MON-367

Unusual Presentation of Hypercalcemia preceding the diagnosis of methotrexate-induced *Pneumocystis Jirovecii* pneumonia from treatment of Necrotizing Myopathy

Background: *Pneumocystis Jirovecii* infection is a common opportunistic infection often seen severely immunocompromised individuals, such as those with HIV/AIDs. This is an unusual case where the patient displayed persistent hypercalcemia, with an eventual diagnosis of PCP likely due to immunosuppression from methotrexate (MTX) therapy.

Case: A 79 year old male was brought to the hospital for acute change in mental status and hypercalcemia (13.4mg/dl). The patient was acutely encephalopathic, oriented to self only; his baseline was a high level executive at a company. An extensive neurologic workup including CT, MRI, EEG, spinal fluid examination was negative with a persistent hypercalcemia. Additional workup showed no increase in bone turnover, suppressed PTH, non-elevated pPTHrP. He was found to have diffuse mild PET avidity of bilateral lungs on PET scan, with bronchoscopy for evaluation of potential granulomatous disease. PCR of the BAL fluid obtained during bronchoscopy was positive, and the patient was ultimately treated with an extended course of Atovaquone for *Pneumocystis Jirovecii* pneumonia (PCP). The patient was felt to have an immunosuppressed state secondary to being treated for a necrotizing myopathy with methotrexate. The patient's mentation slowly but substantially improved with a combination of a prednisone taper and Atovaquone, with discontinuation of the MTX. The patient's hypercalcemia improved with treatment of PCP.

Conclusion: Although a cause of hypercalcemia secondary to primary hyperparathyroidism causing necrotizing myopathy is known in the literature, it is unusual to see the opposite, where few case reports have documented hypercalcemia due to immunosuppression from low-dose methotrexate treatment for necrotizing myopathy resulting in pulmonary pneumocystis and hypercalcemia. Additionally, MTX induced immunodeficiency is often associated with severe immunosuppression or lymphoproliferative disorders - however the patient had an extensive work up with negative results for malignancy

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS II

Carney Complex Due to a Contiguous Gene Deletion Syndrome (17q24.2-17q24.3)

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MON-917

Background

While genomic rearrangements of chromosome 17 are not uncommon, deletions of chromosome band 17q24.2-q24.3 are rare, and associated features include cardiac abnormalities, characteristic facial appearance, short stature, obesity, syndactyly, intellectual disability, seizures, delayed dentition, and features of Carney Complex. It has been suggested that the involvement of *KCNJ2*, *PRKCA*, *CACNG* gene cluster (*CACNG1, CACNG4, CACNG5*), and *PRKAR1A* genes contribute to this phenotype. A case of a child with a 3.7 Mb deletion at chromosome band 17q24.2-q24.3, as well as a 2.1 Mb gain at chromosome 17q22, is described.

Clinical Case

A now 6 year old female was born at 34 weeks gestational age with prenatal course complicated by oligohydramnios and intrauterine growth restriction. Birth weight was at the 9th percentile, and birth length was at the 92nd percentile. She was noted to have a patent ductus arteriosus (PDA), poor suck and swallow, and dysmorphic features. Chromosome microarray revealed a 3.7 Mb deletion at Chromosome 17q24.2-q24.3, involving *KCNJ2*, *PRKCA*, *CACNG* gene cluster (*CACNG1, CACNG4, CACNG5*), and *PRKAR1A*, as well as a 2.1 Mb gain at Chromosome 17q22, involving *C17orf112* and *KIP2B*.

At 6 years old, she continues to be small for weight (-4.5 SDs), BMI (-4.22 SDs), and height (-2.5 SDs), though with appropriate pre-pubertal linear growth velocity. She is minimally verbal and continues to receive physical, occupational and speech therapies. Examination showed dysmorphic facial features, including triangular face with pointed chin, prominent forehead with low-set ears, retro-micrognathia, almond-shaped eyes with up-slanting palpebral fissures, bulbous nose, thin lips, and irregularly-shaped teeth. She had bilateral 5th digit clinodactyly, tapering of the distal aspects of bilateral first digits of the hands, and syndactyly of bilateral 2nd/3rd digits of the feet. She had scant freckling over the nasal bridge and cheeks, as well as freckles of the left arm, left groin, and back. She had no clinical stigmata of hypercortisolism. Echocardiogram continues to show a PDA with no cardiac myxomas. Thyroid ultrasound was normal. However, she does have mild hypercalcemia, most recently 2.61 mmol/L (2.15-2.55), and mildly elevated alkaline phosphatase of 341 U/L (96-297).

Conclusion

This case highlights a child with many of the previously reported findings associated with 17q24.2-q24.3 deletions. However, she also was noted to have a 2.1 Mb gain at chromosome 17q22 involving *C17orf112* and *KIP2B* genes, which have not yet been associated with a clinical phenotype. It is therefore unclear if her phenotype is partially explained by the chromosomal gain. Clinicians should suspect a contiguous gene deletion syndrome in a patient with Carney Complex and atypical features. Patients with this condition have also been described as "Carney Complex-plus", a term that we do not recommend be used.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Multiple Recurrent Lipomatoses with Thiazolidinedione Therapy in Familial Partial Lipodystrophy, Dunnigan Variety (FPLD2)

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MON-695

Background: FPLD2, a rare autosomal dominant disorder due to heterozygous missense mutations in *LMNA*, is

characterized by gradual loss of subcutaneous (sc) fat from the limbs starting during late childhood and predisposition to metabolic complications, such as diabetes, dyslipidemia and hepatic steatosis. Some patients, especially females, accumulate excess sc fat in the chin, neck, supraclavicular and perineal regions. We report disfiguring and disabling lipomatoses in unusual locations with thiazolidinedione therapy in two women with FPLD2.

Clinical Cases: A 57-year-old white female with FPLD2, due to heterozygous p.R482Q *LMNA* mutation, developed recurrent large lipomatoses in the axillae at age 33 years, and later in the posterior neck (buffalo hump), mons pubis and above sacrum. She developed diabetes at age 30 and was started on pioglitazone 45 mg daily, which was switched to rosiglitazone 8 mg daily at age 43 years. Supra-sacral lipomatoses were approximately 40 cm X 20 cm bilaterally and continued to grow despite lipectomy and multiple liposuctions. Rosiglitazone was stopped at age 56 years, and she reported no further increase in the size of lipomatoses. Her other medications included colesevelam, atorvastatin, metformin, glimepiride, lisinopril, losartan, hydrochlorothiazide, aspirin, insulin and dulaglutide. Her 54-year-old younger sister with FPLD2 (heterozygous p.R482Q *LMNA* mutation) was treated with lisinopril, metoprolol, atorvastatin, liraglutide, and insulin glargine and aspart, but no history of taking thiazolidinediones, and she never developed any lipomatoses. Another 43-year-old white female with FPLD2, due to heterozygous p.S583L *LMNA* mutation, was noticed to have lipomatous deposits in the axillae, medial gluteal region, labia and perineal regions. She developed diabetes mellitus at age 36 years and took metformin for 6 years and pioglitazone 30 mg daily for one year before she noticed the lipomatoses. Her other medications included atorvastatin, aldactone and vitamin D3. Pioglitazone was stopped and after one year, she reported reduction in the size of lipomatoses.

Conclusion: Thiazolidinediones are selective peroxisomal proliferator-activated receptor-γ agonists and induce weight gain by increasing fat mass, especially subcutaneous depots. Our cases suggest that thiazolidinediones can cause undesired growth of non-lipodystrophic adipose tissue in patients with FPLD2 and thus should be avoided.

Adipose Tissue, Appetite, and Obesity

OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Effect of Liraglutide Treatment on Proglucagon-Derived Peptides

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MON-591

Liraglutide is a glucagon-like peptide 1 receptor agonist (GLP-1ra) and has 97% homology to native GLP-1. Native GLP-1 derives from proglucagon, which is also a prohormone for other peptides including GLP-2, glucagon, oxytomodulin, glicentin, and major proglucagon fragment. Aside from GLP-1 and glucagon, the actions and roles of the other proglucagon-derived peptides remain unclear. In addition, the effect of liraglutide treatment on these peptides are unknown. The aim of this study was to evaluate the effect of treatment with liraglutide compared with placebo on proglucagon-derived peptides. Adults who were overweight/obese (BMI 27-40 kg/m^2) with prediabetes were randomized to liraglutide 1.8mg daily vs placebo for 14 weeks. All participants met regularly with a registered dietitian and were advised to decrease calorie intake by 500 kcal/day. Proglucagon-derived peptides were measured during mixed-meal tolerance test (MMTT) at baseline and after 14 weeks in a subset of individuals with saved samples (n=16 on liraglutide, n=19 on placebo). The MMTT involved eating breakfast at 08:00 (20% of daily energy intake) and lunch at 12:00 (40% of daily energy intake). Blood was collected before breakfast and hourly from 08:00 to 16:00. The area-under-the curve (AUC) was calculated for all proglucagon-derived peptides using the trapezoidal method. Individuals treated with liraglutide lost twice as much weight as those assigned to placebo injections (mean ± SD, 6.1 ± 1.9 vs 3.2 ± 2.2 kg, $p<0.002$). Treatment with liraglutide also was associated with a significant ($p < 0.01$) decrease in all proglucagon-derived peptides. In the placebo group, only glucagon AUC significantly decreased after 14-weeks (P=0.002). Our study demonstrates for the first time that liraglutide treatment is associated with decrease in proglucagon-derived peptides, suggesting downregulation of endogenous proglucagon. The effects of this downregulation are unknown and need further study.

Thyroid

THYROID DISORDERS CASE REPORTS III

Biotin Masquerading as Subclinical Hyperthyroidism

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MON-470

Introduction: Thyroid conditions are among the most common endocrine disorders. Diagnosis is dependent on interpretation of laboratory tests. The challenge comes when the clinical picture is discordant with laboratory results.

Case Report: Patient is a 53-year-old male with history of cardiac transplantation, type 2 diabetes mellitus, history of amiodarone-induced hyperthyroidism. He was noted to have labs indicative of hyperthyroidism, while taking amiodarone, in 2016-2017, which was treated with methimazole. He was then noted to have abnormal thyroid function tests with low TSH to 0.3 IU/L, normal T3 and normal T4 levels. Thyroid stimulating immunoglobulin had been checked multiple times, and was normal, which is inconsistent with Graves' disease. Prior radioactive iodine uptake scan, while off amiodarone, was noted to be normal. He was also scheduled for thyroidectomy at another hospital, which was cancelled due to normalization of thyroid function tests. Consultation was received for suppressed TSH to 0.323 IU/L, without symptoms of hyperthyroidism. He had been taking biotin during this time, which he subsequently stopped taking. Repeat TSH following discontinuation of biotin, was within normal range, most recent TSH 2.48 IU/L, free T4 1.03 ng/dL, free T3 2.7 pg/mL.