph tumors) at San Martino University Hospital in Genova, Italy and at the University Clinical Hospital No. 1 in Szczecin, Poland were retrospectively analyzed with regard to patient's sex.

Results: In total 168 patients were included. Men were significantly more often operated in comparison to women (107 vs. 61; $\chi^2(1) = 12.595$, $p < 0.001$). Analysis of mitotic activity (<2 vs. ≥2 mitoses) using Fisher's exact test revealed a borderline association with sex, with ≥2 mitoses more frequent in men ($p = 0.041$ one-tailed). The Ki-67 proliferation index showed a tendency toward higher values in men, although the difference did not reach statistical significance (Mann–Whitney $U = 1171.5$, $z = -1.719$, $p = 0.086$) Maximal tumor diameter, assessed in a single-center cohort (Szczecin, Poland), was larger in men (27.1 ± 2.81 mm) than in women (20.6 ± 2.80 mm; $t(72) = 2.29$, $p = 0.024$, 95% CI: 0.089–12.09). No sex differences were observed in Knosp grade and in the need for multiple interventions.

Conclusion: Differences between men and women occur in the clinical course of NFPAs, which are due to the dynamics of lesion growth characterized by tumor size and proliferation markers.

Keywords: pituitary adenoma, sex-related differences, Ki-67, mitosis

PITUITARY MICROADENOMA WITH GH AND ACTH COSECRETION – CASE REPORT

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Introduction: Pituitary hormone expression is regulated by several transcription factors: PIT-1 regulates the functional differentiation of GH, PRL, and TSH; SF-1 and GATA-2 regulate LH and FSH expression, while ACTH expression is controlled by T-PIT. Functioning pituitary tumors most often secrete a single hormone. Plurihormonal adenomas (PHAs) that do not follow a specific cell lineage are rare, accounting for approximately 0.5–1.3% of PitNETs. Tumors co-secreting GH and ACTH belong to this poorly characterized group. To date, only isolated cases of macro- and microadenomas have been reported in the literature.

Case report: An 18-year-old woman with PCOS was referred to the endocrinology clinic due to irregular menstrual cycles, acne, and a perceived facial rounding. A 1 mg overnight dexamethasone suppression test revealed a cortisol level of 9.3 µg/dL. As a result, the patient was admitted to hospital for further evaluation, which confirmed ACTH-dependent hypercortisolism. Additional tests included an 8 mg dexamethasone suppression test (HDDST) and a desmopressin stimulation test. The dynamic tests clearly indicated a pituitary source of ACTH. Moreover, elevated IGF-1 levels and the lack of GH suppression during a 75 g oral glucose tolerance test were found. Based on the tests performed, a pituitary adenoma co-secreting GH and ACTH was suspected. Pituitary MRI revealed a 1.5 × 1.5 × 2.5 mm microadenoma in the pituitary gland. The patient was referred for Inferior Petrosal Sinus Sampling.

Conclusions:

• Plurihormonal pituitary adenomas with GH and ACTH co-secretion are exceptionally rare and often present with an atypical clinical picture.

• Early diagnosis requires a high index of clinical suspicion and interdisciplinary collaboration.

• PHAs, particularly those secreting ACTH, are associated with a high risk of recurrence and frequently follow an aggressive course; therefore, early recognition of such tumors is of great importance.

Keywords: Pituitary neuroendocrine tumor (PitNET), Plurihormonal adenoma, GH/ACTH co-secretion

VARIOUS ASPECTS OF IMMUNOTHERAPY-RELATED HYPOPHYSITIS – A REPORT OF FOUR CASES

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Introduction: Immunotherapy-induced hypophysitis (IH) is a serious adverse effect, that most commonly occurs in men around 60 years old. The pathogenic mechanism remains unclear. According to the latest reports, antibodies against GNAL (guanine nucleotide-binding protein G subunit alpha) and ITN2B (integral membrane protein 2B) are associated with the development of IH. Proposed diagnostic criteria include: a deficit in >=2 hormonal axes or a deficit in >=1 axis with radiological abnormalities in MRI, in the presence of suggestive symptoms. Inflammation induced by anti-PD-1/PD-L1 therapy most commonly manifests as isolated ACTH deficiency, occurring around the 26th week of treatment, rarely (in 28%) accompanied by pituitary enlargement. Disease induced by anti-CTLA-4 therapy can cause multiple hormonal deficiencies, reveals within 2-3 months from the therapy initiation, with pituitary enlargement in 98% of cases. In combination therapy (anti-CTLA-4 + anti-PD-1/PD-L1) ACTH and TSH deficiencies are most commonly reported. There are isolated case reports of patients with diabetes insipidus induced by this therapy.
Case report: We present four cases of patients treated with combined therapy of ipilimumab and nivolumab, who developed pituitary inflammation. In all four cases, it manifested as adrenal axis insufficiency, in two also as thyroid axis insufficiency, one patient was diagnosed with diabetes insipidus. Abnormalities in the pituitary MRI were recorded in only one case – heterogeneous signal of the pituitary anterior lobe, without enlargement of the gland, without thickening of the stalk.
Conclusions: Symptoms of hormonal deficiencies in IH are similar to the other cancer treatment complications and the cancer itself. Patients may not present any neurological signs. However, diagnostic vigilance and proper treatment of IH are crucial for patient outcomes, as overlooking this complication may lead even to the death. Patients with polyuria, particularly those treated with anti-PD-1/PD-L1 therapy, should be diagnosed for the possible, rare complication - diabetes insipidus.
Keywords: Hypophysitis, Immunotherapy, CTLA-4 inhibitor; PD-1 inhibitor

THE ROLE OF CYTOKINES REGULATING THE FUNCTION OF CD4+ T HELPER 17 (TH17) AND REGULATORY T (TREG) LYMPHOCYTES IN THE COURSE OF SELECTED ENDOCRINE AUTOIMMUNE DISEASES

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Background: The imbalance between T helper 17 (Th17) lymphocytes and regulatory T (Treg) cells is one of the main mechanisms triggering the autoimmune process. Interleukins (IL)-23, 31 and 33 are involved in the regulation of T Th17/Treg cells balance. The role of IL-23, 31 and 33 in non-endocrine autoimmune diseases has been confirmed. Data on the involvement of these cytokines in endocrine autoimmune diseases are limited.
Purpose: This study aimed to determine the involvement of cytokines regulating the Th17 /Treg cells axis in the course of autoimmune endocrine diseases.
Methodology: Eighty participants of the study were divided into 4 groups: the autoimmune polyendocrine syndrome (APS) group consisting of APS type 2 (APS-2) and type 3 (APS-3) subgroups, the Hashimoto's thyroiditis (HT) group, the Graves' disease (GD) group and the control (C) group. Fifteen cytokines related to Th17 and Treg lymphocytes were determined in the serum of all participants.
Results: Higher levels of IL-23 and IL-31 were found in the APS, GD and HT groups compared to the C group. Higher levels of IL-23 and IL-31 were also observed in the APS-2 group, in contrast to the APS-3 group. Correlation analysis of variables in the groups showed a statistically significant correlation between the cytokines IL-23, IL-31 and IL-33 in the APS, APS-2 groups, but no correlation in the APS-3 and C groups.
Conclusion: IL-23 and IL-31 are independent factors in the course of HT, GD and APS-2, in contrast to APS-3. The positive correlation between IL-23 and IL-31, IL-23 and IL-33, and between IL-31 and IL-33 in the APS, APS-2 groups, but the lack of correlation in the APS-3 and C groups may further suggest the involvement of these cytokines in the course of Addison's disease.
Keywords: cytokines, Th17 cells, Treg cells, autoimmune thyroid disease, autoimmune polyendocrine syndrome, Addison's disease.

ASSESSMENT OF THE ALLOSTATIC LOAD INDEX IN PATIENTS WITH PITUITARY TUMOURS

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Background: Chronic exposure to pathogenic stressors leads to exhaustion of adaptive mechanisms and the development of allostatic load (AL). This condition is associated with dysregulation of neuroendocrine axes, metabolic disorders, and chronic inflammation, which contribute to the development of various chronic diseases, including endocrinopathies.

Purpose: The purpose of this study was to determine the AL index in patients with pituitary tumours and compare it to a control group.
Methodology: The study group consisted of 58 patients with hormonally active pituitary tumours, while the control group included 52 patients without pituitary dysfunction. The AL index was calculated based on 16 parameters categorized as follows: anthropometric measurements, cardiovascular indicators, lipid and carbohydrate metabolism parameters, and inflammatory and hormonal markers.
Results: Patients with pituitary tumours reported a statistically significantly higher AL index compared to the control group, regardless of the hormonal activity of the adenoma [7.00 (5.00–9.00) vs. 3.50 (2.00–5.00), p < 0.001]. Age significantly correlated with the AL index, while no relationship was noticed with education level. Analysis of individual AL biomarkers showed that patients with pituitary tumours had significantly higher body mass index (BMI), systolic and diastolic blood pressure, insulin, triglyceride, and interleukin-6 levels, and also significantly lower concentrations of high-density lipoprotein cholesterol, dehydroepiandrosterone sulphate, and albumin compared to the control group.
Conclusion: Our results confirm the utility of the AL index as an integrated measure of cumulative stress load in pituitary diseases. In addition, patients with hormonally active pituitary tumours showed a higher cardio-metabolic risk.
Keywords: allostatic load, allostasis, pituitary tumour, acromegaly, stress

BONE COMPLICATIONS IN CUSHING`S SYNDROME ACROSS EUROPE. DATA FROM THE EUROPEAN REGISTRY ON CUSHING'S SYNDROME (ERCUSYN)

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Background: Bone complications are common in patients with Cushing`s syndrome (CS), because osteoporosis (OP) and bone fractures (BF) affect about half of the patients, often preceding the diagnosis of hypercortisolism. However, the real prevalence of those comorbidities is probably underestimated, partly due to the lack of clinical symptoms and diagnostic delay. Moreover, the optimal clinical management of bone disease in CS is still a matter of debate.

Purpose: Our objective was to investigate bone complications and their management in patients included in the European Register on Cushing`s syndrome (ERCUSYN). We analyzed the prevalence of OP and BF during diagnosis and follow-up.
Methodology: We analyzed the data of 1682 patients with pituitary and adrenal CS, who were included in the ERCUSYN between 2000 and 2021.
Results: DXA examination was performed in 766 patients (45%), while an X-ray in 492 patients (29%) from the initial cohort. OP was found in 157 (21%) and 103 (13%) examinations at spine and hip, respectively, while BF was present in 87 (18%) of X-rays. Older age and lower BMI increased the risk of OP at baseline (p=0.038 and 0.022, respectively), while male sex, muscle weakness and lower bone mass density increased the risk of BF (p values below 0.05 for all). During follow-up, the presence of diabetes mellitus, hypopituitarism and older age were associated with bone mass deterioration.
Conclusion: Bone complications affect a significant number of patients with CS. Selected risk factors, including older age, male sex, muscle weakness and diabetes at baseline, as well as hypopituitarism during follow-up may suggest the need of careful monitoring of skeletal impairment in patients with CS.
Keywords: Cushing`s syndrome; ERCUSYN; osteoporosis; bone fractures

IS THERE STILL A PLACE FOR ETOMIDATE IN THE MANAGEMENT OF CUSHING'S SYNDROME? THE EXPERIENCE OF A SINGLE CENTER OF LOW-DOSE ETOMIDATE AND COMBINED ETOMIDATE-OSILODROSTAT TREATMENT IN SEVERE HYPERCORTISOLISM

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Background: Severe Cushing's syndrome (SCS) is a life-threatening endocrine emergency associated with multiple complications and high mortality, representing a significant therapeutic challenge for endocrinologists. Intravenous etomidate infusion is considered the most effective approach for rapid suppression of cortisol overproduction.
Purpose: This single-center retrospective study aimed to present the safety and effectiveness of intravenous, low-dose, lipid formulated etomidate infusion in patients with SCS.
Methodology: This descriptive, retrospective study was conducted on seven patients with SCS hospitalized in the Department of Internal Medicine, Endocrinology, and Diabetes, Medical University of Warsaw, Poland between April 2019 and April 2024. The patients were included in the study if they met the criteria for SCS and received etomidate infusion as a part of their cortisol-lowering treatment.
Results: A continuous etomidate infusion was initiated at a rate of 0.01–0.02 mg/kg/h. Target serum cortisol concentrations were achieved in all patients, with a median time of 30h (range: 12–48h). Median serum cortisol decreased from 101.9 µg/dL (range: 78.2–119.6 µg/dL) prior to etomidate administration to 19.5 µg/dL (range: 18.3–22.5 µg/dL) after 72h of treatment. The infusion was maintained for a median duration of 14 days (range: 5–19 days).
Normokalemia was achieved with a median time of 18h (range: 6–72h). Mean serum potassium increased from 2.10 ± 0.17 mmol/L before etomidate to 4.20 ± 0.48 mmol/L after 72h of treatment. In four patients, etomidate infusion was continued until osilodrostat therapy could be successfully initiated. Prior to transitioning to osilodrostat monotherapy, patients received combination therapy with etomidate and osilodrostat for a median duration of 7 days (range: 5–19 days).
Conclusions: This study shows that low-dose and short-term lipid formulation etomidate therapy is highly effective in severe hypercortisolism management. Combined therapy with etomidate and osilodrostat is well tolerated and could serve as a bridge in long-term SCS treatment.
Keywords: (Cushing's syndrome, etomidate, osilodrostat, severe hypercortisolism)

VASCULAR ANOMALY AS A RARE CAUSE OF HYPOPITUITARISM – CASE REPORT

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Background: Hypopituitarism in most cases is caused by pituitary adenomas or is a consequence of medical procedures in this area; rare causes include vascular pathologies.
Purpose: to present uncommon cause of acquired hypopituitarism.
Methodology: retrospective analysis of medical data.
Results: We present the case of a 67-year-old woman who was admitted to the emergency department with severe headaches. The symptoms occurred during upper respiratory tract infection. Moderate hyponatremia (125 mmol/l) was detected in basal laboratory tests. Computed tomography scans showed an abnormal, round mass, 30 mm in diameter, filling the sella turcica and a prothesis in the right internal carotid artery. No normal pituitary tissue was visualized. A detailed medical interview revealed a history of surgery for a suprasellar aneurysm seven years earlier. The patient had not been diagnosed with any endocrine disorders prior to admission. The presence of an aneurysmal sac-type lesion was confirmed by magnetic resonance imaging. Insufficiency of adrenal, thyroid and gonadal axes as well as hyperprolactinemia were found in the hormonal assessment. Function of posterior pituitary lobe and somatotropic axis was normal. Adequate hormonal substitution was introduced with subsequent improvement in the patient's general condition. The patient remains under constant endocrinological care.
Conclusion: Vascular changes, although rare, should be considered as a cause of hypopituitarism.
Keywords: hypopituitarism, pituitary gland, aneurysm, tumor

FAMILIAL CASE OF MEN1 WITH ASYMPTOMATIC GONOSOMAL MOSAICISM IN THE FATHER

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Background: Multiple endocrine neoplasia–type 1 (MEN1) is an autosomal dominant cancer syndrome characterized by tumors in at least two of the following: parathyroid, endocrine pancreas, and anterior pituitary. MEN1 mutations may exhibit gonosomal mosaicism - a combination of somatic and germline tissue mosaicism. We present a family with gonosomal mosaicism in MEN1.

Case presentation: A 43-year-old male with type-2 diabetes, hyperuricemia, and a family history of MEN1 presented with sudden neck enlargement. His sister has a history of hyperprolactinemia, hypogonadal axis failure, hypothyroidism, and primary hyperparathyroidism, and she has been diagnosed with a MEN1 mutation. The patient's neck ultrasound revealed two focal lesions in the left supraclavicular fossa. Thin-needle biopsy showed monomorphic cells with a "salt and pepper" chromatin pattern and pink cytoplasm. Differential diagnoses included neuroendocrine neoplasm (NEN) or medullary thyroid carcinoma (MTC). Tests indicated primary hyperparathyroidism with elevated IGF-1 and Chromogranin A. CT and scintigraphy revealed necrotic lymph nodes, chest masses, and pancreatic lesions. Biopsy of a cervical lymph node detected atypical carcinoid (thymic NET G2, Ki-67 10-15%). The patient received Octreotide, radiation therapy, and Everolimus. Genetic analysis identified a pathogenic MEN1 variant. Considering the MEN1 mutation in both siblings, first-degree relatives were examined. Despite the dominant inheritance pattern, the mutation was absent in the parents' blood. Consanguinity was confirmed, suggesting parental genetic mosaicism. DNA from eyebrow hair follicles and cheek swabs confirmed the father's gonosomal mosaicism. The patient's father shows no subjective symptoms.

Conclusions: The patient's father should undergo periodic screening for MEN1 spectrum tumors. This case illustrates divergent MEN1 courses in siblings with the same mutation. Genetic testing should be extended to assess the potential spread of the mutation within the other relatives. Only one case of gonosomal MEN1 mutation was described - it led to symptomatic disease there. No cases have reported asymptomatic gonosomal mosaicism.

Keywords: MEN1, gonosomal mosaicism, neuroendocrine tumor, genetic analysis, familial cancer, asymptomatic carrier