A disruption in this pathway will result in hyperglycemia. Hyperglycemia was reported in 65% of patients with some cases found to be in ketoacidosis. This adverse effect means frequent monitoring of blood glucose is required following initiation of this treatment.4

Conclusion: Alpelisib is a new drug used in the select treatment of breast cancer. It can cause severe hyperglycemia and potential worsening of diabetes. Blood glucose should be monitored closely in patients with diabetes who are treated with alpelisib.

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Cardiovascular Endocrinology

HYPERTRIGLYCERIDEMIA; INFLAMMATION AND MUSCLE METABOLISM IN OBESITY AND WEIGHT LOSS I

Severe Asymptomatic Hypertriglyceridemia

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SAT-577

Background

Case reports of patients with severely elevated serum triglyceride levels (>1000 mg/dL) have been documented where Insulin infusions, heparin and plasmapheresis have demonstrated rapid and successful decrease in serum Triglyceride levels. The benefits of one approach versus the other to prevent major complications such as cardiovascular events or acute pancreatitis has not been well investigated. We present the case of a patient with severely elevated serum triglyceride levels without any manifestations.

Case Description

A 53-year-old male presented from his primary care provider's office due to elevated Triglycerides levels over 6000 as per outpatient lab work. Inpatient labs were unattainable initially due to hemolysis secondary to the severely high lipid content. Patient was admitted to the medical ICU for closer monitoring and initiated on an insulin drip. Two days after insulin initiation patient's triglyceride levels returned as 2,887 with a total cholesterol count of 848. His insulin drip was continued until his TAG levels were less than 1000. Upon discharge his levels were less than 600.

Discussion

Most patients with hypertriglyceridemia are asymptomatic. However, in patients with levels above 1000 mg/dL, the risk of pancreatitis or cardiovascular event is of concern. Hypertriglyceridemia may account for 1 to 14 percent of cases of acute pancreatitis. Treatment is largely based upon symptoms and complications. In the event of pancreatitis or other cardiovascular complication, plasmapheresis is usually recommended. If asymptomatic, Insulin may be used. Insulin promotes synthesis of lipoprotein lipase which functions to hydrolyze triglycerides, and has been shown to be an effective lowering agent in the treatment of such individuals. Case reports of Heparin being used as a lipid lowering agent have also been documented, but was not used in our particular patient.

Normal triglyceride plasma levels are defined as less than 150 mg/dL. Mild hypertriglyceridemia typically ranges between 150-499 mg/dL, moderate between 500-866 mg/dL, and severe is defined as levels greater than 886 mg/dL. Plasma triglyceride levels above 1000 mg/dL occur in fewer than 1 in 5000 individuals. It is said that patients with TAG levels above 2000 mg/dL almost always have both a secondary and a genetic form of Hypertriglyceridemia. For this reason it is very important to identify these patients as early as possible to treat appropriately. Our patient was a known alcohol abuser, yet without the presence of some polygenic familial disorder, the likelihood of our patient having TAG levels >6000 mg/dL, is very unlikely.

Genetics and Development (including Gene Regulation)

ENDOCRINE DISRUPTING CHEMICALS

Historical Occurrence of Intersex in Largemouth Bass (Micropterus Salmoides) and Smallmouth Bass (Micropterus Dolomieu)

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SAT-732

The widespread occurrence of gonadal intersex (presence of testicular oocytes) has been recently reported in populations of Largemouth Bass (*Micropterus salmoides*) and Smallmouth Bass *Micropterus dolomieu*) from populations across North America. To evaluate the historical occurrence of intersex in bass species, gonads were examined visually and histologically from Largemouth Bass and Smallmouth Bass from museum specimens collected from 16 States. These fishes were collected between 1823-1965, before the widespread discharge of estrogenic chemicals to surface waters via wastewater effluents. All females examined had normal ovaries. Intersex gonads were identified in 17.8 % of male Largemouth Bass, and in 14.2% of male Smallmouth Bass. The intensity of testicular oocytes in some males was as great as observed since 2000. These results indicate that the occurrence of this form of intersex in these bass species is not a recent phenomenon.

Adipose Tissue, Appetite, and Obesity

ADIPOSE TISSUE BIOLOGY AND OBESITY II

IDH1-Dependent Alpha-KG Regulates Brown Fat Differentiation and Function by Modulating Histone Methylation

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SUN-587

ABSTRACT

Brown adipocytes play important roles in the regulation of energy homeostasis by uncoupling protein 1-mediated non-shivering thermogenesis. Recent studies suggest that brown adipocytes as novel therapeutic targets for combating obesity and associated diseases, such as type II diabetes. However, the molecular mechanisms underlying brown adipocyte differentiation and function are not fully understood. We employed previous findings obtained through proteomic studies performed to assess proteins displaying altered levels during brown adipocyte differentiation. Here, we performed assays to determine the functional significance of their altered levels during brown adipogenesis and development. We identified isocitrate dehydrogenase 1 (IDH1) as upregulated during brown adipocyte differentiation, with subsequent investigations revealing that ectopic expression of IDH1 inhibited brown adipogenesis, whereas suppression of IDH1 levels promoted differentiation of brown adipocytes. Additionally, *Idh1* overexpression resulted in increased levels of intracellular α-ketoglutarate (α-KG) and inhibited the expression of genes involved in brown adipogenesis. Exogenous treatment with α-KG reduced brown adipogenesis during the early phase of differentiation, and ChIP analysis revealed that IDH1-mediated α-KG reduced trimethylation of histone H3 lysine 4 in the promoters of genes associated with brown adipogenesis. Furthermore, administration of α-KG decreased adipogenic gene expression by modulating histone methylation in brown adipose tissues of mice. These results suggested that the IDH1–α-KG axis plays an important role in regulating brown adipocyte differentiation and might represent a therapeutic target for treating metabolic diseases.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING I

Implementation of Whole Exome Sequencing for Clinical Diagnostics: A Prospective Busan Kyung-Sang Regional Co-Work Team Experience

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SUN-721

Purpose: Next Generation Sequencing (NGS) technology is a highthroughput method for genome sequencing which assists clinicians with diagnosis of patients with suspected genetic disorders. This study was to investigate diagnostic yield and clinical utility of whole exome sequencing prospectively in the rare genetic diseases. Method: WES was performed a total of 178 patients with suspected genetic disorder. Buccal swab samples were collected from the patients to extract genomic DNA. WES and variant interpretation was conducted in 3 Billion Inc (Seoul, Republic of Korea), based on their own software. Patients' phenotype was interpreted by clinical geneticists. Results: WES reported 117 variants (66.7%). According to the ACMG/AMP guidelines, there were 25 pathogenic variants (14%), 37 likely pathogenic variants (32%), and 55 VUS (31%). Among the 117 patients who detected variants, genotype-phenotype correlation was analyzed and resulted that 44 (38%) were found to be apparently causal mutation of the disease, 37 (32%) were not considered the cause of the disease, and 36 (31%) were withheld judgement. Of the VUS variants, 13% were likely to be the causal variants of the disease considering phenotype of patients. Conclusion: This study showed 38% of diagnostic yield in patients with unidentified genetic condition by using prospective WES based on automating variant interpretation system. In the diagnosis of rare genetic disease, we identified the need for a multi-disciplinary team to select appropriate subjects and interpret the clinical significance of the found genetic variants.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY

Ipilimumab Immune-Related ACTH Deficiency Is of Acute Onset and Severe.

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MON-290

Introduction

Immune checkpoint inhibitors (ICIs) are immunomodulatory molecules that downregulate T-cell inhibiting-receptors or ligands to promote an enhanced anti-tumour response. Ipilimumab is a human monoclonal antibody directed against cytotoxic T-lymphocyte antigen-4 (CTLA-4) that has been shown to significantly improve survival in patients with metastatic melanoma. Immune-related adverse events (irAEs) occur in some patients with increased T-cell activation, of which ipilimumab-related hypophysitis (IH) is an