for whom medical therapy is not effective and who have concomitant secondary hyperparathyroidism, subtotal parathyroidectomy is a reasonable treatment option.

Thyroid

THYROID NEOPLASIA AND CANCER

RET Mutations in the MEN1 Syndrome: Is It an Innocent Bystander?

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MON-509

RET Mutations In The MEN1 Syndrome: Is it an innocent bystander?

Introduction

MENIN and RET mutations in MEN1 families, are rare, and, when they co-exist either mutation may predominate the clinical picture.

We report a family, with both mutations, and, suspect that the RET mutation may not be an innocent bystander.

Clinical Cases

GM (36M): 2009: Presented with skin lesions and a lactotroph adenoma causing chiasmal compression. Treatment: Hypophysectomy and Cabergoline. This resulted in restoration of sexual function and fertility. 2013: Developed hyperparathyroidism [Calcium 10.6mg% (8.5-10.5); PTH 610pg/ml (10-65); MIBG Scan: parathyroid adenomas]. Treatment: Subtotal parathyroidectomy with allotransplant.

2015: Developed Zollinger-Ellison Syndrome [multiple gastric ulcers; S Gastrin: 516pg/ml; (0-180)]. Treatment: Pantoprazole.

MRI Abdomen: Calcific atrophic pancreas and bilateral non-functioning adrenal adenomas.

HM (32M): 2008: Skin lesions and Lactotroph adenoma. Treatment with Cabergoline resulted in restoration of sexual function and a reduction in breast and tumour size. 2013: Hyperparathyroidism [Calcium 10.9mg%; PTH: 166pg/ml; Calcium excretion: 1160mg/24hrs (100-250)]; BMD: Osteopenia. MIBG 123 Scan: Avid uptake in Right Inferior parathyroid gland. He underwent a subtotal parathyroidectomy with allotransplant.

2015: Recurrent Hyperparathyroidism (Calcium 10.7mg%; PTH: 116pg/ml; MIBG 123 scan: Hyperfunction of the transplanted gland). Stable on treatment with Cinacalcet. Their mother, AM (42F): 1980: Detected to have a lactotroph adenoma when investigated for primary infertility and galactorrhea. She was treated with Bromocriptine and delivered the boys in 1980 and 1984 respectively. She had recurrent renal calculi and hydrenephrosis (? hyperparathyroidism). She succumbed to renal failure following surgery for a benign pancreatic cystadenoma in 1990.

Discussion

Whole exome sequencing of GM and HM showed pathogenic mutations of both, MENIN and RET gene. The precise mutation was a stop gain mutation at exon 3 MENIN.C511T.p. Q171X. They (GM/HM) also harboured a mutation in the RET gene at exon 14 c. G2492T: p.G831V; g. chr10. This may be the first family in which the rare combination of these two mutations has been reported.

The genomics and the clinical presentation suggest that the MENIN mutation predominates in the family, but the presence of bilateral adrenal adenomas in GM are significant on account of RET mutation. The latter may be a harbinger of serious disease in the future. The situation is further compounded by the recurrence of hyperparathyroidism in the allograft of HM. This may be caused due to chance or an unknown genetic/ epigenetic phenomenon in the two MEN mutated genes and RNA sequencing of the tumur tissue may explain the genetic phenomenon. The latter two events suggest that the RET mutations in MEN1 may not be an innocent bystander.

Neuroendocrinology and Pituitary

CASE REPORTS IN CLASSICAL AND UNUSUAL CAUSES OF HYPOPITUITARISM II

Primary Pituitary Lymphoma - an Unusual Guest in the Sella!

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MON-237

Background

Primary Pituitary Lymphoma (PPL) is a rare differential diagnosis for a sellar / suprasellar lesion. Less than 40 cases have been reported.

Case presentation

A 75-year old Chinese lady with known subclinical hypothyroidism presented with 3-day history of dull frontal headache, giddiness and diplopia. Incomplete left cranial nerve (CN) III palsy was noted with no other neurological deficit or hemodynamic instability. MRI brain and pituitary showed a T1- and T2 isointense, 2.0 x 1.1 x 1.3 cm enhancing mass arising from the left sellar region, extending to the left sphenoid and cavernous sinuses, displacing the pituitary stalk towards the right, with no optic chiasm compression. There was no imaging evidence of apoplexy.

Evaluation of anterior pituitary hormones revealed hypocortisolism (peak cortisol post 1mg Synacthen 344 nmol/L, ACTH 3.5 ng/L [10 - 60]), subclinical hypothyroidism (free T4 9.6 pmol/L [8.8 - 14.4], TSH 7.19 mU/L [0.65 - 3.70]), normal prolactin 7.4 ug/L [5.0-27.7], mildly hypocortisolism (peak cortisol post 1mcg Synacthen 193.7 mcg/L [67.0 - 189.0] with normal GH 1.0 ng/ml, and elevated FSH appropriate for menopause. Glucocorticoid replacement was started.

Though the clinical presentation was not typical of a pituitary macroadenoma, in view of symptomatic improvement and neurological stability, she was conservatively managed with plans for early repeat imaging outpatient.

Patient was readmitted 1 month later for headache and decreased left-sided visual acuity. A complete CN III palsy, and new CN II, IV and VI deficits were noted (orbital apex syndrome). Repeat MRI showed increase in the size of the sellar lesion to 2.6 x 2.1 x 1.3 cm, surrounding the optic nerve and with left cavernous and sphenoid sinus invasion.

Again, there was no suggestion of apoplexy. Biopsy of the lesion was performed, and histology was consistent with...
Diffuse Large B-cell Lymphoma and Grade 3A Follicular Lymphoma with high proliferative index (Ki67 70%). Immunohistochemistry excluded carcinoma, meningioma and pituitary tumor. PET-CT and bone marrow aspirate confirmed the diagnosis of PPL without metastasis. After 3 cycles of chemotherapy (Methotrexate, Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone), significant decrease in the size of the lesion was noted on repeat MRI. Only mild asymmetric soft tissue thickening remained noticeable over the left sella and cavernous sinus. Cranial nerve deficits had since completely resolved. Glucocorticoid replacement was continued in the meantime while awaiting the completion of chemotherapy.

Conclusion

PPL may present in a similar manner as pituitary apoplexy. Absence of typical imaging characteristics of apoplexy in patients with rapid symptom progression and CN involvement should alert clinicians to consider alternative diagnosis including aggressive neoplastic, inflammatory and infective lesions.

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I

The Influence of Thyroid Autoimmunity on Pregnancy Outcome in Infertile Women

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SAT-433

Background: Women with subclinical hypothyroidism (SCH) and thyroid autoimmunity (TAI) reportedly have high risks of miscarriage and preterm birth. Infertile women undergoing assisted reproductive technology (ART) are recommended for levothyroxine (L-T4) supplementation to maintain TSH levels below 2.5 mIU/mL according to ATA guideline; however, insufficient evidence exists to determine whether L-T4 treatment for infertile women with TSH levels between 2.5 and 5.0 mIU/mL. Objective: To clarify the influence of TAI on pregnancy in infertile women under L-T4 treatment to maintain TSH levels below 2.5 mIU/mL, and to compare its influence depending on fertility treatments. Methods: A total of 595 infertile women who visited a fertility clinic between January 2013 and December 2015 were prospectively recruited to this study. Five patients with Graves’ disease were excluded and remained 590 women were included in the analysis. Infertile women with TSH levels above 2.5 mIU/mL were treated with L-T4 followed by evaluation of fertility status and pregnancy outcomes. Factors affecting pregnancy were analyzed statistically depending on fertility treatments. Written informed consent was obtained from all patients, and the study protocol was approved by the Ethics Committee. Results: The proportion of SCH and thyroid peroxidase antibodies (TPOAb) positivity was 19.6% and 10.4%, respectively. Women who did not become pregnant were older than those who became pregnant (p=0.003), but no influence of thyroid-associated factors on pregnancy was confirmed. Pregnancy outcome contrarily showed that women who had a miscarriage were older (p<0.001) and higher TPOAb titers (p=0.038) than those who had a live birth. In addition, higher age (OR 26.4, p<0.001) and high TPOAb titer (OR 11.8, p=0.043) were decided as risk factors for miscarriage through multiple logistic regression analysis. Among women who treated with intrauterine insemination, TPOAb titers were higher in women who had a miscarriage than in those who had a live birth (p=0.040). We further focused on the difference between ART methods including in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). Women undergoing IVF had higher TPOAb titers in women who had miscarriage than those who had a live birth (p=0.023), but in women undergoing ICSI there was no association between TPOAb titers and pregnancy outcome. Conclusion: Infertile women with high TPOAb titers are susceptible to miscarriage despite appropriate L-T4 treatment. The influence of TPOAb titers as well as TPOAb positivity on pregnancy should be considered, when undergoing fertility treatments.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS I

Risk Factors Associated with 30-Day and 90-Day Readmission in Persons with Diabetic Foot Ulcers

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SAT-628

Background Diabetic foot ulcers (DFU) are the leading cause of lower-extremity amputations among patients with diabetes (DM). 15% of patients with DM develop DFU, with the potential for progression to osteomyelitis or gangrene with suboptimal glycemic control. Repeated readmissions are not only a negative prognostic indicator for these patients, but also contributes to increasing healthcare costs. Areas of Uncertainty Previous studies have examined associations among demographics, comorbidities and DFU, and the value of Hemoglobin A1c (HbA1c) and C-reactive protein (CRP) as a prognostic indicator and monitoring tool for progression and regression, respectively. However, no studies to date have examined medical or pharmaceutical factors contributing to 30-day and 90-day readmission. Methods A retrospective chart review was conducted examining 397 patients with type 2 diabetes readmitted for