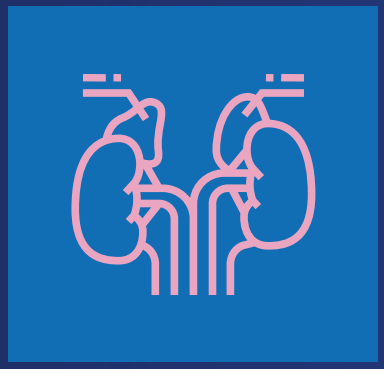
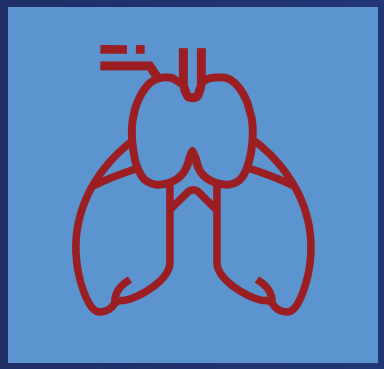
DIABETES CANADA/CSEM

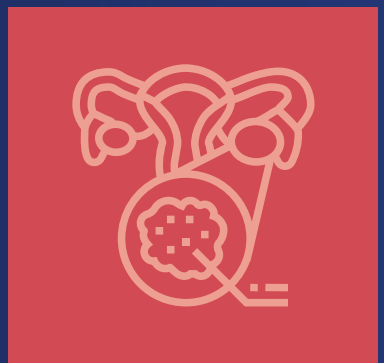
PROFESSIONAL CONFERENCE

NOVEMBER 9–12, 2022

2022







RESIDENT CLINICAL VIGNETTES

RESEARCH PROJECT ABSTRACTS

ORAL PRESENTATIONS

THURSDAY, NOVEMBER 10, 2022 9:45–11:45 AM MT · MODERATOR: BREAY PATY, MD, FRCPC

9:45 AM · INTRODUCTION

BREAY PATY, MD, FRCPC

9:50 AM · PRESENTATIONS

Slowing Down the Osteoclasts: Potential New Treatment for Fibrous Dysplasia-related Bone Pain

- MOHAMMAD JAY, MD

A Case Series of Hypophosphatasia: Presentation and Response to Asfotase Alfa

- FARRAH ALSARRAF, MD

A Rare Case of Succinate Dehydrogenase Enzyme Complex B1 Mutation Leading to Hereditary Paraganglioma

- ZACHARY RAIZMAN, MD, FRCPC

Recurrent Hypervitaminosis D with Spurious High Calcitriol Levels

- UMAIR SAJID, MD

A Rare Case of Parathyroid Carcinoma in MEN1 Syndrome

- MEIYING ZHUANG, BSC, MD

A 680 kb Duplication at the FTO Locus in a Subject with Extreme Weight

- GURLEEN GILL, MD

Renal Tubular Acidosis as a Cause of Hypophosphatemic Rickets in a Young Child

- KRISTINA PABEDINSKAS, MD

A Case of Adipsic Hypernatremia due to Antibody-mediated Hypothalamic Injury

- RYAN LE, MD

Co-secretion of Cortisol and Aldosterone from Metastatic Adrenocortical Carcinoma

- HAMNA TARIQ, MD

Optimal Therapeutic Strategy for a Novel Pathogenic Variant of Maturity-Onset Diabetes of the Young Type 4 (MODY-4)

- JUSTIN BHULLAR, MD

11:39 · CLOSING REMARKS

ABSTRACTS

YIQIAO WANG*, JIALIN HE, STEPHEN WANG, COLIN TAN, CATHERINE JI, CATHERINE YU

UNIVERSITY OF TORONTO

USE OF ACR-TIRADS — A SURVEY OF CANADIAN PRIMARY CARE PROVIDERS

Background: The American College of Radiology — Thyroid Imaging Reporting and Data System (ACR-TIRADS) is an ultrasound-based tool used to assess the risk of malignancy in thyroid nodules. Since primary care providers commonly identify and manage thyroid nodules, we aimed to determine 1) current diagnostic approach to thyroid nodules and 2) perceived utility of ACR-TIRADS in Canadian primary care providers.

Methods: We conducted a cross-sectional survey study for family physicians and nurse practitioners working in Canada. The 23-question survey was distributed electronically on Qualtrics using convenience sampling from August 31 2021 to January 3 2022.

Results: One hundred and four primary care providers responded to our survey. Of these, 90 met enrolment criteria and were included. For thyroid nodules, only 47% were confident in their ability to risk-stratify, and only 57% reported using a risk stratification tool. Although 64% percent of participants agreed with being familiar with ACR-TIRADS, only 28% used this scoring system. After being shown a diagram demonstrating the ACR-TIRADS, 93% thought that the ACR-TIRADS was useful. Most respondents learned about the ACR-TIRADS through ultrasound reports. To improve use, respondents suggested education and increased reporting by radiologists.

Conclusion: In this Canadian survey study, most primary care providers reported being familiar with ACR-TIRADS, however most were not confident with risk stratification and only half used a risk stratification tool. With education, almost all participants thought ACR-TIRADS was useful. Further interventions, including standardization of ACR-TIRADS on ultrasound reports, may be beneficial to improve management of thyroid nodules.

XUN YANG HU*, JIAHUI WU, RALF PASCHKE

UNIVERSITY OF CALGARY

IMPROVEMENT IN THYROID ULTRASOUND REPORT QUALITY WITH RADIOLOGISTS' ADHERENCE TO 2015 ATA OR 2017 TIRADS, A POPULATION STUDY

Objectives: There has been slow adoption of thyroid ultrasound guidelines with adherence rates as low as 30% and no population-based studies investigating adherence to guideline-based malignancy risk assessment. We therefore evaluated the impact of adherence to the 2015 ATA guidelines or 2017 ACR-TIRADS guidelines on the quality of thyroid ultrasound reports in our healthcare region.

Methods: We reviewed 899 thyroid ultrasound reports of patients who received fine needle aspiration biopsy and were diagnosed with Bethesda III or IV nodules or thyroid cancer. Ultrasounds were reported by radiology group 1, group 2, or other groups, and were divided into pre-2018 (before guideline adherence) or 2018-onwards. Reports were given a utility score (0 to 6) based on how many relevant nodule characteristics were included.

Results: Group 1 had a pre-2018 utility score of 3.62 and 39.4% classification reporting rate, improving to 5.77 and 97.0% among 2018-onwards reports. Group 2 had a pre-2018 score of 2.8 and reporting rate of 11.5%, improving to 5.58 and 93.3%. Other radiology groups had a pre-2018 score of 2.49 and reporting rate of 32.2%, improving to 3.28 and 61.8%. Groups 1 and 2 had significantly higher utility scores and reporting rates in their 2018-onward reports when compared to other groups' 2018-onward reports, pre-2018 group 1 reports, and pre-2018 group 2 reports.

Conclusions: Dedicated adherence to published thyroid ultrasound reporting guidelines can lead to improvements in report quality. This will reduce diagnostic ambiguity and improve clinician's decision-making, leading to overall reductions in unnecessary FNA biopsy and diagnostic surgery.

XUN YANG HU*, JIAHUI WU, SANA GHAZNAVI, PAULA SEAL, RALF PASCHKE

UNIVERSITY OF CALGARY

REDUCTION IN FALSE POSITIVE POST OPERATIVE US REPORT (POUR) POST THYROID CANCER TREATMENT WITH IMPROVEMENT IN POUR QUALITY, A PROSPECTIVE POPULATION STUDY

Objectives: We performed the first prospective evaluation of the population-wide impact of adherence to the 2013 ETA guidelines on quality and false positive rates of post operative US report (POUR).

Methods: We followed 579 patients from our prospective thyroid cancer database after implementation of ETA POUR guidelines with radiology group 1. POURs were given a utility score based on the number of relevant characteristics included. Of the indeterminate and suspicious lesions seen, we evaluated those that went on to receive FNA biopsy.

Results: A total 1716 POURs for 579 patients with differentiated thyroid cancer were obtained, 1244 by group 1 and 472 by other groups, identifying 390 neck lesions (177 suspicious, 213 indeterminate). Of 293 lesions in group 1, 33 (11%) were biopsied, of which 25 (76%) were malignant and 2 (6%) were indeterminate, indicating a false positive rate of 18%. Of the 97 lesions in other groups, 17 (18%) were biopsied, of which 8 were malignant, indicating a false positive rate of 53% ($p = 0.03$ for true positive, $p = 0.01$ for false positive). Group 1's POURs had significantly higher utility score than other groups (4.18 vs 3.44).

Conclusion: Strict adherence to ETA guidelines for neck US reporting improves their quality and allows for better recurrence risk estimation, leading to a significant reduction in false positive rates among FNA biopsies for ultrasound lesions.

REZA MIRZA*, DALAL S. ALI, MOHAMED EL-RABBANY,
GORDON GUYATT, ARCHIBALD MORRISON,
SALVATORE L. RUGGIERO, SOTIRIOS TETRADIS, ALIYA A. KHAN

MCMASTER UNIVERSITY

ANTIRESORPTIVE THERAPY AND DENTAL IMPLANT OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Background: To inform the 2022 update by the International Taskforce on Osteonecrosis of the Jaw (ONJ), we conducted a systematic review and meta-analysis evaluating the excess risk of dental implant failure and ONJ related to antiresorptive therapy (bisphosphonates or denosumab) in osteopenia and osteoporosis (OP).

Methods: An experienced health-services librarian conducted a search of 5 databases between 1946 and January 2022. We included case series (5 or more patients), observational, and interventional studies reporting rates of dental implant failure or ONJ in those with OP. Two reviewers independently screened all titles, abstracts and eligible full-texts. Risk of bias was assessed with the modified Ottawa-Newcastle scale, and the evidence was assessed using GRADE.

Results: Seven comparative studies that could inform the risk of dental implant failure in patients taking antiresorptive therapy for OP were included. A random-effects meta-analysis revealed a non-significant increased risk with antiresorptive agents with wide confidence intervals (RR 1.56, 0.43 – 5.70, Figure 1). A sensitivity analysis at the implant level did not change the outcome substantially. The risk of bias is high in 6 out of 7 studies included. All but one study failed to adjust for confounders.

Conclusion: The limited evidence does not suggest an association between antiresorptive therapy and dental implant failure or ONJ. Decisions regarding antiresorptive therapy should be based on other factors including harms and benefits to bone health.

KIMBERLEY LAU*, BONNIE CHEUNG, ETHAN SHAMIS, JULIE GILMOUR, CATHERINE YU

UNIVERSITY OF TORONTO

IDENTIFYING THE BARRIERS TO TIMELY INPATIENT HYPOGLYCEMIA MANAGEMENT AT A QUATERNARY CARE HOSPITAL: A QUALITY IMPROVEMENT PROJECT

Background and Objective: A hypoglycemia order set was implemented February 2019 at a quaternary care hospital to facilitate prompt treatment of hypoglycemia. After its implementation, only modest improvement of time-to-treatment was observed. This quality improvement study aims to identify barriers limiting order set effectiveness using the Model for Improvement.

Methods: Inpatient nurses, inpatient nurse practitioners, inpatient pharmacists, and resident physicians were recruited via email. A semi-structured interview guide was followed to conduct one-on-one and focus group interviews over phone or in-person. Audio-recorded interviews were transcribed. Two researchers independently performed descriptive analysis of interview transcripts to identify themes using statistical software (NVivo 12).

Results: Altogether, 12 semi-structured interviews were conducted (8 one-on-one interviews and 4 focus groups) with 19 participants (1 nurse practitioner, 12 nurses, 2 pharmacists, 2 resident physicians, 2 nurse educators). Participants worked on general medicine or surgical wards. The following main themes regarding barriers were identified: 1) order set not ordered by physician delays hypoglycemia management initiation by nurses, 2) delayed identification of hypoglycemia by nurses and residents due to lack of experience with hypoglycemia, 3) unawareness of protocol instructions by nurses and residents delays time between steps of protocol, and 4) lack of juice and snacks on wards increases time spent searching for supplies.

Conclusion: Barriers currently exist at the individual healthcare provider and institutional level. Future Plan-Do-Study-Act cycles will implement strategies to address these barriers. A potential change idea includes adding the hypoglycemia order set to pre-existing admission order sets to facilitate ordering by physicians.

ADAM SINCLAIR*, INDRA BUDIYANTO, LAURIE MEREU,
ANDREA OPGENORTH, MAHUA GHOSH,
DENISE CAMPBELL-SCHERER, ROSEANNE O. YEUNG

UNIVERSITY OF ALBERTA

CO-CREATING AN ADRENAL INSUFFICIENCY PATIENT TOOLKIT USING HUMAN-CENTERED DESIGN

Objective: To describe the application of Human-Centered Design (HCD) in development of an adrenal insufficiency patient education toolkit.

Overview: HCD is an iterative process that involves context-informed user-driven design and evaluation. In healthcare, HCD has been used to develop shared decision-making tools and interventions. In partnership with the Physician Learning Program, the Division of Endocrinology and Metabolism identified adrenal insufficiency as a clinical area of focus to collaborate with patients and Human-Centered Designers to explore ways to enhance patient care.

Methods: Through co-creation sessions, a team of endocrinologists, Human-Centered Designers, and patient volunteers explored patient care issues and agreed to create a standardized patient care toolkit as a potential solution. The HCD process involved 3 phases: toolkit design, user feedback, and usability testing.

Results: 2 handouts were produced: 1) Patient resource with basic information on symptoms of adrenal insufficiency/ crisis, treatment, circumstances to seek healthcare, and additional web resources. 2) Personal treatment plan with individualized information on stress dosing of adrenal hormone replacement and common example scenarios with suggested dosages. Usability testing with 11 patients demonstrated that the toolkit was intuitive, practical, and participants appreciated the recommended web resources and stress-dosing examples. Additionally, all participants reported that they would use the toolkit to guide self-management decisions.

Conclusion: Our toolkit development process illustrates the value of Human-Centered Design in healthcare. By collaborating with Human-Centered Designers and patient partners we created an educational resource that was intuitive and practical for those affected by adrenal insufficiency.

NATALIE RAKOCEVIC*, HEIDI DUTTON, ERIN KEELY

UNIVERSITY OF OTTAWA

BARIATRIC SURGERY IN PATIENTS WITH TYPE 1 DIABETES: A SINGLE CENTRE EXPERIENCE WITH PERI-OPERATIVE GLYCEMIC MANAGEMENT

Background: With rising obesity rates, individuals with type 1 diabetes mellitus (T1DM) are increasingly undergoing bariatric surgery. While bariatric surgery is considered a relatively safe procedure, this population is at increased risk of peri-operative diabetic ketoacidosis (DKA) and hypoglycemia, and no guidelines currently exist for optimizing peri-operative glycemic management. Our study aims to describe our centre's experience with glycemic management and outcomes in this population.

Methods: This was a retrospective case series including all patients with T1DM who underwent bariatric surgery between 2016 and 2022 in a single centre. Extracted data included patient demographics, baseline insulin regimen, and incidence of peri-operative glycemic complications.

Results: Eight patients with T1DM were identified; all underwent Roux-en-Y gastric bypass (RYGB). The cohort had a mean age of 42.5 years (range 29–57); 7 female and 1 male. Mean pre-operative insulin requirements were 75.7 units; 75% were on multiple daily injections and 25% on an insulin pump. Five patients experienced hypoglycemia; 3 pre-operatively and 2 post-operatively. One episode was severe and none required hospital admission. Four incidences of DKA were noted amongst three patients. All four cases were related to insulin omission; one patient received intra-operative dexamethasone which may have contributed.

Conclusion: This study aims to identify areas for quality improvement in patients with T1DM undergoing bariatric surgery. We identified hypoglycemia and DKA as potential complications, highlighting the importance of avoiding insulin omission, adjusting insulin doses carefully, and closely monitoring glucose levels in the perioperative period.

MONA VAHIDI RAD*, CHRISTOPHER FILLITER, KRISTIAN FILION, CHRISTEL RENOUX, ROBERT PLATT, ROLAND GRAD, ORIANA HOI YUN YU

MCGILL UNIVERSITY

LEVOTHYROXINE THERAPY AND ADVERSE RENAL OUTCOMES AMONG INDIVIDUALS WITH MILD SUBCLINICAL HYPOTHYROIDISM

Objective: To determine whether levothyroxine treatment is associated with the risk of adverse renal events among individuals with mild subclinical hypothyroidism (mild-SCH).

Overview: Mild-SCH is defined as an elevated thyroid stimulating hormone level < 10 mU/L with a normal thyroxine level. Cross-sectional studies have associated SCH with renal insufficiency. However, few studies have evaluated the association between levothyroxine and adverse renal outcomes among individuals with mild-SCH. Methods: Using the Clinical Practice Research Database Aurum, we conducted a population-based cohort study assessing individuals with incident mild-SCH between 1998 and 2018, with follow-up until 2019. Individuals who used levothyroxine were matched to non-users on time-conditional propensity score (TCPS). The primary endpoint was major adverse renal outcomes, defined as a composite endpoint of end stage renal disease, doubling of creatinine levels, and reduction of the estimated glomerular filtration rate of ≥50%. Cox proportional hazards models estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of adverse renal outcomes with levothyroxine versus non-use.

Results: From a cohort of 11,058 individuals with mild-SCH, we matched 5529 levothyroxine users to 5529 non-users. The mean age was 76.2 (standard deviation: 11) years, and 70.7% were female. The rate of adverse renal outcomes per 1,000 person-years was 14.9 (95% CI: 12.7–17.3) with levothyroxine and 15.0 (95% CI: 13.3–16.9) with non-use. Levothyroxine use was not associated with the risk of renal outcomes compared to non-use (HR: 1.03; 95% CI: 0.84–1.27).

Conclusion: Levothyroxine treatment was not associated with adverse renal outcomes among individuals with mild-SCH.

MARTIN GUAY-GAGNON*, JONATHAN LEGAULT, NADIA GAGNON, YOEL BITTON, SAMER MANSOUR, ISABELLE BOURDEAU

UNIVERSITÉ DE MONTRÉAL

SCREENING FOR PHEOCHROMOCYTOMA IN A COHORT OF PATIENTS WITH TAKOTSUBO CARDIOMYOPATHY: NEW INSIGHTS ON PREVALENCE AND SCREENING TESTS RELIABILITY SURROUNDING THE ACUTE CARDIAC EVENT

Background: According to Takotsubo cardiomyopathy (TCM) diagnostic criteria, pheochromocytoma and paraganglioma (PPGL) should be excluded as secondary causes.

Objective: Assess the prevalence and the reliability of PPGL screening in the setting of acute TCM. Method: Retrospective study of patients admitted in a tertiary hospital between 2012 and 2021 with a diagnosis of TCM who were screened for PPGL by plasma metanephrines/normetanephrines (pM/NM).

Results: Among 64 patients identified with TCM, 42 underwent pM/NM screening (34 females, 8 males, mean age 67.4±9.9 yo. 10 out of 42 (23.8%) patients had a positive result. Of those, 8 patients had a weakly positive result (1–2 × upper limit of normal [ULN]) and 2 had a strongly positive result (>2 × ULN). Of those 10 patients, 6 underwent subsequent screenings that came out negative. The 4 other patients who could not undergo a 2nd screening (3 died of other causes, 1 lost to follow up) all had normal adrenal glands on abdominal CT. Average time between TCM diagnosis and PPGL screening in all patients and in patients with a positive initial screening was 4.57±3.91 and 3.38±2.12 days, respectively. A linear regression model suggested an inverse relationship between pM/NM and time between TCM diagnosis and screening, with $R2 = 0.2275$.

Conclusion: In our cohort of patients, PPGLs were not a prevalent cause of TCM. A shorter delay between TCM diagnosis and PPGL screening may be associated with more false positives. Optimal timing and cut-offs for PPGL screening in acute TCM remain to be determined.

SAI MAN MUNG*, SAFA ELMAKKI, SHAZLI AZMI, JONATHAN SCHOFIELD, LAXMI BALMURI

MANCHESTER ROYAL INFIRMARY, UNITED KINGDOM

IDENTIFICATION AND MANAGEMENT OF HYPOGLYCEMIA IN ADULT PATIENTS ON HEMODIALYSIS WITH DIABETES

Background: Hypoglycemia is common in patients with diabetes on hemodialysis. Insulin reduction on dialysis days, flash glucose monitoring (FGM) and review in joint diabetes-renal clinic may mitigate this. We reviewed current practice in identification and management of 30 patients with diabetes who experienced hypoglycemia across satellite dialysis units.

Method: Clinic letters and capillary glucose (CBG) from June 2021 to June 2022 were obtained from Electronic Medical Record. Number of hypoglycemic and serious hypoglycemic events (CBG ≤2.5mmol/L or required third party assistance), hypoglycemic events occurring on dialysis days and whether insulin reduction advice was offered were analysed. We reviewed their duration of diabetes and hemodialysis, whether they were reviewed in joint clinic and whether FGM was offered.

Results: 30% of patients were reviewed in joint clinic. 288 hypoglycemic events occurred annually, of which 20% were considered serious. 60% of hypoglycemic events occurred on dialysis days. 37% were offered insulin reduction advice. All patients had CBG check before and after dialysis. Median duration of diabetes and hemodialysis was 22.5 years and 3 years respectively. There was no correlation between frequency of hypoglycemia and duration of diabetes or dialysis ($p=0.10$). 47% of 15 patients eligible were offered FGM. No patients seen in renal clinic were offered FGM whereas 67% of patients in joint clinic were offered FGM.

Discussion: Hypoglycemia on dialysis is common. Advice on insulin reduction on dialysis days, offering FGM and review in joint clinic may mitigate this but is not readily practised.

ALAA MOHAMED*, ERIN KEELY, LISA MIELNICZUK, DELVINA HASIMJA

UNIVERSITY OF OTTAWA

PRESCRIPTION PATTERNS OF SGLT2 INHIBITORS IN PATIENTS WITH T2DM AND HFrEF ADMITTED TO A TERTIARY CARE CENTRE WITH DECOMPENSATED HEART FAILURE

Objective: To assess prescription patterns of SGLT2i and prescriber variability in patients with T2DM and HFrEF and identify gaps in practice.

Methods: A retrospective chart review of patients with T2DM and HFrEF admitted to TOH (under Cardiology or GIM) with decompensated heart failure from June 2019–May 2021 was conducted. Patterns were assessed at 8-months intervals (3 periods). Exclusion criteria included those with eGFR<30, EF>40 or history of DKA. Baseline patient characteristics, co-morbidities and prescriber information was collected. SPSS software was used for descriptive statistical analysis.

Results: Of the 98 patients that met the inclusion criteria, 36.7% had a prescription for an SGLT2i either on admission, discharge or follow-up. Trends gradually increased over time. On admission, 9.8% of patients were on an SGLT2i in period 1, 19.2% in period 2 and 23.3% in period 3. Patients receiving a prescription for SGLT2i on discharge were 0% in period 1, 7.7% in period 2 and 6.7% in period 3. On follow-up, 12.2% of patients were started on an SGLT2i in period 1, 15.4% in period 2 and 26.7% in period 3. Cardiology provided 100% of inpatient prescriptions. Endocrinology took the lead for outpatient prescriptions providing >50% of prescriptions, followed by Cardiology. GIM provided 0% of prescriptions both as inpatient and outpatient.

Conclusion: Despite an increase in SGLT2i use over time, they remain underutilized. Communication with family physicians to initiate these agents in the outpatient setting for eligible patients who cannot be initiated on discharge is essential to improve uptake over time.

SARAH ZANKAR*, GURLEEN GILL, ERIN KEELY, CLARE LIDDY, AMIR AFKHAM

UNIVERSITY OF OTTAWA

EVALUATING DIABETES CLINICAL QUESTIONS AND ANSWERS PROVIDED VIA eCONSULTS

Background: The Champlain BASE eConsult service facilitates communication between primary care providers (PCPs) and specialists. Endocrinology, one of the most common specialties, receives 7% of all eConsults.

Aim: The primary aim of this study is to identify the most common diabetes-related questions asked by PCPs, and the answers provided by endocrinologists. A secondary aim is to evaluate the impact of the COVID-19 pandemic by comparing the changes in question and answer types from 2018 to 2020.

Methods: Endocrinology eConsults submitted to the Champlain BASE eConsult service between 2018–2020 were categorized by 3 researchers using predetermined taxonomies for the type of clinical questions and answers. Results: 326/2223 (14.7%) of all Endocrinology eConsult cases were diabetes-related with 128/700 (18.3%) in 2018, 126/735 (17.1%) in 2019, and 72/788 (9.1%) in 2020. There were 3 main types of questions: treatment related (70.1%), management related (13.7%), and diagnosis related (15.1%). The most commonly asked question was "What drug to choose next" (52.5%). In 50% of answers a specific name/class of drug was provided, however only 31% of them included a dose. The indication/rationale for medication choice was outlined in 34.4% of cases. A referral to an endocrinologist was recommended in 16% of cases.

Conclusion: eConsult is a feasible way for PCPs to get advice on patient specific diabetes questions. Continuing professional development could be developed around common medication related questions and provision of high quality eConsult replies. Fewer diabetes questions were asked during COVID. The reason for this should be further explored.

YOUSSEF HSHEIMI*, AGNIESZKA MAJDAN

MCGILL UNIVERSITY

ABERRANT ESTRADIOL IMMUNOASSAY MEASUREMENTS DURING FULVESTRANT ADMINISTRATION

Introduction: Estradiol levels measurement is used to inform treatment decisions in women with estrogen receptor positive breast cancer; however, certain assay interferences may result in falsely elevated measurements and unnecessary therapy modifications.

Case Description: A forty-two year old female known for a history of macroprolactinoma, metastatic breast cancer (hormone receptors positive; HER2 negative), and ovarian cancer status post bilateral mastectomy and bilateral salpingo-oophorectomy. She was being actively treated with cabergoline for her macroprolactinoma and with abemaciclib and fulvestrant for her metastatic breast cancer. She was referred to the care of her endocrinologist after elevated serum estradiol measurements (121 pmol/l) were discovered by her oncologist. Extensive work-up was undertaken to rule out cancer recurrence or an ectopic site of estradiol production including serial FDG-PET scans which did not reveal any evidence of cancer recurrence. Tandem measurement of estradiol using mass spectroscopy and immunoassays revealed discrepantly low levels of estradiol using mass spectroscopy (< 10 pmol/L) compared to that of the immunoassays (88 pmol/l).

Discussion: While the effect of fulvestrant on immunoassays measuring estradiol levels is reported in the literature, better clinician awareness of this phenomenon is needed to avoid protracted investigations, patient distress, and increased costs to the healthcare system. This case serves to raise awareness regarding measuring estradiol levels during fulvestrant administration for breast cancer and values that can result from immunoassays during administration of this medication. In such instances estradiol measurement with mass spectrometry should be favored to guide clinical decision making.

CAROLYN PAVONI*, VINCENT LAROUCHE, MARC PUSZTASZERI, ORIANA YU

MCGILL UNIVERSITY

HYPERCALCEMIC CRISIS SECONDARY TO A GIANT PARATHYROID ADENOMA

Primary hyperparathyroidism is frequently caused by a parathyroid adenoma. The presentation ranges from asymptomatic to, rarely, hypercalcemic crisis, defined as a corrected calcium >3.5 mmol/L with multi-organ failure. We discuss the medical and surgical management of a case of hypercalcemic crisis secondary to a giant parathyroid adenoma, defined as an adenoma weighing more than 3.5g. An 82-year-old female known for hypertension and type 2 diabetes presented with acute altered mental status. She was found to have a corrected calcium of 5.08 mmol/L (2.12–2.62 mmol/L) and a parathyroid hormone (PTH) level of 2858 ng/L (10–70 ng/L). She also had an incidental 5mm non-obstructing renal stone on imaging and mild renal injury. She was managed in hospital for 15 days using fluids, diuresis, zoledronic acid, calcitonin, and cinacalcet. Subsequently, serum calcium decreased to 2.68 mmol/L. She was then managed with daily cinacalcet, and elective surgery took place 2–3 weeks after discharge. A giant parathyroid adenoma weighing 15g was found intra-operatively. Two years later, her serum calcium and PTH levels remain normal. This case contributes to the controversial literature about the relationship between parathyroid adenoma weight and calcium and PTH levels. To our knowledge, this is the highest documented serum corrected calcium and second highest PTH level caused by a giant parathyroid adenoma, excluding atypical and cystic adenomas. We highlight successful pre-operative medical management including cinacalcet, which was not used in similar cases. Furthermore, the appropriate timing of surgery in these cases remains unclear. We describe successful surgical delay for pre-operative medical optimization.

FREDERICK WONG*, RYAN LE, SHOHINEE SARMA, SATYA DASH

UNIVERSITY OF TORONTO

MEGESTROL-INDUCED CENTRAL ADRENAL INSUFFICIENCY

Background: Megestrol is commonly used for improving appetite in cancer patients. Several previous case reports suggest that megestrol can lead to central adrenal insufficiency.

Case: A 56-year-old male inpatient with a past medical history remarkable for acute myeloid leukemia (AML), William's syndrome, pulmonary embolism, hypertension, aortic stenosis and cholecystitis was referred to the inpatient endocrinology team due to adrenal insufficiency with symptoms of mild dizziness and investigations suggestive of central adrenal insufficiency: ACTH $<$ 1.0 pmol/L and AM cortisol of $<$ 28 nmol/L. Ferritin was elevated at 7371 likely secondary to multiple blood transfusions given history of AML. There was no previous history of pituitary surgery and MRI sella was normal with no enlargement or features typical of iron deposition. There was no prolonged history of steroid use. Megestrol was initiated nine months prior due to poor appetite. One week after megestrol was discontinued, morning cortisol was 117 nmol/L. The patient was initiated on hydrocortisone 10mg in the morning and 5 mg in the evening. Bloodwork at 3 months following discontinuation of megestrol revealed an improved but blunted ACTH 250 mcg stimulation test: initial ACTH 5.3 pmol/L, AM cortisol 166 nmol/L, cortisol 401 nmol/L at 30 minutes after ACTH given and cortisol 282 nmol/L at 1 hour.

Discussion: More common causes of central adrenal insufficiency include pituitary tumors, surgery, irradiation, and infiltrative pituitary processes. The rapid but partial recovery of cortisol production after stopping megestrol implicates it as a major contributor to secondary adrenal insufficiency in this patient.

MEAGAN MCLAVISH*, SANDRA KIM

UNIVERSITY OF TORONTO

"STONE BONES": A CASE OF HIGH BONE MASS

We describe a 50-year-old female incidentally found to have diffusely osteosclerotic bones on imaging. Medical history was notable for normocytic anemia and osteoarthritis. There was no history of fracture, hearing loss, dental concerns, renal or liver disease. She was not on prescribed medications and denied excess fluoride ingestion. There was no family history of metabolic bone disease or unusual fractures. Physical exam was notable for short stature (148cm) and hand joint deformities. Radiographs demonstrated diffusely osteosclerotic bones, particularly of the spine and pelvis, associated with diffuse bone marrow signal abnormality on MRI suggestive of an infiltrative disease. DXA showed significantly increased bone density (Z-scores:11.4, 5.0, 6.1, at the lumbar spine, femoral neck, and total hip, respectively). Biochemistry demonstrated mild anemia and ALP elevation. Calcium, phosphate, 25OHD, and PTH were normal. Although an attempted bone marrow biopsy was unsuccessful, primary hematologic disorders were felt to be very unlikely from hematology evaluation. Several genetic causes of high bone mass (HBM) occur from imbalances of bone remodeling, resulting in sclerotic dense bones. In our case of HBM discovered in adulthood, genetic causes include mutations in LRP5 causing increased bone formation but not associated with increased fracture risk (autosomal dominant osteopetrosis type 1). Another possibility is due to mutations in CLCN7 resulting in decreased osteoclastic bone resorption where the benign form (autosomal dominant osteopetrosis type 2) may be asymptomatic or present with fractures, osteoarthritis, compressive neuropathies, or mild anemia. Genetic testing was sent to identify the genetic cause of diffuse HBM for this patient.

OLIVIA COOK*, MEDINA MOHAMED

MCMASTER UNIVERSITY

A CASE OF GESTATIONAL GIGANTOMASTIA

Gestational gigantomastia is a rare, debilitating and potentially lethal complication of pregnancy hypothesized to be secondary to excessive production of estrogen or prolactin, increased hormone receptor sensitivity or an underlying autoimmune disease triggered by pregnancy.[1,2] Our patient is a 30-year-old female who presented at 29 weeks gestational age with rapid breast enlargement and galactorrhea, resulting in skin ulceration with unbearable pain and staphylococcus bacteremia. The differential diagnosis for gestational breast enlargement includes physiologic changes in pregnancy, mastitis, malignancy, fibrocystic or adenomatous changes, and gestational gigantomastia.[2] Gestational gigantomasia effects 1/100,000 pregnancies and is defined as diffuse, extreme, and incapacitating enlargement of one or both breasts.[1] It develops rapidly in the first or second trimester and will recur with subsequent pregnancies. Risk factors include Caucasian background, multiparous and concurrent autoimmune disease.[2] Complications include pain, infection, ulceration, and intercostal nerve damage.[1] Investigations should include prolactin, calcium, ANA, RF, anti-CCP, ESR, CRP, breast ultrasound and breast biopsy to exclude malignancy.[2] Medical management includes bromocriptine to arrest further breast growth and hyperplasia. Ultimately, many patients will require a reduction mammoplasty or total mastectomy.[2] Our patient's investigations showed an elevated prolactin of 1414.6ug/L of which 81.3% was macroprolactin. She was started on bromocriptine, which was up titrated to 2.5mg twice daily. This halted progression of her disease and stopped the galactorrhea. She had an elective cesarian section at 32+5 weeks. Post-partum she had significant reduction in breast size and a normal prolactin level allowing for discontinuation of bromocriptine 1-month post-delivery. She ultimately underwent a bilateral mastectomy.

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A RARE CASE OF AN ADRENOCORTICOTROPIC SECRETING NEUROENDOCRINE CARCINOMA OF THE RECTUM

Background: Ectopic Adrenocorticotropic Hormone (ACTH) secreting neuroendocrine neoplasms are generally bronchial or thymic in origin, with colorectal neoplasms being extremely rare. We describe a case of an ectopic ACTH secreting neuroendocrine carcinoma of the rectum and resulting Cushing's syndrome.

Case: A 66-year-old female presented with a rectal mass which was resected. Pathology confirmed a well-differentiated neuroendocrine carcinoma stage 1 T1 NX M0, Ki-67 about 75%. She had recurrence one year later, presenting with rectal pain, proximal muscle weakness, edema and hirsutism. Imaging showed two new peri-rectal masses and liver lesions, consistent with metastatic disease. Initial workup demonstrated hypokalemia with a potassium of 2.3 mmol/L (normal 3.5–5), hypertension and hyperglycemia. She had an elevated 24-hour urine cortisol of 8266 nmol/d (normal 10–125), and a fasting serum ACTH of 20.0 pmol/L (normal $<$ 10). Magnetic resonance imaging revealed a normal pituitary gland and bloodwork examining the remainder of her pituitary axis was normal. A diagnosis of ectopic ACTH dependent Cushing's syndrome due to her neuroendocrine carcinoma was made. Her neoplasm was treated with Cisplatin/Etoposide, Lanreotide injections and radiotherapy. She was treated with max dose Ketoconazole, along with aggressive management of her hypercortisolism related co-morbidities. Her Cushing's syndrome improved, but her functional status declined, and care was changed to compassionate care.

Discussion: ACTH secreting colorectal neuroendocrine neoplasms have a poor prognosis and Cushing's syndrome is an independent predictor of mortality. It is imperative that management include both appropriate treatment of the neoplasm and of Cushing's syndrome.

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DOES THIS PATIENT HAVE CYCLICAL CUSHING'S DISEASE?

In a 71-year-old male presenting with headaches, MRI showed a 13 × 13 mm pituitary macroadenoma. Evaluation for mild symptoms of Cushing's disease (CD) showed variable a.m. cortisol (14 and 914 nmol/L) and 24-h UFC (3783 and 2219 nmol/d; normal < 786 nmol/d), elevated LNSC, non-suppressed cortisol post 1 mg DST, and elevated ACTH. Desmopressin test, prior to planned pituitary surgery, showed a low cortisol with a modest response to desmopressin stimulation (cortisol 28 to 102 nmol/L; ACTH = 3.7 to 10.3 pmol/L). These unexpected findings without apoplexy signs raised suspicion for nadir phase of cyclic CD. Desmopressin test repeated one week later revealed identical results. Complementary workup showed low LNSC, normal UFC, low LH, and low testosterone values. The patient was admitted, hydrocortisone and testosterone were initiated, and urgent pituitary MRI showed partial pituitary apoplexy. Multidisciplinary evaluation with neurosurgery recommended no pituitary surgery. Upon starting hydrocortisone, the patient presented polyuria and hypernatremia and required oral desmopressin for diabetes insipidus. Low morning cortisol and ACTH responding mildly to desmopressin persisted one and four months later suggesting residual tumor and is predictive of eventual disease recurrence. Repeat pituitary MRI showed stability of the lesion after twelve months. Instructive value: This patient combined an initial presentation evocative of cyclical CD, followed by remission and hypopituitarism secondary to apoplexy. The patient remains at risk of recurrence with a persistent positive response of residual tumor to the desmopressin test. Moreover, diabetes insipidus is a rare complication of apoplexy revealed by hydrocortisone replacement therapy.

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MCMASTER UNIVERSITY

SEVERE PRIMARY HYPERPARATHYROIDISM WITH EXTENSIVE BROWN TUMORS AND MULTIPLE FRACTURES IN PREGNANCY: A CASE REPORT

Background: PHPT in pregnancy is defined as hypercalcemia with high or non-suppressed PTH. During pregnancy, PTH levels may decline due to the physiological rise in PTHrP. Severe maternal hypercalcemia may suppress the development of fetal parathyroid glands and cause hypoparathyroidism in the neonate.

Case: 30y.o female presented at 33weeks' gestation with leg pain and severe PTH-mediated hypercalcemia; serum corrected calcium 4.2mmol/L, PTH 147.9pmol/L. She reported polydipsia and constipation for 2yrs and history of kidney stones in 2019; renal US showed 10–20 non-obstructing renal calculi. Xrays of the femur demonstrated an aggressive bony lesion (Figure1), identified as brown tumor, on histopathology. Additional bone lesions were found on skeletal survey post-partum (R-humerus and L-iliac bone). Multiple Endocrine Neoplasia (MEN) workup was unremarkable. Hypercalcemia was managed with IV fluids, calcitonin and cinacalcet 30mg BID due to the severity of the hypercalcemia. Neck-CT showed a 4cm parathyroid adenoma with no overt malignant features. Subtotal parathyroidectomy (PTX) was performed at 33+2weeks, PTH dropped to 4.7pmol/L postop. Histopathology reported atypical parathyroid adenoma.

Conclusion: This case of severe PHPT with brown tumors is rare in pregnancy. Fortunately, she did not have parathyroid cancer and the femoral lesion was a Brown tumor and not a metastatic lesion from parathyroid cancer. Surgery was well tolerated in the third trimester with excellent maternal outcome. The baby did have hypoparathyroidism requiring therapy.

NISHA GUPTA*, SRINIVASAN KRISHNAMURTHY, DONG BACH NGUYEN, MARK SHERMAN

MCGILL UNIVERSITY

STORM WARNING: MOLAR PREGNANCY INDUCED HYPERTHYROIDISM — THE IMPORTANCE OF EARLY RECOGNITION AND TIMELY PREOPERATIVE MANAGEMENT

Background: Hyperthyroidism due to gestational trophoblastic disease (GTD) is a rare clinical presentation, and thyroid storm happens even less. Early preoperative detection and management through a multidisciplinary approach are paramount as untreated hyperthyroidism can trigger a thyroid storm, a potentially life-threatening complication of GTD. The problem is frequently described, however sparse literature exists regarding the optimal perioperative management.

Case: A 32-year-old woman G1 at 10 weeks gestation was transferred to our institution for a suspected molar pregnancy that was discovered during routine first trimester ultrasound. Further investigations revealed a beta-human chorionic gonadotropin (hCG) of over 420 million IUs/L and a thyroid profile consistent with overt biochemical hyperthyroidism without symptoms and/or signs of hyperthyroidism. A uterine evacuation was promptly organized, at which time the anesthesia providers urgently consulted endocrinology given the concern for impending thyroid storm. The patient was started on intravenous corticosteroids and an antithyroid agent but did not require beta blockade. She underwent an uncomplicated dilation and evacuation. Close thyroid function monitoring during post-molar evacuation follow-up showed subsequent resolution of her biochemical hyperthyroid status that correlated with declining hCG levels within two weeks. The antithyroid drugs were discontinued, and the patient remained asymptomatic during follow-ups.

Discussion: This case highlights the importance of recognising the link between GTD and thyrotoxicosis and initiating appropriate preoperative treatment of hyperthyroidism as soon as possible. Furthermore, our report highlights the significance of a multidisciplinary approach during the perioperative period, as early recognition facilitated timely management in our patient and prevented complications.

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LESSON LEARNED FROM CASE OF RECURRENT POSTPARTUM THYROIDITIS (PPT)

A 38-year-old woman experienced postpartum thyroiditis after each of her four pregnancies around 10 weeks postpartum. She required cardioversion for unstable atrial fibrillation with her first and fourth pregnancies. During her first two pregnancies she received methimazole which was stopped due to hypothyroidism; this did not occur during her last two pregnancies which were treated with beta-blockade only. Duration from onset of hyperthyroidism to euthyroid state varied from 10–18 months. Anti-thyroid peroxidase antibody titres were high while TSH receptor antibodies were negative during all pregnancies The prevalence of postpartum thyroiditis in North America is 2%, with recurrence rates of 70% for women with positive anti-thyroid peroxidase antibodies and history of postpartum thyroiditis(1). Anti-thyroid drugs are rarely required and most cases can be treated with beta-blockade and close monitoring. Treatment of the hypothyroid state may not be necessary unless TSH is >10, symptomatic or trying to conceive Selenium 200 mcg daily given intra- and postpartum has been reported to normalize anti-thyroid peroxidase antibodies titre which could reduce the risk of progression to postpartum thyroiditis.

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WESTERN UNIVERSITY

RENAL HILAR PARAGANGLIOMA IN PREGNANCY: A RARE PRESENTATION DEMONSTRATING THE IMPORTANCE OF INTERDISCIPLINARY AND INDIVIDUALIZED CARE

Background: Pheochromocytoma and paraganglioma (PPGL) during pregnancy is extremely rare, occurring in 0.007% of all pregnancies. Advancements in obstetric, medical and surgical technologies have led to significant improvements in maternal and fetal outcomes.

Case: An otherwise healthy 20-year-old woman presented to clinic at 13 weeks of gestation for assessment of chronic hypertension and a peri-renal lesion. Family history was significant for hypertension and an undiagnosed renal lesion in her mother. Biochemical testing performed at the initial visit revealed plasma norepinephrine 4.2 (0.5 – 3.1) nmol/L and normetanephrine 2.48 (</ 0.89) nmol/L. All other serum testing was within normal limits. MRI neck, chest and pelvis revealed a right retroperitoneal mass measuring 3.0 × 1.0 cm in its maximum dimension and did not identify any metastases. Urgent Urology and Obstetric consultations were obtained to assist with further management. The decision was made to proceed with surgical resection in the second trimester. In the preoperative period she was managed with Doxazosin and Metoprolol and closely followed with weekly clinic visits. She underwent successful robotic assisted resection at 19 weeks of gestation. Pathology confirmed the diagnosis of paraganglioma, and genetic studies identified an SDHB heterozygous mutation. Postoperative investigations revealed biochemical remission. Her pregnancy went to term with no further complications.

Conclusion: This case will explore the unique considerations of care for patients with PPGL in pregnancy and review recent updates in management practices. To our knowledge, this is also the first reported robotic resection of renal hilar paraganglioma in pregnancy.

CHAITANYA GANDHI*, MAHUA GHOSH

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POST COVID-19 ENDOCRINE EMERGENCY: NEW PRESENTATION OF GRAVES' DISEASE WITH THYROTOXIC PERIODIC PARALYSIS

Thyrotoxic periodic paralysis (TPP) represents an uncommon manifestation of Graves' disease, occurring in 0.1–2% of patients. Despite the female predominance in Graves' disease, TPP occurs more commonly in men, leading to a paucity of literature delineating TPP in women. We describe the case of a 34-year-old Asian woman with no known history of Graves' disease who presented with TPP after COVID-19 infection. Our patient presented to the emergency department via EMS with acute lower extremity paralysis. She endorsed a history of tremor, anxiety, and unintentional 30–40 lbs weight loss after COVID-19 infection three months prior. On examination, she had tachycardia (heart rate 130), tremor, thyromegaly, and subtle lid retraction. She had eaten a fast-food meal the night before and was on a 3-day course of prednisone 50mg for environmental allergies. Investigations showed a very low potassium (2.2 mmol/L) and subsequently, TSH $<$ 0.01 mIU/L, free T4 85.6 pmol/L, free T3 31.9 pmol/L, and a positive TSH-receptor antibody (7.33 IU/L). Her weakness improved with intravenous potassium replacement. She was discharged home on metoprolol and methimazole. She also needed potassium replacement for two weeks. In follow-up clinic, she had improved symptoms and biochemistry. While COVID-19 commonly causes subacute thyroiditis, it can trigger Graves' disease, possibly by altering autoimmunity in susceptible individuals. Although not a classic precipitant, glucocorticoids have been identified to cause TPP, perhaps through hyperinsulinemia. Physicians should be aware that COVID-19 infection may trigger Graves' disease and TPP in female patients, particularly after glucocorticoid use.

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PAXLOVID AND FLUTICASONE: AN UNDERAPPRECIATED INTERACTION INFLUENCING THE ACTH STIMULATION TEST

We describe the case of an unvaccinated 70-year-old woman with a history of asthma who presented to hospital with nausea, emesis, and diarrhea three days after starting nirmatrelvir 300mg with ritonavir 100mg (Paxlovid) for COVID-19 infection. Initial investigations showed a sodium of 116mmol/L (reference range: 135–145mmol/L), which initially improved to 125mmol/L with IV fluid rehydration. A morning cortisol level obtained for workup of hyponatremia was undetectable at < 28nmol/L (reference range: 101–536nmol/L). An ACTH stimulation test was performed, which yielded cortisol undetectable at < 28nmol/L with ACTH < 1.0pmol/L (reference range: less than 10.2pmol/L) at baseline, followed by cortisol levels of 217nmol/L at 30 mins and 256nmol/L at 60 mins, respectively. Medication history revealed fluticasone propionate 250mcg / salmeterol 50mcg (Advair Diskus 250) inhaler used twice daily. Paxlovid was discontinued and the ACTH stimulation test was repeated 2 days later, at which point the baseline cortisol level made adrenal insufficiency unlikely at 600nmol/L with ACTH 3.5pmol/L and cortisol levels of 329nmol/L and 586nmol/L at 30 mins and 60 mins, respectively. Bioavailability of fluticasone propionate delivered by Advair Diskus is 5.5%. Fluticasone propionate is extensively metabolized by CYP3A4 with a reduction of peak plasma concentrations by 98% within 3–4 hours. Ritonavir, the protease inhibitor component of Paxlovid, inhibits CYP3A4 metabolism and thereby may have precipitated an exogenous Cushing syndrome physiology with suppression of endogenous cortisol production and ACTH secretion. This case highlights an underappreciated pharmacokinetic interaction that can affect the interpretation of ACTH stimulation tests in patients treated for COVID-19 infection.

RIDHA ALI*, HEATHER A. LOCHNAN

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MYSTERY METASTASES: A CURIOUS CASE OF PAPILLARY THYROID CANCER WITH UNKNOWN LUNG NODULES

A 66-year-old male was seen by ENT for a large solitary neck mass determined to be a thyroid mass on CT Neck. CT Neck also revealed multiple small nodules in the upper lung lobes. He underwent total thyroidectomy for compressive multinodular goiter. Pathology revealed papillary carcinoma (2.0cm) involving the left lobe. A post-operative CT Thorax confirmed previously seen multiple sub-centimeter pulmonary nodules and revealed a few enlarged mediastinal lymph nodes suggestive of a metastatic process. The lesions were deemed too small for percutaneous CT-guided biopsy. He was referred for consideration of radioactive iodine in the context of likely metastatic disease. FDG PET scanning indicated numerous indeterminate hypermetabolic lesions in the bilateral lung nodules, bone and spleen along with mediastinal/hilar lymphadenopathy consistent with lymphoproliferative disease or metastatic disease. In absence of a biopsy and noting his thyroglobulin was consistently undetectable on suppressive doses of levothyroxine, an iodine-123 whole body scan was done with Thyrogen pretreatment to determine if the lung nodules were iodine avid and they were not. Imaging revealed uptake only in the remnant and stimulated thyroglobulin remained low (0.5 ug/L). Likelihood of metastatic thyroid cancer was low given negative iodine-123 scan and low-undetectable thyroglobulin levels. He was referred for bronchoscopy guided biopsy which demonstrated sarcoidosis. This case highlights the importance of maintaining a broad differential diagnosis before pursuing treatment of presumed metastatic thyroid disease with radioactive iodine. Low thyroglobulin led to concern there was a second process ongoing. The patient did not proceed to radioactive iodine therapy.

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ROLE OF CHOLESTYRAMINE IN REFRACTORY AMIODARONE-INDUCED THYROTOXICOSIS

Background: Amiodarone-induced thyrotoxicosis (AIT) is divided into type 1 (AIT1; treated with thioamides) and type 2 (AIT2; treated with glucocorticoids). Combined therapy is utilized in mixed or indefinite forms. When medical treatment is unsuccessful, radioiodine ablation or thyroidectomy are considered.

Case: A 76-year-old gentleman, with a history of atrial fibrillation treated with amiodarone, presented with recurrent atrial fibrillation refractory to cardioversion. Investigations revealed TSH $<$ 0.01, FT4 58.1 (ref 10.0–20.0 pmol/L), FT3 16.0 (ref 3.5–6.5 pmol/L), TPO negative and TRAB negative. As thyroid ultrasound revealed absence of focal nodules or hypervascularity and technetium pertechnetate scan demonstrated no thyroid activity, AIT2 was suspected. Prednisone was initiated and amiodarone discontinued. Due to minimal response after a month, a mixed type was suggested and methimazole added. Despite intensification of the antithyroid regimen, FT4 increased to 59.5. Methimazole was discontinued for radioiodine ablation assessment. Given low thyroid uptake ($<$ 3%), ablation was deemed unlikely beneficial. After patient refused thyroidectomy, cholestyramine was initiated, resulting in significant improvement, with FT4 declining from 46.0 to 29.0 in 2 weeks. Euthyroidism was achieved after 2 months of cholestyramine treatment and medications were stopped. At 6 months post presentation, he developed amiodarone-related hypothyroidism and began levothyroxine.

Discussion: Previous reports propose that cholestyramine, an ion exchange resin, interrupts enterohepatic circulation of thyroid hormone. Given amiodarone primarily undergoes hepatic metabolism, cholestyramine may also enhance amiodarone elimination, which is particularly important due to its lengthy half-life. Thus, we suggest consideration of cholestyramine as a treatment option in refractory AIT.

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AN ATYPICAL PRESENTATION OF A CORTICOTROPH MACROADENOMA

Background: Corticotroph adenomas (CA) are pituitary tumours that express ACTH. The majority of CAs are microadenomas (< 10mm in size), while only 4–20% of cases are macroadenomas. Corticotroph macroadenomas tend to be less responsive to therapy and require multiple treatment modalities to achieve remission.

Case Presentation: A 42-year-old woman presented with several weeks of vision blurring. She had no prior medical issues and pituitary review of systems was unremarkable. Physical examination revealed bitemporal hemianopsia and no Cushingnoid features. MRI demonstrated a 1.9×2.0×2.8cm adenoma displacing the optic chiasm and invading the right cavernous sinus (Knosp grade 4). Preoperative endocrine assessment showed elevated 24hr UFC 1562 nmol/d (ref < 275), non-suppressed morning cortisol 609 nmol/L following 1mg DST (ref < 50), and baseline ACTH 49.3 pmol/L. Remainder of pituitary hormones were normal.

Preoperative 8mg DST was unable to suppress cortisol, raising concern for ectopic ACTH secretion (EAS). Pan-body CT showed no evidence of malignancy. She underwent transsphenoidal surgery and incomplete resection due to anatomy. Postoperatively, she did not have cortisol excess or deficiency. Surgical pathology confirmed a sparsely granulated corticotroph adenoma.

Discussion: This case illustrates the importance of completing biochemical screening for hypersecretion syndromes such as hypercortisolism in all patients with pituitary adenoma prior to surgical management regardless of clinical suspicion. Our patient had Cushing disease (CD) based on biochemical parameters but was clinically asymptomatic. Furthermore, corticotroph macroadenomas compared to microadenomas are less likely to suppress post-8mg DST. Biochemical tests attempting to differentiate CD from EAS must be interpreted with caution.

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NOVEL ANGPTL3 INHIBITOR, EVINACUMAB, FOR THE TREATMENT OF HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA: A CASE REPORT

Introduction: Homozygous familial hypercholesterolemia (HoFH) is an ultra-rare, life-threatening condition characterized by extremely elevated levels of low-density lipoprotein cholesterol (LDL-C) usually due to loss-of-function variants in the LDLR gene. Standard lipid-lowering therapies only modestly reduce LDL-C in these patients, and serial apheresis is the mainstay of treatment. Evinacumab is a monoclonal antibody against angiopoietin-like protein 3 that lowers LDL-C levels via a novel receptor-independent mechanism. We present here the second patient with HoFH in Canada to be treated with evinacumab.

Case presentation: A 17-year-old male in [province] was diagnosed with severe HoFH in infancy due to compound heterozygous LDLR variants. Treatment has included statin, ezetimibe, and apheresis (initially plasmapheresis then LDL-apheresis) every 2 weeks, with minimal effect on LDL-C levels, although he remains asymptomatic. At age 17 years, he started evinacumab 15 mg/kg administered intravenously every 4 weeks. After 11 months of treatment, his mean pre-apheresis LDL-C was reduced from 9.81 to 5.90 mmol/L, and time averaged LDL-C level has decreased by 40.7% from 8.75 to 5.19 mmol/L, despite a reduction in frequency of LDL-apheresis from biweekly to every 4 weeks.

Conclusions: This patient has been on evinacumab for 11 months with significant improvement in his LDL-C, reduction in apheresis frequency, and no adverse events. The FDA has approved the use of evinacumab for HoFH, but it is only available in Canada via clinical trials or compassionate use. Evinacumab shows great promise as an effective treatment option for patients with HoFH, a difficult-to-treat and potentially life-threatening condition.

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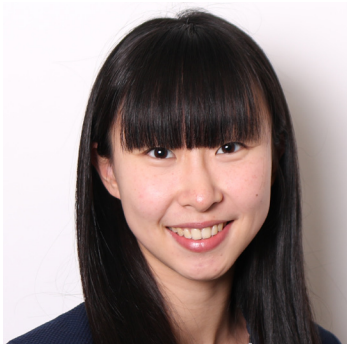

AN UNUSUAL CASE OF GLUCOCORTICOID RESISTANCE SYNDROME

Glucocorticoid resistance syndrome (GRS) results mostly from mutations in the NR3C1 gene, encoding the glucocorticoid receptor (GR). Affected patients are devoid of Cushing's syndrome (CS) features despite high cortisol levels and may present adrenal hyperplasia, hypertension, hirsutism, and hypokalemia. A 60-year-old man was referred for bilateral adrenal incidentalomas. Blood pressure was normal without diabetes, signs of CS or pheochromocytoma. Repeated 1 mg dexamethasone tests (DST) showed morning cortisol of 52 to 74 nmol/L. Urinary free cortisol (UFC) was constantly 3–4 fold >ULN. An ACTH test (250 mcg) showed normal cortisol and 17 OHP responses. Plasma ACTH was inappropriately normal despite impaired DST and elevated UFC. Salivary cortisol, DHEAS, aldosterone-to-renin ratio, potassium and 24-hr urine metanephrines were normal. There was no ACTH/cortisol response to 10 mcg desmopressin i.v. and a normal response to CRH test. A 4 mg IV DST combined with vasopressin 10 IU IM at 14h demonstrated an incomplete suppression of cortisol post-DST and an absence of elevation of cortisol post-vasopressin. The targeted sequencing of the NR3C1 gene found no pathogenic mutation of the GR. A whole exome sequencing may help elucidate the mechanism by which this patient with normal NR3C1 gene has a GRS phenotype. A mutation of another gene involved in the complex GR signaling pathway may impair his glucocorticoid sensitivity. Another hypothesis would be a mutation in NR3C1 promoter resulting in reduced GR expression. This patient illustrates that some patients may present a milder phenotype of GRS without any mutation of the NRC31 gene.

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A CASE OF PERMANENT NEONATAL DIABETES MELLITUS DUE TO INS GENE MUTATION

Introduction: Neonatal diabetes mellitus (NDM) is a monogenic disease that results in diabetes mellitus in the first 6 months of life. NDM can be transient or permanent, depending on the specific gene that is implicated. We present the case of an infant who presented with hyperglycemia and was subsequently diagnosed with permanent NDM.

Case Presentation: A 9-week-old male infant presented to acute care with a viral gastrointestinal illness and was incidentally found to have hyperglycemia (blood glucose in the range of 8–12 mmol/L). There was no evidence of ketoacidosis at that time. Family history was significant for his father having been diagnosed with diabetes mellitus (presumed type 1) at 9 months of age. The patient had persistent hyperglycemia following resolution of his acute illness. He was started on insulin therapy injections at the time of the first assessment and then transitioned to an insulin pump and CGMS, with improvement of his blood glucose into normal range. Given the early age of presentation and family history, genetic testing was completed, and he was confirmed to have monogenic diabetes due to a heterozygous known pathogenic mutation (Gly32Ser) in the INS (insulin) gene.

Conclusion: Our patient was found to NDM on the basis of a missense variant in INS. While the outcome of the genetic testing did not change management in our case, it does provide the diagnosis of a permanent form of NDM. It also has implications for screening of other family members and genetic counselling. Paternal testing is now underway.

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A CURIOUS CASE OF SEVERE PTH-MEDIATED HYPERCALCEMIA OF PREGNANCY

Background: Primary hyperparathyroidism is rarely diagnosed in pregnancy as symptoms may overlap with those of pregnancy and biochemical diagnosis may be masked by physiologic changes in calcium homeostasis. Hyperparathyroidism in pregnancy is associated with increased maternal and fetal complications. While mild disease is treated conservatively, moderate to severe disease is generally treated surgically in the second trimester. Safe pharmacotherapy options are limited in pregnancy.

Case: A 35-year-old woman G3P1 at 10 weeks presented to our institution with polyuria, bone pain and weakness with labs demonstrating severe hypercalcemia (Calcium total: 3.82mmol/L (normal: 2.12–2.62); PTHi: 12pmol/L (normal: 1.5–9.3)). PTHrP was suppressed. She had a prior history of PTH-mediated hypercalcemia in her first pregnancy. She previously underwent three exploratory surgeries in which only three parathyroid glands were found and removed. She also required intravenous fluids, calcitonin and cinacalcet. There were no complications. Between pregnancies, she developed hypoparathyroidism and hypocalcemia. Throughout the current pregnancy, despite aggressive hydration, calcitonin and cinacalcet, total calcium and PTH levels consistently rose reaching peaks of 4.06mmol/L and 45.4pmol/L, respectively. Parathyroid sestamibi scan and genetic testing were negative. Given hypercalcemia severity and associated neurological symptoms, she was also given bisphosphonates (pamidronate 60mg and zolendronate 4mg). She underwent C-section at 25+3 weeks due to fetal decelerations and placental insufficiency. She again developed hypoparathyroidism and hypocalcemia 1-week post-partum.

Discussion: This is a unique case of severe PTH-mediated hypercalcemia in that the exact mechanism is unknown but appears pregnancy-mediated and reversible. Investigations (including placental pathology) to better elucidate this mechanism are ongoing.

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DOEGE-POTTER SYNDROME: IGF-2 MEDIATED HYPOGLYCEMIA THAT MIMICS SURREPTITIOUS INSULIN USE

Background: Doege-Potter syndrome (DPS) is a rare form of non-islet cell tumour hypoglycemia seen in fewer than 5% of patients with mesenchymal tumours. Patients with DPS have tumours that produce excess IGF-2, which suppresses endogenous insulin and binds to IGF-1 receptors to promote hypoglycemia. Definitive management involves resection of the underlying malignancy.

Case: A 28-year-old woman with depression presented to an emergency department after being found unresponsive with a glucose of 1.2 mmol/L. She responded promptly to administration of intravenous dextrose, but continued to have unexplained fasting hypoglycemia for days, necessitating a continuous dextrose infusion. A three-hour fast revealed an undetectable C-peptide, undetectable insulin, low beta-hydroxybutyrate, and negative sulfonylurea screen with a serum glucose of 2.1 mmol/L. Administration of glucagon increased the glucose to 4.3 mmol/L. Given this pattern of glucagon-responsive hypoglycemia with low ketones and C-peptide, exogenous insulin use was the presumptive diagnosis. However, psychiatry found the patient to be euthymic with no reason to suspect surreptitious insulin use, while biochemistry found no detectable insulin analogues. An abdominal CT then identified a 16 cm retroperitoneal mass. Further investigation revealed an elevated IGF-2/IGF-1 ratio of 14.6 (normal < 10) during a hypoglycemic episode, confirming the diagnosis of DPS. The patient underwent successful tumour resection, resulting in normalization of IGF-2 and cessation of hypoglycemia.

Discussion: IGF-2 mediated hypoglycemia is a rare neoplastic syndrome that is nearly indistinguishable from exogenous insulin-mediated hypoglycemia. Early recognition of this entity allows for timely surgery, drastically improving clinical outcomes.

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ECTOPIC PITUITARY ADENOMA OF THE SPHENOID SINUS — TSHoma OR PITUITARY HYPERPLASIA?

Background: Ectopic TSH secreting adenomas (TSHomas) are rare with about 12 reported cases.

Objectives: We describe a case of ectopic TSH-secreting pituitary macroadenoma of the sphenoid sinus in a 73-year-old man whose thyroid function tests were interestingly consistent with primary hypothyroidism. Methods: An aggressive appearing mass in the sphenoid sinus was incidentally discovered on imaging after the patient presented with loss of consciousness. At the time, his TSH was elevated at 167 mIU/mL, with no free hormone levels available. He had no symptoms of hyperthyroidism. After debulking and biopsy, the pathology was positive for Pit-1 and TSH suggestive of a TSHoma. MRI of the sella revealed a normal appearing pituitary gland.

Results: Post-op pituitary function showed ongoing elevation in TSH at 187 mIU/mL, suppressed free T4 and free T3, and positive anti-TPO antibodies. Upon questioning, he had mild symptoms of hypothyroidism, including cold intolerance and fatigue. Pathology was reevaluated for ectopic pituitary hyperplasia due to chronic hypothyroidism. However, reticulin staining was consistent with an adenoma. Three months after initiation of levothyroxine 100 mcg daily, his TSH, fT4 and fT3 normalized.

Conclusion: Currently, the primary process driving patient's presentation is unclear. His TSH levels increased post-op making primary functioning TSHoma less likely. Pathology makes hyperplasia less likely. We suggest that his presentation may best fit with an ectopic silent TSHoma with concurrent primary hypothyroidism responding to levothyroxine treatment.

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AN 'UNFAMILIAR' CASE OF 'FAMILIAL' PRIMARY HYPERPARATHYROIDISM: EXPLORING PARATHYROID TUMOUR RISK IN BIRT-HOGG-DUBÉ SYNDROME

Background: Birt-Hogg Dubé (BHD) syndrome is an autosomal dominant condition characterized by benign cutaneous lesions, pulmonary cysts with spontaneous pneumothoraces, and renal neoplasms. There have been case reports of other associations with BHD syndrome including parotid, thyroid, and parathyroid tumours . Here, we discuss a patient with known BHD syndrome presenting with primary hyperparathyroidism.

Case: A 49-year-old gentleman with BHD syndrome presented with incidental parathyroid nodules on CT chest screening for pulmonary cysts. His calcium (3.07 mmol/L) and PTH (36.5 pmol/L) were elevated with low phosphate (0.42 mmol/L), consistent with primary hyperparathyroidism. Nuclear scan confirmed a hyperfunctioning right superior parathyroid adenoma measuring 2.7×1.7 cm along with a left soft tissue nodule measuring 4.1×2.3 cm. He underwent surgical resection of his left and right superior parathyroid glands with postoperative normalization of his calcium and PTH levels. Pathology revealed enlarged and hypercellular tissue in both glands.

Discussion: Primary hyperparathyroidism has been linked to numerous familial syndromes including multiple endocrine neoplasia types 1 and 2A. The genetic variant often predicts the phenotype, such as four gland hyperplasia in multiple endocrine neoplasia type 1 which necessitates more extensive surgical resection. There is limited literature surrounding BHD syndrome and the phenotype of parathyroid disease. This is the first reported case of hyperparathyroidism in BHD syndrome presenting as a double adenoma and the subsequent hyperplasia evident on pathology suggests an increased risk of future recurrence. Further understanding of parathyroid tumour pathogenesis in BHD syndrome will help guide appropriate parathyroid disease monitoring for patients with this condition.

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DALHOUSIE UNIVERSITY

ATYPICAL PRESENTATION OF CUSHING'S DISEASE WITH WEIGHT LOSS AND HYPOKALEMIA — A CASE REPORT

Background: ACTH secreting pituitary adenoma causing Cushing's disease (CD) classically present with weight gain, whereas weight loss and hypokalemia in Cushing's patients are suggestive of ectopic ACTH production. We report a case of CD presenting with atypical features of weight loss and hypokalemia.

Methods: Patient's hospital records were reviewed.

Results: A 75-year-old female presented with serum potassium of 2.4 mmol/L, a weight loss of 90 lbs over 2 years, uncontrolled hypertension and hyperglycemia, as well as, profound proximal muscle weakness. Initial inpatient workup showed an elevated 24-hour urinary free cortisol (UFC) level of 1908 ug/L (ULN = 486 ug/L) prompting referral to Endocrinology. Repeat outpatient 24h UFC was 1750 ug/L, serum ACTH level was 37.5 pmol/L (ULN = 10.1 pmol/L) and post-48h low dose dexamethasone suppression serum cortisol was 1238 nmol/L. Localizing studies showed no lesion on chest CT, Ga68 Dotatate PET/CT and Sella MRI. Bilateral inferior petrosal sinus sampling showed a post-CRH central to peripheral ACTH ratio of 3. A clinical diagnosis of CD was made and due to the lack of clear surgical target, patient was given a combination of ketoconazole and cabergoline. Her 24h UFC, serum potassium and blood pressure normalized and the most recent 24hr UFC was 67 ug/L. She has regained 60 lbs and is able to mobilize without assistance. Her blood pressure and hyperglycemia medications have been reduced.

Conclusion: This case illustrates that CD can present with symptoms and biochemical findings that would otherwise suggest ectopic ACTH production.

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WESTERN UNIVERSITY

CLOMIPHENE-ASSOCIATED HYPERTRIGLYCERIDEMIA IN A MALE PATIENT

Background: Clomiphene is a selective estrogen receptor modulator used off-label in men with low sperm count and normal to mildly low serum testosterone to stimulate gonadotropin secretion. There are several case reports of clomiphene exacerbating existing hypertriglyceridemia in women, but none in men.

Case: A 37-year-old man with infertility was referred for hypertriglyceridemia. His initial triglyceride level was 7.2 (reference < 1.7) mmol/L, which decreased to 2.58 mmol/L with lifestyle changes. However, his triglycerides subsequently rose to 17.92 mmol/L within months of starting clomiphene for fertility treatment. Lipid profile included an HDL-C of 0.51 (reference >1) mmol/L and non-HDL cholesterol 7.31 (reference < 4.29) mmol/L. Baseline total testosterone level was 10 (7.6–31.4) nmol/L. Baseline estradiol level was unavailable. His body mass index was 30 kg/m^2. We ruled out other secondary causes of hypertriglyceridemia including diabetes, hypothyroidism, and nephrotic syndrome. Since he wished to continue taking clomiphene, we started fibrate therapy and await repeat triglyceride levels.

Discussion: Although obesity contributed to this man's hypertriglyceridemia, the sharp rise in triglyceride levels may also be explained by clomiphene. Studies on the use of clomiphene in men did not find differences in post-treatment triglycerides, however patients with baseline hypertriglyceridemia were not included. Clomiphene significantly increases estradiol levels in men and is also structurally similar to tamoxifen, which has been shown to increase triglyceride levels by impairing catabolism of triglyceride-rich lipoproteins. Therefore, our report highlights a potential adverse effect of clomiphene on men with pre-existing hypertriglyceridemia. We suggest checking a lipid profile before and during treatment.

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NOVEL HETEROZYGOUS MISSENSE MUTATION IN LRP5 GENE ASSOCIATED WITH VERY-HIGH RISK EARLY-ONSET OSTEOPOROSIS

Background: Wnt/β-catenin signaling is an essential pathway in regulating bone homeostasis. Crucial to this pathway is low-density lipoprotein receptor related-protein 5 (LRP5), a co-receptor that binds Wnt ligand, thereby preventing β-catenin degradation and signalling for osteoprotegerin transcription.

Case: We evaluated a previously healthy 45-year-old man in clinic for recurrent low-energy fractures. Bone mineral density (BMD) testing at age 33 found T-scores of −3.5 at the lumbar spine, −2.5 at the left femoral neck, and −3.7 at the left total hip. He took alendronate briefly but was switched to denosumab for over 10 years. Supplements include vitamin D 2000 IU daily and calcium citrate 300mg TID. Conventional workup for secondary causes of osteoporosis was negative. Family history was negative for osteoporosis except in his maternal grandmother.

Outcome: Genetic testing identified a novel variant of uncertain significance in the LRP5 gene: a heterozygous missense mutation at c.1090G>A resulting in protein defect p.Asp364Asn. Since diagnosis, T-scores have risen to −1.8 at the lumbar spine, −2.1 at the left femoral neck, and −2.4 at the left total hip.

Discussion: Genetic causes of low bone density should be suspected in young patients with multiple fragility fractures. Our case represents a novel missense mutation in the LRP5 gene leading to early-onset osteoporosis that responded well to anti-resorptive therapy. Despite Wnt-β-catenin signaling disruption in these patients, favourable responses to anti-sclerostin antibody treatment have been reported in animal models, likely through maintained LRP6 function.

BONNIE CHEUNG*, ILANA HALPERIN

UNIVERSITY OF TORONTO

LYMPHOCYTIC HYPOPHYSITIS IN PREGNANCY: A CASE REPORT

Background: Lymphocytic hypophysitis (LYH) is a rare immune-mediated disorder causing pituitary gland inflammation via lymphocytic infiltration, with an annual incidence of 0.1 cases per million. 78% of patients with LYH are women, of which 15% involve the peripartum period.

Case Presentation: A 37-year-old pregnant female at 27 weeks' gestation presented to hospital with headaches, dense hemianopsia, and hypotension. Bloodwork showed TSH 0.19, free T4 6, random cortisol 26, Na 138, with normal IGF-1 and prolactin. MRI sella without gadolinium showed a 13×23×20 mm sellar/suprasellar mass with optic chiasm compression felt to be in keeping with pituitary macroadenoma. She underwent transsphenoidal resection with pathology showing LYH. Post-operatively, she developed diabetes insipidus with Na 156 and low-normal serum osmolality 270–280s despite significant polyuria of greater than 6 litres/day. She was discharged on desmopressin, hydrocortisone, and levothyroxine. At one-month post-resection, her vision had improved significantly but she was still experiencing headaches and extreme fatigue. Repeat MRI showed prominent residual pituitary tissue suggesting residual LYH versus physiologic from pregnancy. Prednisone 40 mg daily was recommended at tumour boards but the patient opted not to start this. Ultimately, she had an uncomplicated delivery at 38 weeks' gestation induced with oxytocin. She remained on replacement for panhypopituitarism with improvement in symptoms.

Discussion: This case illustrates an approach to managing LYH in pregnancy with surgical resection due to mass effect and highlights an indication for steroids post-operatively. There is currently no unified treatment guideline for LYH. Additional research is needed to determine the most effective treatment modalities.

MEGGIE STAINFORTH-DUBOIS*

UNIVERSITÉ LAVAL

AGGRESSIVE CUSHING'S DISEASE PRESENTING AS ATYPICAL THIRD CRANIAL NERVE PALSY

Cushing's disease typically presents with symptoms of hypercortisolism due to a microadenoma. The purpose of this clinical vignette is to highlight an unusual presentation of Cushing's disease to facilitate diagnosis of similar cases. A 35-year-old male presented with a brief, self-limiting episode of diplopia. Head CT was non-contributory. Five years later, symptoms recurred. Ophthalmologic assessment demonstrated complex strabismus of unclear etiology. Cerebral MRI was unremarkable. One year later, the patient was referred to a specialized ophthalmologist who remarked that the strabismus mimicked a left third cranial nerve palsy with absence of ptosis and pupillary involvement. Repeat cerebral MRI revealed a 40 by 40 by 35mm sellar mass involving the sphenoid and cavernous sinuses with optic nerve and mild optic chiasm compression. The patient had no remarkable stigmata of Cushing's disease, but early morning cortisol and ACTH were elevated (819 nmol/L and 48pmol/L respectively). Central hypothyroidism and hypogonadism were noted, and levothyroxine was initiated. 1mg dexamethasone suppression test was abnormal (cortisol 821 nmol/L). Salivary cortisol and 24h urinary cortisol were elevated (62 nmol/L and 8,463 nmol/d respectively). There was no response to desmopressin stimulation. Shortly afterwards, the patient underwent complete transsphenoidal resection. Post-operative cortisol levels declined (68 nmol/L) and hydrocortisone was prescribed. Pathology reported a sparsely granulated corticotroph tumor with high Ki-67 (13%) and 20% of cells were positive for p53. The case awaits discussion in tumor board. This vignette describes a case of aggressive Cushing's disease with atypical features and illustrates the importance of repeat cerebral imaging.

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SEVERE VITAMIN D TOXICITY DUE TO ADMINISTRATION ERROR IN AN ELDERLY PATIENT

Introduction: Vitamin D toxicity is a rare cause of hypercalcemia. However, incidence has risen in recent years due to recommendation for routine supplementation and avoidance of monitoring levels. Administration errors (especially with liquid formulations) are most commonly implicated.

Case Description: A previously healthy 76-year-old gentleman presented with a few weeks' history of functional decline, memory deficits, abdominal discomfort, and 60 lb weight loss. His home medications included Vitamin D 1000 units and Vitamin B12 1000 units daily. Initial investigations revelated AKI (Creatinine 315umol/L), hypercalcemia (Calcium 3.4mmol/L, ionized 1.74mmol/L), low PTH (1.2pmol/L), high 25-hydroxyvitamin D level >500 nmol/L (later confirmed to be 685 nmol/L), and high 1,25 dihydroxy vitamin D level (367pmol/L). A malignancy work up was completed which was unremarkable (including normal PTHrP). Further review of medications with family revealed he was taking 1 teaspoon of liquid vitamin D daily (equivalent to over 100,000 IU) for over a year due to misunderstanding. His hypercalcemia was managed with fluids, calcitonin and pamidronate. His calcium and Vitamin D levels slowly improved but continue to be elevated to date (2 months post discharge).

Discussion: Administration errors are among the leading causes of Vitamin D toxicity, especially in vulnerable pediatric and elderly populations. Liquid formulations present an increased risk for toxicity due to lack of familiarity with dosing and gaps in communication. It is essential for physicians and care providers to closely review method of administration to avoid toxicity and related morbidity.

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UNIVERSITY OF CALGARY

THE DIAGNOSTIC DILEMMA OF POSTMENOPAUSAL HYPERANDROGENISM: A CASE REPORT

Introduction: Hyperandrogenism in postmenopausal patients is a diagnostic challenge because differentiating between adrenal or ovarian sources based on hormone levels and imaging is often not possible, and malignancy is an important differential diagnosis.

Case: A 51-year-old postmenopausal woman presented with 9-months of hirsutism and no other virilization. Testosterone was elevated at 6 nmol/L (reference range ≤1.9 nmol/L), while her luteinizing hormone (40.0 IU/L), follicle-stimulating hormone (63.2 IU/L), and estradiol (82.0 pmol/L) were consistent with post-menopause. Her dehydroepiandrosterone sulfate was 3.1 umol/L. At the time of these tests, she was exposed to exogenous testosterone through her partner. However, after 4-weeks of eliminating exposure, symptoms persisted and her testosterone remained elevated. Pelvic ultrasound and CT scan were unremarkable for ovarian or adrenal abnormalities. A gonadotropin-releasing hormone (GnRH) suppression test was subsequently pursued. Androgen levels were measured prior to injecting 3.75mg of intramuscular leuprolide, and again 4 weeks after the GnRH agonist dose. With this test, the patient's testosterone level decreased by >50% from 6.4 nmol/L to 2.3 nmol/L, consistent with an ovarian source of androgen excess, such as ovarian hyperthecosis or a small virilizing ovarian tumor.

Conclusion: Imaging is often insufficient when investigating hyperandrogenism in postmenopausal women given the possibility of finding an adrenal incidentaloma or missing a small ovarian tumor. There is also no hormone pattern that reliably differentiates adrenal versus ovarian causes. The GnRH suppression test is a less invasive method for determining the source of hyperandrogenism in these patients compared to venous sampling or surgery for histopathological examination.

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HCG-MEDIATED THYROTOXICOSIS SECONDARY TO METASTATIC, GERM-CELL TUMOR OF THE TESTES

Background: We present a case of HCG-mediated hyperthyroidism secondary to a metastatic, non-seminomatous germ-cell tumor. We highlight the challenges of diagnosis and typical management approach.

Case: A 34-year-old male presented with progressive testicular pain, intermittent chills, nausea/vomiting, and 15 pounds of weight loss. Investigations showed a testicular mass suspicious for malignancy, as well as probable metastatic disease to the lung, liver, brain, and an abdominal mass extending from the region of the right adrenal gland to the inferior vena cava. A CT guided biopsy of the abdominal mass was completed which confirmed the diagnosis of metastatic choriocarcinoma and did not identify any other germ cell component. Initial HCG was extremely elevated at 763,269 IU/L and climbed to 1,073,000 IU/L just prior to treatment. His TSH was < 0.01, FT4 33.4 (10.0–25.0 (pmol/L)), and TSH receptor antibody titre was negative. Management of the hyperthyroidism consisted of propranolol 20 mg TID and methimazole 7.5 mg daily, which was later increased to 15 mg due to worsening symptoms corresponding with a surge in HCG with the start of chemotherapy (HCG level = 1,454,500 IU/L). Following two rounds of cisplatin and etoposide, his HCG level fell to 704 IU/L, and methimazole was tapered off due to the resolution of hyperthyroidism.

Discussion: HCG-mediated hyperthyroidism can arise in conditions with HCG levels $> 50{,}000$ such as hyperemesis gravidarum, hydatidiform moles, and germ cell tumors. Temporizing treatment of the hyperthyroidism includes thioamides and beta-blockers, however, definitive management requires treating the underlying condition, thus resolving the HCG-mediated hyperthyroidism.

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QUEEN'S UNIVERSITY

ALEMTUZUMAB-INDUCED GRAVE'S DISEASE IN MULTIPLE SCLEROSIS

Background: Alemtuzumab (ALZ)-induced thyroid disease in patients with multiple sclerosis (MS) occurs with a prevalence of 34 to 41%, with Grave's Disease (GD) being the most common etiology. We discuss a case of ALZ-induced GD with complex features.

Case presentation: A 46-year-old male with known relapsing-remitting MS and known seizure disorder was admitted with status epilepticus and signs of thyrotoxicosis. His labs revealed low TSH < 0.01, with elevated fT4 34pmol/L, and fT3 13pmol/L. His last cycle of alemtuzumab was in January 2019 with good response. Prior to hospitalization, he had no signs of hyperthyroidism. He was initially started on methimazole and cholestyramine while awaiting results of further thyroid testing. Subsequently, he developed atrial fibrillation requiring amiodarone for rhythm control. After 3 days he developed a diffuse purpuric rash, and methimazole was stopped. Thyroid ultrasound showed no focal nodules, and TRAb was positive at 4.1 IU/L, in keeping with a diagnosis of GD. Although fT4 steadily decreased on cholestyramine alone, 5 months later the fT4 peaked again at 41 pmol/L. He was started on propylthiouracil 50 mg daily and was monitored for adverse effects.

Discsussion: ALZ-induced GD is commonly reported, but these cases are often complex. Though ALZ efficacy is known to be associated with secondary autoimmunity, the pathophysiology remains unclear.

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UNIVERSITÉ DE MONTRÉAL

A RARE CASE OF MEN-1 WITH ACTH-SECRETING ADENOMA AND GLUCAGONOMA

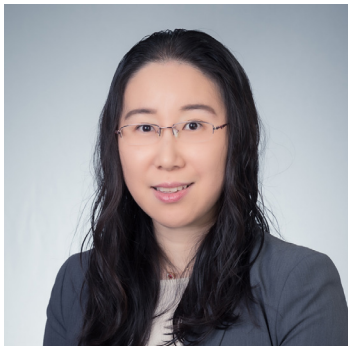
Context: Multiple endocrine neoplasia type 1 (MEN1) is characterized by the presence of two or more endocrine and non-endocrine tumors. ACTH-secreting anterior pituitary adenomas and glucagon-secreting pancreatic tumors are both rare presentations of MEN-1. To our knowledge, there has been no reported cases of the association of these two conditions.

Case: We evaluated a 26-year-old female with a family history of MEN-1 and genetic testing positive for a mutation in the menin gene. She presented with slightly elevated parathyroid hormone (PTH), but her calcium levels were normal. Her imaging studies showed two microadenoma in the anterior pituitary and a 2 cm pancreatic mass. Her glucagon levels were slightly elevated, but she didn't show any symptoms of glucagon excess. An FNA biopsy of the pancreatic lesion confirmed the diagnosis of glucagonoma. The pituitary hormone testing was normal except for an abnormal dexamethasone suppression test. Further investigations showed an elevated late-night salivary cortisol, 24h urinary free cortisol and ACTH. The intravenous dexamethasone suppression test and desmopressin stimulation test were compatible with an ACTH-secreting anterior pituitary adenoma.

Conclusion: We have a 26-yr-old female with MEN-1 syndrome confirmed with genetic testing that presents with an ACTH-secreting anterior pituitary adenoma, glucagon-secreting neuroendocrine pancreatic tumor and hyperparathyroidism. She is scheduled for a transsphenoidal surgery in the coming weeks that will be followed by the resection of her pancreatic tumor and parathyroid adenoma in the next months.

XING SUN*, JUN YI, MARIO KONTOLEMOS, PALOMA O'MEARA, IRENA DRUCE

UNIVERSITY OF OTTAWA



EVOLVING RADIOLOGIC FINDINGS IN PITUITARY APOPLEXY

A 93-year-old man presented to the emergency department with 1-day history of headache and nausea/vomiting. Past medical history was significant for non-functioning pituitary macroadenoma. The headache was described as the worst headache of his life, waking him from sleep. Computed tomography (CT) angiogram of the head revealed a stable sellar mass and otherwise no acute intracranial abnormality. As his headache persisted, repeat CT head was performed and showed interval development of fluid with mucosal thickening in bilateral sphenoid sinuses. Further investigation with magnetic resonance imaging (MRI) of the brain revealed signs of hemorrhage within the pituitary adenoma resulting in apoplexy, mass effect on the cavernous sinuses and decompression into the sphenoid sinuses. Neurosurgery was consulted and due to frailty and comorbidities, conservative management was recommended. Full panhypopituitarism testing was significant for suppressed adrenocorticotropic hormone levels (1.2 pmol/L) consistent with central adrenal insufficiency, as well as undetectable prolactin levels. On post-admission day 5, the patient developed right-sided ptosis, mydriasis, ophthalmoplegia and binocular diplopia, consistent with cavernous sinus syndrome with frozen globe. Dexamethasone therapy was started to reduce edema in the cavernous sinuses with subsequent improvement in his ocular symptoms. This case was notable due to the evolution of interesting radiological findings and clinical features of pituitary apoplexy. Although initial imaging revealed no acute changes, a suspicious clinical presentation prompted repeat imaging with eventual confirmation on MRI. During his admission, the patient was managed conservatively for complications secondary to pituitary apoplexy, including central adrenal insufficiency and cavernous sinus syndrome.

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A CASE MODY5 CAUSED BY 17q.12 RECURRENT DELETION SYNDROME

Background: Mature onset diabetes of the young (MODY) accounts for 2–5% of diabetes cases. HNF1B gene mutations cause MODY 5, which accounts for 5% of MODY cases. 17q.12 recurrent deletion syndrome causes HNF1B deletion and is characterized by MODY 5, kidney and neurodevelopmental disorders.

Case: A 24-year-old female was diagnosed with diabetes with an A1C of 19.4% and random glucose 60.6mmol/L on routine bloodwork. She had hypomagnesemia but no ketoacidosis and negative autoantibodies. Shortly after insulin was started, she developed blurred vision and abdominal pain. Ophthalmology diagnosed bilateral cataracts. Imaging did not identify an etiology for her abdominal pain, but noted pancreatic hypoplasia, renal cysts, mild hydronephrosis, and a uterine anomaly. She was referred to endocrinology for diagnostic clarification. She had atypical features for type 1 and type 2 diabetes. Presence of renal cysts and hypomagnesemia prompted genetics referral for suspected MODY 5 due to HNF1B mutation. Initial genetic testing suggested HNF1B gene deletion. Subsequent chromosome microarray testing revealed 1781kb loss of chromosome 17q.12, also known as 17q.12 recurrent deletion syndrome, explaining her various clinical sequelae.

Discussion: 17q.12 recurrent deletion syndrome is nearly always present in the context of HNF1B deletion, and therefore in about 50% of MODY 5 cases. Key clinical features include structural and/or tubulointerstitial kidney disease (especially hypomagnesemia), MODY, and neurodevelopmental/ neuropsychiatric disorders. Hyperparathyroidism, elevated liver enzymes, eye abnormalities, and uterine abnormalities in females are also common. Establishing this underlying diagnosis in the setting of MODY 5 is important in order to guide further investigations, follow-up, and management.

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MULTIFOCAL NON-METASTATIC RADIOACTIVE IODINE AVIDITY ON WHOLE BODY SCAN AFTER TREATMENT OF THYROID CANCER

Objective: Radioactive iodine (RAI) I-131 ablation is used to treat high-risk differentiated thyroid cancer following thyroidectomy, to reduce the risk of recurrence, and to allow for long-term monitoring. However, false-positive iodine uptake can occur. We describe a patient with multifocal non-metastatic RAI avidity on whole body scan.

Results: A 42-year-old female with high-risk follicular thyroid cancer was treated with total thyroidectomy followed by RAI ablation. She had undetectable thyroglobulin and anti-thyroglobulin antibodies. Whole-body scan post-RAI showed multifocal I-131 avidity in the left hip and in several vertebral bodies (left 7th thoracic, left 4th lumbar, and right 5th lumbar). She had no corresponding morphologic abnormalities on localizing CT scan. Spine MRI showed no suspicious lesions. Additionally, she had a small I-131 avid focus on her right breast, for which diagnostic mammography confirmed no suspicious lesions. In the absence of morphologic abnormalities on correlating scans, and no clinical or biochemical features of metastatic disease, these were felt to likely represent non-metastatic avidity. She is awaiting a thyrogen-stimulated Positron Emission Tomography scan to confirm their benign nature.

Discussion: False-positive uptake of I-131 can mimic metastasis and is commonly described in organs with sodium-iodine symporter (NIS) expression. We discuss a unique case of uptake in musculoskeletal tissues. One hypothesis could be individual variances in location and degree of NIS expression, which could result in non-metastatic and atypical areas of RAI uptake. Confirmatory imaging and biochemical markers are essential in distinguishing metastatic from non-metastatic RAI foci. Further studies are necessary to elucidate the mechanism.

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SLOWING DOWN THE OSTEOCLASTS: POTENTIAL NEW TREATMENT FOR FIBROUS DYSPLASIA-RELATED BONE PAIN

Fibrous dysplasia (FD) is a disorder of bone growth. Decreased osteoblast formation and osteoclast overactivity are a part of its proposed mechanism. Common symptoms include pain, fracture, and uneven bone growth. Bisphosphonates are the mainstay of treatment with the primary goal of pain relief. Other RANK ligand inhibitors have also been shown to reduce bone pain. Here, we present a potential novel treatment for FD-associated pain A 50-year-old woman presented to ophthalmology in March 2011 with proptosis, diplopia, and orbital pain. CT head revealed a skull base lesion which was confirmed to be fibrous dysplasia on bone biopsy. She was started on IV pamidronate monthly for pain control in November 2011. Repeated attempts to decrease the frequency of IV pamidronate was unsuccessful due to breakthrough pain. She was transitioned to oral bisphosphonates given the duration of IV bisphosphonate but had inadequate pain control. In August 2021, she was diagnosed with metastatic melanoma and started nivolumab, while staying on an oral bisphosphonate. After starting nivolumab, her pain completely resolved for the first time in ten years. While nivolumab, a human programmed death receptor-1 blocking antibody, has been utilized in the treatment of bone associated malignancy, it has not been studied in FD. Nivolumab suppresses RANK ligand-related osteoclastogenesis. This mechanism is proposed to prevent bone destruction and reduce cancer bone pain. Our case is unique as it suggests a potential role of Nivolumab in treating FD-associated pain. Future studies should determine if anti-PD1 therapy could be an innovative therapy for FD.

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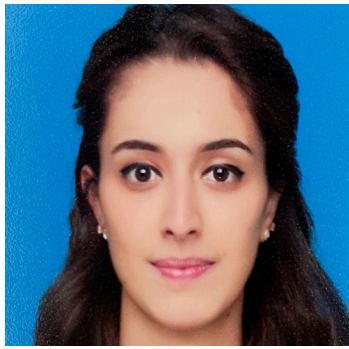
MCMASTER UNIVERSITY



A CASE SERIES OF HYPOPHOSPHATASIA: PRESENTATION AND RESPONSE TO ASFOTASE ALFA

Introduction: Hypophosphatasia (HPP) is a rare inherited metabolic bone disorder characterized by a deficiency in the tissue non-specific alkaline phosphatase (TNSALP) due to loss of function mutation in the ALPL gene. HPP is associated with impaired skeletal mineralization due to elevations in inorganic pyrophosphate and altered phosphate: pyrophosphate ratio. Asfotase alfa (AA) was approved for treatment of HPP in 2015. We present a case series of 7 patients with HPP, 5 with pediatric-onset and 2 with adult-onset, treated with AA and describe its efficacy and safety. Case presentation: 7 patients aged 19–68 years with HPP were included. AA was administered in doses of 6mg/kg/week with a mean follow-up of 6 months (SD=5).

Management outcome: Muscle strength and pain improved by up to 70% from baseline as quantified subjectively by patients. Walking distance improved by up to 100% with a reduction in the use of gait aids. Patients also reported up to 90% improvement in mood and 75% improvement in energy levels. 4 out of 6 patients first noted clinical signs of improvement after 3 months of being on therapy. 1 out of the 7 patients sustained a toe fracture while on AA. AA was well-tolerated with injection site reactions being the most commonly reported adverse effect.

Discussion: HPP treatment with AA in both pediatric and adult-onset forms resulted in significant improvement in musculoskeletal and cognitive manifestations and patients' quality of life. It was well tolerated in 6 patients. 1 patient discontinued therapy because of minor adverse effects with myalgias.

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A RARE CASE OF SUCCINATE DEHYDROGENASE ENZYME COMPLEX B1 MUTATION LEADING TO HEREDITARY PARAGANGLIOMA

Background: Paragangliomas are rare neuroendocrine tumors that arise from extra-adrenal autonomic paraganglia. These are located in the sympathetic paravertebral ganglia of the thorax, abdomen and pelvis. The majority are sporadic, however, approximately ⅓–½ are associated with inherited syndromes. Some linked to variants in the genes encoding subunits of succinate dehydrogenase enzyme (SDH) complex SDHA, SDHB, SDHC, SDHD. Case 39yo male referred for thyroid nodule found to have history of panic attacks, anxiety, sense of doom. His maternal grandmother had metastatic paraganglioma. His mother had a positive constellation of symptoms, negative urine screen however, positive genetics. Initial testing showed plasma normetanephrine 5.55nmol/L (< 0.89nmol/L) and metanehprine 0.22nmol/L (< 0.49nmol/L). 24hr urine testing showed normetanephrine 11.2umol/L (0.6–2.3umol/L) and metanephrine 0.8umol/L (0.2–1.3umol/L). This was done on Wellbutrin. Repeated two years later and revealed consistently elevated normetanephrines. Chromogranin A 152ng/mL (< 110ng/mL). He had a normal adrenal workup. Abdominal ultrasound revealed normal adrenals. PET/CT whole body discovered a hypermetabolic paravertebral mass posteromedially in the right hemithorax measuring 6.6cm. Bone scan negative for metastases. Genetic testing consistent with SDHB1 mutation. The patient underwent removal of the mass. Pathology confirmed paraganglioma with a Ki67 of 2%. Postoperative catecholamines and chromogranin A were normal.

Conclusion: Paraganglioma syndrome 4 (PGL4) is associated with SDHB autosomal dominant mutation which commonly secrete normetanephrines over metanephrines and has a higher morbidity and mortality in comparison to other mutations as it can metastasize and present at much younger ages. It is important to consider coexisting tumors such as renal, breast, thyroid and prostate.

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RECURRENT HYPERVITAMINOSIS D WITH SPURIOUS HIGH CALCITRIOL LEVELS

Hypercalcemia is a common problem encountered in inpatient adult medicine. Determining the etiology requires measurement of parameters involved in maintaining calcium homeostasis. A 69-year-old man was found to have multiple complications of acute, severe hypercalcemia including delirium and renal impairment while taking several complementary medicine tablets. The presenting calcidiol serum concentration was 1495 nmol/L (50–200), with a corrected calcium of 3.86 mmol/L and PTH 6 ng/L (7–37). However, an elevated calcitriol level of 1225 pmol/L raised concerns of excess 1-hydroxylation of calcidiol to calcitriol via co-existing granulomatous disease or malignancy. PET-CT revealed no pathologically hypermetabolic lesion. The 25-OH-D3: 24,25-(OH)2D3 ratio was normal, excluding CYP24A1 mutations. Interestingly, serial dilution of the sample demonstrated a non-linear response, suggesting interference from heterophile antibodies or possible downstream vitamin D metabolites cross reacting with the calcitriol assay. Given incongruent findings, vitamin D measurements were re-evaluated with mass spectrometry. Research-based measurement of the vitamin D metabolome demonstrated high concentrations of di-hydroxy and tri-hydroxyvitamin D metabolites, which may explain the immunoassay interference and contribute to a biologic effect via the Vitamin D receptor. The patient's calcium level improved after supplement discontinuation, but the patient remained unconvinced of the diagnosis. On two subsequent occasions, he re-started the supplements, incurring a marked increase in calcium, calcidiol and reduction in eGFR each time. Eventually the supplements were permanently discontinued, and all biochemistry normalized save moderate ongoing renal impairment. Vitamin D intoxication may be inadvertent, causing impaired organ function and may show spurious high calcitriol levels when immunoassay methodology is used.

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A RARE CASE OF PARATHYROID CARCINOMA IN MEN1 SYNDROME

Parathyroid carcinoma has a prevalence of 0.005% among all malignancies and occurs in less than 1% of all primary hyperparathyroidism cases. Primary hyperparathyroidism is the most common manifestation of multiple endocrine neoplasia type 1 (MEN1). However, only 17 cases of parathyroid carcinoma have been reported in the literature among those with MEN1. Here we describe a case of severe hypercalcemia leading to a new diagnosis of parathyroid carcinoma and MEN1 (c.196_200dupAGCCC frame shift mutation). A 40-year-old previously healthy Caucasian female presented to hospital with nausea, vomiting, fatigue, and unintentional weight loss. Investigations revealed calcium 4.23 mmol/L, parathyroid hormone 146.20 pmol/L, bone specific ALP 453 U/L, and 25-OH-vitamin D 89 nmol/L. Imaging demonstrated a 5 cm right parathyroid mass with inferior extension, a 2.7 cm pancreatic mass, and a 4 cm left adrenal mass. No pituitary lesion was identified on MRI sella. The patient underwent subtotal right parathyroidectomy, right thyroid lobectomy and isthmusectomy. Pathology confirmed subtotal resection of 3 cm of parathyroid carcinoma invading into the thyroid with positive margins. The pancreatic and adrenal masses were both non-functioning and resected given concern for metastatic parathyroid carcinoma. Pathology revealed two well-differentiated pancreatic neuroendocrine tumours, with no extension or metastasis, and a benign adrenal cortical adenoma. Following parathyroidectomy, calcium and PTH remained elevated at 2.95 mmol/L and 170.0 pmol/L, respectively. With cinacalcet and radiation therapy, calcium level normalized to 2.54 mmol/L. Parathyroid carcinoma is a rare manifestation of MEN1 that brings unique management challenges and benefits from a multidisciplinary care team.

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A 680 KB DUPLICATION AT THE FTO LOCUS IN A SUBJECT WITH EXTREME WEIGHT

Background: Common intronic single nucleotide polymorphisms (SNPs) in the human fat mass and obesity associated (FTO) gene are strongly associated with body mass index. In mouse models, inactivation of the FTO gene results in a lean phenotype, whereas over-expression leads to increased food intake and weight. The latter finding suggests that copy number variants at the FTO locus might be associated with extremes of adiposity. We present a case of a 68-year-old patient with a 680 kb duplication between ~rs11859825 and rs9932411. Methods A cohort of unrelated Caucasian subjects with obesity (n=985) and lean subjects (n=869) was searched for rare, private or de novo copy number variation (CNV), genotyped on Affymetrix 6.0 arrays.

Results: Single marker analysis confirmed previously shown associations between intronic SNPs in FTO and obesity. Additionally, a ~680 kb duplication was confirmed by real time PCR and G-to-FISH analyses between rs11859825 and rs9932411 in a 68-year-old patient with obesity since childhood. The affected phenotype was characterized by increased fat distribution in the shoulders and neck, and was accompanied by increased peripheral blood expression of RBL2 with no alteration in expression of FTO or other genes in the region.

Conclusion: We have identified a novel ~680 kb duplication at the FTO locus. No other duplications or deletions in this region were identified, suggesting that large, rare CNVs surrounding the FTO gene are not a frequent cause of obesity. Further studies are required to explore the possibility of a functional link between RBL2 and obesity.

Citation for previous publication:
Davies RW, Lau P, Naing T, Nikpay M, Doelle H, Harper ME, Dent R, McPherson R. A 680 kb duplication at the FTO locus in a kindred with obesity and a distinct body fat distribution. Eur J Hum Genet. 2013 Dec;21(12):1417-22. doi: 10.1038/ejhg.2013.63. Epub 2013 Apr 17. PMID: 23591406; PMCID: PMC3831078.

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RENAL TUBULAR ACIDOSIS AS A CAUSE OF HYPOPHOSPHATEMIC RICKETS IN A YOUNG CHILD

Background: Hypophosphatemia due to renal phosphate wasting is often secondary to hyperparathyroidism or FGF23 excess. We present the case of a young girl with hypophosphatemic rickets secondary to an uncommon cause of renal phosphate wasting.

Case: A 7-year-old girl, previously healthy, presented for evaluation of rickets. On exam, she had bilateral genu valgum and short stature (height 103.5 cm, Z-score −3.24). Blood work demonstrated an elevated alkaline phosphatase (701 U/L), low phosphate (0.9 mmol/L), normal calcium (2.24 mmol/L), normal 25-hydroxyvitamin D (78 nmol/L), and normal PTH (2.6 pmol/L). Tubular reabsorption of phosphate was low (71%), consistent with renal phosphate wasting. Urine calcium/creatinine ratio was also elevated. X-ray chest showed paraspinal calcifications suggesting medullary nephrocalcinosis. X-rays of the extremities showed bilateral flaring of the distal femurs and ulnar metaphyses. The patient was started on phosphate supplementation without calcitriol given her pre-existing hypercalciuria. Blueprint Genetics Hypophosphatemic Rickets Panel was negative. Three months later, the patient was incidentally found to have a metabolic acidosis. Repeat testing demonstrated low venous pH (7.28) and low bicarbonate (20 mmol/L) with an inappropriately elevated urine pH (8.0) and polyuria (2.6 L/m2/day). A diagnosis of renal tubular acidosis (RTA) was made. Investigations to determine the specific RTA etiology are ongoing.

Conclusion: RTA is an uncommon cause of renal phosphate wasting and hypophosphatemic rickets in children. It is important to recognize this diagnosis as it will help guide management decisions. Screening for RTA should be completed in all children presenting with hypophosphatemic rickets due to renal phosphate wasting.

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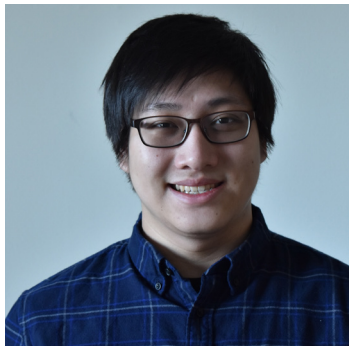

A CASE OF ADIPSIC HYPERNATREMIA DUE TO ANTIBODY-MEDIATED HYPOTHALAMIC INJURY

Adipsic hypernatremia (AH) is a rare condition resulting from failure of thirst response leading to free water deficit. We describe a 23-year-old woman who presented with serum sodium (SNa) 158 mmol/L; hypernatremia had also been noted at age 13. She was cognitively normal. Her urine was concentrated (osmolality averaged 700 mosm/kg), she reported minimal thirst (0 or 1 on 10-point visual analog scale) and since childhood had always needed to be reminded to drink. She had normal blood pressure and pulse without orthostatic changes, and normal jugular venous pressure. Notwithstanding, she had evidence of complications of volume depletion, with impaired renal function (creatinine 120 umol/L), hyperuricemia (uric acid 598 umol/L) with gout, frequent leg cramps, and hemoconcentration (hematocrit 0.483). MRI showed no pituitary structural abnormalities and pituitary hormone testing was unremarkable. Her plasma copeptin was 3 pmol/L, far below expected when serum osmolality was 334 mosm/kg. With prescribed daily fluid intake of 1.6L she diluted her urine (urine osmolality 210 mosm/kg) while still hypernatremic (SNa 151) suggesting a reset osmostat. Her serum was positive for antibodies to the Na(x) channel found in the hypothalamic thirst centre. Given her adipsia, and her excretion of free water when still hypernatremic, she was prescribed daily 1.6 L fluid intake and twice daily DDAVP. Her average SNa is now 149, serum creatinine has improved (87 umol/L), and hematocrit has fallen (0.452). Less hemoconcentration may reduce the risk of deep vein thrombosis. Here we review the unique investigations and clinical management of this challenging case.

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CO-SECRETION OF CORTISOL AND ALDOSTERONE FROM METASTATIC ADRENOCORTICAL CARCINOMA

Introduction: Adrenocortical carcinoma is a rare condition that can be hormonally functional, most often with hypercortisolemia (Cushing's syndrome). We present the case of a metastatic adrenocortical carcinoma that co-secretes cortisol and aldosterone.

Case Description: A 40-year-old male with no past medical history presented with severe hypertension, 30 lbs weight gain and congestive heart failure. Physical exam was consistent with Cushing's syndrome with central adiposity with large violaceous striae. He was found to have an 8.7 cm left adrenal tumor suspicious for adrenocortical carcinoma with numerous pulmonary nodules. Adrenal biopsy and endobronchial ultrasound guided biopsy of pulmonary lymph nodes confirmed the diagnosis of metastatic adrenocortical carcinoma. Secondary workup of hypertension revealed hypercortisolemia with 24-hour urine cortisol secretion of 2821 nmol/day and hyperaldosteronism with aldosterone level of 1515 pmol/L, renin of 9.4 ng/L and aldosterone to renin ratio of 161 pmol/L/ng/L. He demonstrated typical sequelae of hypercortisolemia, along with hypertension and hypokalemia between 2–3.4 mmol/L from hypercortisolemia and hyperaldosteronism. He was deemed to be a non-operative candidate with poor prognosis. He was thus managed medically with ketoconazole and four antihypertensive agents including spironolactone. 24-hour urine cortisol two weeks after titrating to maximum dose ketoconazole was 704 nmol/day and hypertension was controlled.

Discussion: Metastatic adrenocortical carcinoma with hypersecretion of cortisol and aldosterone is an extremely rare entity. While surgical resection would provide cure of the sequelae of hypersecretion, in those who are not candidates, medical management with agents such as ketoconazole and spironolactone can improve patient parameters.

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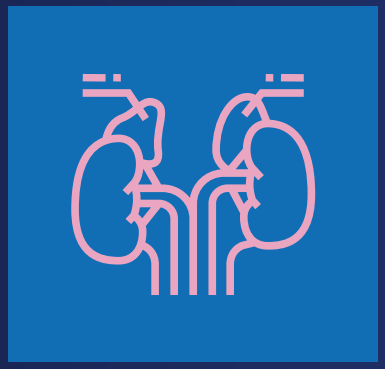
OPTIMAL THERAPEUTIC STRATEGY FOR A NOVEL PATHOGENIC VARIANT OF MATURITY-ONSET DIABETES OF THE YOUNG TYPE 4 (MODY-4)

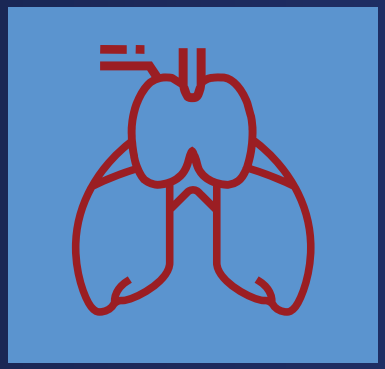
A 32-year-old non-obese female presents with a 15-year history of tremors, scintillations in peripheral vision, and paresthesia involving the extremities and face. Initial capillary glucose testing revealed glucose of 2 mmol/L. Further investigations included: elevated fasting blood glucose 6.2 mmol/L, c-peptide 645 (325–1090 pmol/L), insulin 49 (< 95 pmol/L), and negative anti-GAD65 antibody. With a multi-generational family history of diabetes and impaired fasting glucose, she was investigated for monogenic diabetes. Subsequent whole genome sequencing revealed the missense variant c.486A>C (p. Glu162Ala) in the PDX1 gene. Current human genetic database analysis identified this as a novel and pathogenic genetic variant causing Maturity-Onset Diabetes of the Young Type 4 (MODY-4). She was eventually initiated on basal insulin followed by multiple daily injection insulin therapy, completely resolving her symptoms and normalizing glucose readings. MODY-4 is exceedingly rare and accounts for less than 1% of all causes of MODY.

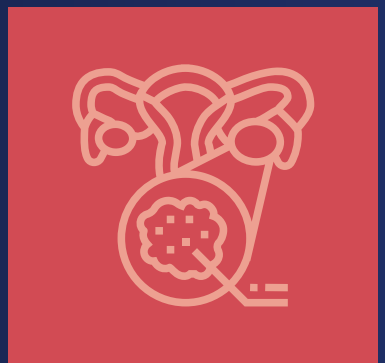
The pathogenesis involves a mutation in the PDX1 gene, which encodes a transcription factor (Insulin Promoter Factor-1) responsible for pancreatic function and development[1]. Among only a small subset of pathogenic variants, we report a novel mutation as the causative variant in MODY-4. Given the rarity of this disease, the optimal therapeutic approach remains debated. This case demonstrates the utility of insulin therapy as an effective treatment for a subset of patients with MODY-4.

References:

[1] *R. Aarthy et al. Journal of Diabetes and Its Complications 35 (2021) 107640.*







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