an increased risk for heart disease. Using a mouse model of mental stress induced by restraint, we mimic the biochemical and physiologic changes observed in chronically stressed humans, which is characterized by an increase in circulating glucocorticoids, such as cortisol. Middle-aged mice (6 months old) as well as old-aged mice (18 months old) were used to differentiate the effects of aging on the burden of mental stress associated cardiovascular disease. Genes implicated in cardiomyopathy and CVD were found to be significantly up-regulated, not only immediately after a two-week stress period, but remained significantly up-regulated after the mice were allowed to recover stress-free for 5 weeks. Gene expression of the glucocorticoid receptor was down-regulated following exposure to chronic stress, suggesting an involvement of the hypothalamic-pituitary axis negative feedback loop. Gene expression of markers for hypertrophy (MHY7, ACTA1, NPPB) were upregulated and persisted in upregulation after mice were allowed to recover. Hypertrophy was further indicated by heart weight to tibia length ratios. Significant changes in aortic samples also implicate an involvement of the vasculature. Chronic stress in humans and mice leads to an increase in inflammatory and pro-coagulant markers. In our study, inflammatory markers (LCN, IL-6, IL-17c, PTGS2) were shown to be significantly increased immediately after the period of chronic stress, however the markers return to non-significant levels when mice were allowed a recovery period. Chronic mental stress has a lasting and direct deleterious effect on the cardiovascular system and it is essential to understand these implications in an aging population.

Thyroid

THYROID NEOPLASIA AND CANCER

In Silico Analysis of Polymorphism rs2228638 in Neuropillin-1 Demonstrated That This Variant May Hinder EBV Entry into Epithelial Cells.

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The Epstein-Barr virus (EBV) is the first herpesvirus identified to be associated with human cancers and our group has demonstrated its association to thyroid cancer. It infects the vast majority of the world population causing latent and persistent infection, interfering in the metabolism of the host cells and triggering tumorigenic processes. Neuropillin-1 (NRP-1) is a type I transmembrane glycoprotein distributed on the cell surface of the virus, and considered vital for tumorigenesis. It has been demonstrated that EBV infection was increased by NRP1 expression. However, a conformational alteration of NRP1 could interfere with virus internalization into epithelial cells. The rs2228638 polymorphism of *NRP1* may modify the molecule tridimensional configuration. In order to better understand the role of this polymorphism, based on NCBI dbSNP and UniProt databases, we evaluated the effect of the amino acid change in the protein structure using bioinformatics tools including SIFT, Align GVGD, PolyPhen-2, SNAP, PANTHER, PredictSNP, nsSNPAnalyzer, PROVEAN, SNP&GO, PMut and MuPRO. PANTHER prediction indicated that the polymorphic variant could produce a change in function. MuPRO indicated that the amino acid exchange produced by the polymorphism decreases protein stability. However, none of these tools showed conformational alteration. In conclusion, the presence of the rs2228638 polymorphism of *NRP-1* may cause functional but not morphological changes that hinder EBV entry into the epithelial cells.

Pediatric Endocrinology

PEDIATRIC ENDOCRINE CASE REPORTS I

Gigantism and Hypothalamic Obesity: Rare Endocrine Manifestations of Neurofibromatosis Type 1

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Background: Neurofibromatosis type 1 (NF-1) is a heritable, autosomal dominant, multisystem disorder caused by mutations or deletions in *NF1*, with approximately 30-50% of cases arising from de novo mutations. In the pediatric population, growth hormone deficiency is among one of the most commonly described endocrine sequelae, although aberrations of pubertal development are also commonly seen.

Clinical Case: A 3-year-old female, who was clinically diagnosed with NF-1 at the age of 4 months based on the presence of multiple café-au-lait macules, underwent screening MRI, which noted a left optic glioma and a hypothalamic mass favored to represent a hypothalamic glioma. Review of her growth chart showed a height much greater than the 99th percentile, with an increase in height velocity beginning 1 year prior. Weight was also noted to be much greater than the 99th percentile, with an increase in weight gain coinciding with the timing of alterations in linear growth. Mid-parental height is at the 95th percentile, and the patient's height had tracked between the 86th and the 99th percentiles until age 2 years. Weight had tracked between the 68th and the 95th percentiles during that period. Initial laboratory evaluation showed an IGF-1 of 644 ng/mL (26-164 ng/mL). Gonadotropins were prepubertal; prolactin and thyroid studies were normal. ACTH stimulation demonstrated a rise in serum cortisol from 6.8 mcg/dL to 30.2 mcg/dL at 60 minutes. Growth hormone failed to suppress following an oral glucose load with a baseline GH of 4.4 ng/mL and values of 3.7, 6.5, 6.8, and 9.0 ng/mL at time +30, +60, +90, and +120 minutes respectively. Leuprolide stimulation did not