necrosis factor in the VAT and a trend (evident by effect size analysis only) for an increase in SAT and PCAT and 3) significant increase in PRAT and a trend toward increase in the macrophage marker CD68 expression in VAT. Among the thermogenic gene markers, the expression of UCP1 was significantly increased in VAT and PCAT with a trend for an increase in PRAT. The expression of UCP2 and PPAR gamma co-activator 1 beta (PPARGC1B) were also significantly elevated in VAT with a trend for an increase in SAT. These findings are indicative of depot-specific differences in prenatal T-induced inflammatory status with effects being pronounced in VAT compared to other depots. The increases in thermogenic markers in adipose depots do not support our hypothesis but rather are reflective of a compensatory response to promote adipose depot insulin sensitivity and may have a bearing on function of organs in the proximity of respective depots. These findings are likely of translational significance in metabolic disorders associated with hyperandrogenic state.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS II

Primary Neuroendocrine Tumor of the Central Nervous Sistem, a Case Report and Literature Review

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Introduction

Neuroendocrine Neoplasms are rare, with an incidence of 5 to 100,000 inhabitants, constituting 1% of all malignancies, presenting high survival rates in general, even in metastatic diseases. However, in those poorly differentiated, as in the following case, survival is around 4% in 5 years. We will describe a case of primary neuroendocrine tumor in the brain, of which is uncommon in the literature.Clinical case

A 26 years women was referred to the ER of Santa Casa de São Paulo, in January 2019, to be evaluated by neurosurgery, due to progressive left hemiparesis and headache for 3 months, which got worse in 4 days. On CT scan, there was a 6 x 6 cm solid-cystic, expansive, lesion in the right frontal lobe, with perilesional edema and contralateral midline 1.3cm deviation and subfalcine herniation.

Thus, the tumor was resected soon, with anatomopathological analysis showing poorly differentiated tumor of cells with scarce cytoplasm, hyperchromatic nuclei and high mitotic activity.

Immunohistochemical analysis finds 50% Ki67, with focal p53, TTF1, CD99, CD 56 and synaptophysin positivity. The main hypotheses, then, consisted of Neuroendocrine Carcinoma.

Four months after surgery, the patient reported worsening deficit, headache, pain, weight loss, being referred to the Emergency Room, once more. In RM an expansive lesion was found 6.6 x 4.4 cm, in the right

frontoparietal surgical cavity, edema, compression and 0,4 cm midline deviation.

The patient was once again submitted to emergency neurosurgery, with microsurgical resection. The pathology was identical to the previous one.

We proceed with hormonal evaluation, regarding to Medular Thyroid carcinoma, Gastrinoma, Insulinoma, Pheochromocytoma, Carcinoid tumor and others.

Imaging exams were also performed to investigate other primary sites: no changes in CT scan of the chest and abdomen and PET CT FDG. However, this one showed recurrence of the intracranial lesion, with three sites of involvement, all hypermetabolic: one of 4.1 x 2.9 cm (SUV 4.9) and another of 3.9 x 3.3 cm (SUV 8, 4) in the right frontoparietal region and medial nodule to the right thalamus of 1.2 cm (SUV 6.1).

Patient currently maintain left hemiparesis, frequent pain, taking carbamazepine due to epileptic seizures, and considerable weight loss. She has an important limitation of daily activities and basic self-care, with 50% Karnofsky scale. Due to relapse, palliative radiotherapy was initiated in the region of the tumors.

Conclusion

The patient had a poor outcome in relation to cancer, with little possibility of treatment due to poor tumor differentiation and poor performance status.

Adipose Tissue, Appetite, and Obesity

RARE CAUSES AND CONDITIONS OF OBESITY: PRADER WILLI SYNDROME, LIPODYSTROPHY

Identification of NASH Using Data from NHANES III

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Nonalcoholic steatohepatitis (NASH) is a serious liver condition marked by hepatic steatosis (HS), cell damage and inflammation. Patients with NASH are at risk for developing cirrhosis and hepatic cancer. Currently, the definitive method of diagnosing NASH is by liver biopsy. To avoid the costs and risks associated with biopsy procedures, there has been considerable effort to develop a non-invasive method of identifying patients with NASH. However, none of these methods has become accepted as a "gold standard." Our objective was to compare three non-invasive methods of identifying NASH by using data from NHANES III (1988-1994) to determine variables associated with published formulas to identify NASH. We used ultrasound data to identify subjects with moderate - severe HS. Among those with HS, we identified the NASH population using either the HAIR score, the NASH liver fat score, or the Gholam score. The HAIR score was developed in a sample of obese patients, is based on hypertension, insulin resistance and alanine transaminase (ALT) levels, and had an AUROC of 0.9, a sensitivity of 0.8, and a specificity of 0.89. The NASH liver fat score was developed in a Finnish population undergoing gastric bypass, and validated in an Italian population of liver biopsy patients. This score incorporates metabolic syndrome, type 2 diabetes, serum insulin, AST, and ALT. In the Finnish and Italian populations, respectively,

it had AUROCs of 0.73 and 0.74, sensitivities of 59.5 and 92.9, and specificities of 79.7 and 32.7. The Gholam score was developed in a sample of obese patients and uses aspartate aminotransferase (AST) and type 2 diabetes diagnosis. It had an AUROC of 0.82, a sensitivity of 0.76, and a specificity of 0.66. We performed multinomial logistic regression to compare each NASH population to the normal population (those with no or only mild HS). We identified 1236 subjects as having NASH by at least one method. 18% of these were identified by all 3 methods, while 20% were identified by 2 methods. All three methods identified significant risk factors for NASH ($p<0.05$) as being overweight or obese, having elevated AST or ALT levels, and having elevated C-peptide, serum glucose, or serum triglyceride levels. However, the HAIR and Gholam methods also identified being Mexican-American as a significant risk factor, with the NASH liver fat score did not. Being a former alcohol drinker and not meeting guidelines for physical activity were significant risk factors when using the NASH liver fat score. Further refinement of a noninvasive method for identifying NASH is required. Considerable care must be taken in interpreting risk factors, because the results differ depending which method is used. This could have implications in clinical practice as well, where patients and their risk factors may be mis-identified if formulas are used and not liver biopsy.

Diabetes Mellitus and Glucose Metabolism

TYPE 1 DIABETES MELLITUS

Transient Neonatal Diabetes Mellitus Triggered by EIF2AK3 and PTF1A Mutation

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SAT-681

Background: Neonatal diabetes mellitus (NDM) occurs within the first 6 months of life. Advances in molecular genetics have identified various causatives genes. Mutations in *EIF2AK3* causes Wolcott-Rallison syndrome characterized by NDM, multiple epiphyseal dysphasia and growth retardation. *PTF1A* is associated with the development of pancreas and cerebellum. Both *EIF2AK3* and *PTF1A* mutations are causative genes for permanent NDM with spontaneous and autosomal recessive inheritance. We report a neonate with transient NDM with both *EIF2AK3* and *PTF1A* variants confirmed by Sanger sequencing where each parent found to be a heterozygous carrier of each mutation. **Case presentation:** A two-day old boy was transferred from a local hospital due to hyperglycemia (blood glucose of 385 mg/dL) and glycosuria. Serum c-peptide (0.06 ng/mL) and insulin (0.64 μU/mL) were low. The patient did not present sings of ketoacidosis and was screened negative for pancreatic autoantibodies. The patient did not have any family history of diabetes. Molecular genetic analysis was performed and continuous infusion of intravenous insulin with pre-prandial bolus was started. Oral sulfonylurea therapy was attempted to prevent adverse neurocognitive outcome however, it showed no response and unable to stabilize blood glucose level. Targeted panel sequencing identified two different novel variants: a heterozygous missense mutation (c.3272G>T) in exon 17 of *EIF2AK3* gene and heterozygous missense mutation (c.53C > T) in exon 1 of *PTF1A* gene; both of which have not been previously reported and were no likely pathogenic variants. The patient's father confirmed to be heterozygous carriers of the *EIF2AK3* mutation while mother being heterozygous carriers of the *PTF1A* mutation. Blood glucose level gradually began to stabilize with insulin therapy, and upon discharge the patient switched to continuous subcutaneous insulin infusion (pump) with continuous glucose monitoring. **Conclusions:** NDM caused by in combination of *EIF2AK3* and *PTF1A* gene mutation is a rare condition and could resemble the disease progress of transient form of NDM. Although hyperglycemia might not be an issue of lifelong period, early genetic screening and prompt insulin initiation with consistent glucose monitoring are able to prevent further diabetic complications. In addition, the result of genetic testing in our patient raises the possibility of NDM as polygenic form of diabetes.

Diabetes Mellitus and Glucose Metabolism

ISLETS, LIVERS, PLACENTA, AND VASCULATURE — THE MULTITISSUE IMPACT OF DIABETES

Circadian Regulation of Chromatin State Mediates Pancreatic Islet Incretin Response

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Circadian Regulation of Chromatin State Mediates Pancreatic Incretin Response

The circadian clock is programmed by an autoregulatory transcription feedback loop present in brain and peripheral tissues that coordinates metabolism with nutritional state and the sleep-wake cycle. Epidemiologic and genetic studies indicate circadian disruption as a risk factor in the development of diabetes. We have demonstrated that conditional ablation of the β cell clock in adult life leads to hypoinsulinemic diabetes, and through mRNA-sequencing in mouse and human islets we revealed clock control of gene networks involved in insulin secretion, nutrient sensing, and exocytosis. A remaining question is: How does the core molecular clock modulate time-of-day dependent chromatin state to regulate pancreatic islet response to glucose and insulin secretagogues? Here we report that loss of the pancreatic β cell molecular clock results in closed chromatin at cAMP-responsive gene regulatory elements and dysregulated cAMP-dependent coregulator recruitment following cAMP agonism, consistent with a role for the molecular clock in mediating cell response to environmental stimuli. Further, tandem analyses of ATAC- and ChIP-sequencing in synchronized islets revealed dynamic chromatin accessibility across the 24-hour cycle at genes regulating insulin secretion and at genomic regions