with PPARγ mutation leading to numerous metabolic complications. A 19 year old female with FPL3 was seen by adult endocrinology as a transition from pediatric endocrinology. She was found to have hypertriglyceridemia on routine labs done at the age of 11. Patient reported loss of subcutaneous fat from her extremities and eruptive xanthoma on flexor surfaces at the time of diagnosis along with a positive family history of hypertriglyceridemia induced pancreatitis and Myocardial infarction at the age of 40 in her father. Her triglyceride level has varied between 600 and 3000 (normal 20–149 mg/dl) over the years. FPL3 was diagnosed based on genetic testing. She was prescribed fenofibrate and fish oil, and statin was added thereafter. She developed type 2 diabetes and was started on metformin and pioglitazone. She was noted to have hypertension and was treated with amlodipine and lisinopril. She also was found to have Polycystic Ovarian Syndrome (PCOS) based on menstrual irregularities, hirsutism and ultrasound showing multiple ovarian cysts, and was treated with spironolactone. Her most recent labs show triglyceride level of 2400 mg/dl and HbA1c of 8.3. PPARγ gene mutation in FPL3 leads to insulin resistance and hence patients often develop hypertriglyceridemia, type 2 diabetes, PCOS and hypertension. In terms of treatment options, we are still limited to pioglitazone, metformin, statins and fish oil. Often these are not sufficient in addressing the complexity of metabolic derangements in these patients who have an increased risk of cardiovascular events at a young age. Further research about agents targeting this gene in particular would be beneficial. 1. Agarwal et al. A novel heterozygous mutation in peroxisome proliferator-activated receptor-gamma gene in a patient with familial partial lipodystrophy. J Clin Endocrinol Metab. 2002 Jan; 87(1):408–411. 2. Garg A. Lipodystrophies: Genetic and Acquired Body Fat Disorders. J Clin Endocrinol Metab. 2011;96(11): 3313–3325.

Cardiovascular Endocrinology

CARDIOVASCULAR ENDOCRINOLOGY AND LIPIDS DISORDERS CASE REPORT

Diet-Responsive Hypercholesterolemia With Cardiofaciocutaneous Syndrome Type 3

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Background: Molecular basis of diet responsive hypercholesterolemia remains unclear. We report diet-responsive severe hypercholesterolemia in a young female with cardiofaciocutaneous syndrome type 3 (CFC3) due to a heterozygous pathogenic *MAP2K1* variant, suggesting a role of common MAPK variants in LDL-cholesterol (LDL-C) response to diet. Clinical case: A 3-year-old Caucasian female with CFC3 (macrocephaly, frontal bossing, wide nasal root with depressed bridge, anteverted nares, low set fleshy ears, congenital pulmonic valve stenosis, postnatal growth deficiency, hypotonia, and neurocognitive impairment) due to a *de novo* heterozygous c.389A>G, p.Tyr130Cys pathogenic variant in *MAP2K1,* presented with extremely elevated serum total cholesterol of 446 mg/dL, triglycerides of 239 mg/dL, HDL-cholesterol of 53 mg/dL, LDL-C of 335 mg/dL (normal range < 110 mg/dL) and serum apolipoprotein B level 219 mg/dL (normal range < 90 mg/dL). Her LDL-C was 252 mg/dL a year ago and 215 mg/dL one month prior to presentation. Reducing total dietary fat to 20–25% of total energy and saturated fat to <6% of total energy over the next 4 months lowered LDL-C to 104 mg/dL. However, her weight decreased by 0.5 kg and liberalization of fat intake again increased LDL-C to 222 mg/dL. Her father has mildly elevated LDL-C of 160 mg/dL and her mother had normal LDL-C of 80 mg/dL. Her plasma phytosterol levels were normal and she had ApoE3/E3 genotype. Targeted genetic testing of the patient and parents showed a benign heterozygous LDL receptor (*LDLR*) variant c.2242G>A; p.Asp748Asn, (Minor allele frequency 0.00008) in the patient and her father. Whole exome sequencing of the patient and both parents showed no known disease-causing variants in *LDLR, APOB, PCSK9, LDLRAP1, APOE, STAP1, LIPA, ABCG5, ABCG8* and other known hyperlipidemia-related genes. There are no previous reports of hypercholesterolemia in patients with CFC3. MAP2K1 stimulates various MAP kinases upon wide variety of extra- and intracellular signal and is involved in cell proliferation, differentiation, transcription regulation and development. Previous studies of the relationship between $p42/44^{MAPK}$ activation and *LDLR* expression in human hepatoma HepG2-derived cell line showed that that activation of the Raf-1/MEK/$p42/44^{MAPK}$ cascade induces *LDLR* expression and modulation of the Raf-1 kinase signal strength can determine *LDLR* expression levels. Thus, extent of MAPK activation can alter signaling of LDLR, resulting in hypercholesterolemia. Conclusion: Our case report suggests that MAP2K1 may play a significant role in LDLR signaling, and some MAP2K1 variants may be associated with diet-responsive hypercholesterolemia. Larger studies are required to assess dietary response to LDL-C in subjects with MAP2K1 variants.

Cardiovascular Endocrinology

CARDIOVASCULAR ENDOCRINOLOGY AND LIPIDS DISORDERS CASE REPORT

Familial Partial Lipodystrophy: A Case Study and Review of Recent Literature

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Introduction: Familial partial lipodystrophy (FPLD) is a rare genetic disorder characterized by loss of subcutaneous adipose tissue, mainly from the extremities and gluteal region. FPLD is associated with a variety of metabolic abnormalities including severe hypertriglyceridemia (HTG), insulin resistance (IR), and hepatic steatosis. We present a case of FPLD and summarize recent literature on the metabolic features and their management in patients with this rare disease. Case: A 44 year old female with medical history of Type 2 DM, hypertension, hypothyroidism and recurrent pancreatitis from severe HTG was referred to our clinic. She was diagnosed with Type 2 DM in her 30s. Over the ensuing years she had significant IR requiring increasing doses of concentrated insulin (up to 250 units/day). She reported progressive loss of subcutaneous fat from extremities in the preceding 2–3 years. She