gene expression for selected markers of beige adipocytes, including PAT2, CD137 and C/EBPβ, compared to control females. More crucially, thermogenically relevant UCP1 expression also did not differ between ERaKD females and controls. Taken together, these results suggest that knockdown of VMN ESR1 in adult female monkeys, while inducing modest weight gain after 1.5 years, may not markedly alter beige adipose gene expression of initially selected thermogenically relevant genes.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY

Expression of Programmed Death-Ligand 1 (PD-L1) in Human Pituitary Neuroendocrine Tumor

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MON-287

Introduction

Some Pituitary NeuroEndocrine Tumors (PitNET) present an aggressive evolution and are resistant to standard management. Immunotherapy have shown durable efficacy in a variety of malignancies. The aim of this study was to explore the programmed death-ligand 1 (PD-L1) expression in varied subtypes of pituitary adenomas with assessment of their clinical behavior at diagnosis and follow-up.

Methods

We conducted a retrospective monocentric study, including all patients operated a PitNET between 2012 and 2018. PDL-1 immunostaining were performed using an European Conformity-In-Vitro-Diagnostic labeled anti-PDL1 antibody (Clone 22C3). PD-L1 immunostaining was evaluated as the percentage of tumor cell showing positive membrane staining, into four grades: grade 0 = <1%, grade 1 = 1 to 5%, grade 2 = 6 to 49% and grade 3 = ≥ 50%. PD-L1 expression was compared with tumor features (secretion, proliferation, invasion) and outcome.

Results

The study included one hundred and thirty-nine PitNET, including 84 (60%) nonfunctioning adenomas. Twenty-five PitNET were PD-L1 positive (18%), including 3 grade 3, 8 grade 2 and 14 grade 1. PD-L1 expression was not different between functioning and non-functioning adenomas (p=0.26). Among sixteen tumors with proliferative markers (Ki-67 ≥ 3% and p53 positive), only one was PD-L1 positive.

Conclusion

In our series, pituitary tumors rarely exhibit PD-L1 expression and this immune marker did not seem to be associated with any biological characteristic or behavior of the pituitary

tumors. Thus, PD-L1 staining is necessary before considering PD-L1 blockage in PitNET, in case of therapeutic impasse.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY

TSH Deficiency in Patients on Somatostatin Analog for TSH-PitNET

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MON-288

Background: Somatostatin analogs (SSA) are efficiently used to control central hyperthyroidism in patients with thyrotropin-secreting pituitary neuroendocrine tumor (TSH-PitNET). The aim of this study was to describe the frequency of thyrotropin (TSH) deficiency under SSA in patients with TSH-PitNET. *Methods*: We retrospectively recruited patients presenting a central hyperthyroidism due to TSH-PitNET. Inclusion criteria were patients treated in first, second or third line by short or long-acting SSA, with central hyperthyroidism before SSA. Patients treated by radiotherapy or dopamine agonist were excluded. TSH deficiency was defined by either a low FT4 or low FT4 and FT3, associated with non-elevated TSH concentrations during SSA therapy. We analyzed the frequency of TSH deficiency and the characteristics of patients with or without TSH deficiency. *Results:* 46 patients were included in the study. SSA were used as the first-line therapy in 21 of 46 patients (46%). Central hyperthyroidism was controlled in 36 of 46 patients (78%). TSH deficiency appeared in 7 of 46 patients (15%), after a median time of 4 weeks (4–7) after the starting of SSA, and for a median duration of 3 months (2.5–3). The TSH deficiency occurred after 1 to 3 injections of long-acting SSA. There were no differences in terms of clinical and hormonal features and size of adenomas between patients with or without TSH deficiency. *Conclusions:* In patients with central hyperthyroidism due to TSH-PitNET, SSA can induce TSH deficiency. Thyrotropic function should be assessed before each injection of SSA in order to adapt the frequency of injection when control of thyrotoxicosis rather than tumor reduction is purpose of the treatment.

Reproductive Endocrinology

REPRODUCTIVE ENDOCRINOLOGY: REPRODUCTIVE FUNCTION AND DYSFUNCTION ON DEVELOPMENT

Does Androgen Exposure Result in Germline Transmission of PCOS-Like Phenotypes and Can It Be Reversed?

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MON-035

Daughters of women with polycystic ovary syndrome (PCOS) are more likely to be diagnosed with PCOS, including reproductive and metabolic dysfunctions. Our recent research has demonstrated that dihydrotestosterone (DHT) exposure during late pregnancy results in transgenerational transmission of PCOS susceptibility to female offspring. But it remains unclear whether the transmission of the PCOS-like phenotypes is induced by *in utero* environment or via germ cell reprogramming, and whether treatment by exercise or androgen receptor blocker, flutamide, can prevent disease transmission. To model PCOS condition, donor mice were implanted with a continuous releasing DHT or vehicle pellet at 4 weeks of age. A subset of DHT exposed F0 donors had either free access to running wheels or were implanted with a slow-releasing flutamide pellet. Mice were exposed with or without treatment for either 6 weeks before IVF or 10 weeks prior to phenotypic testing. Here we present the phenotype of the F0 donors and the result of IVF to generate first (F1) and second (F2) generation offspring. Donors weigh more already after 2 weeks of DHT exposure and had more fat mass with larger adipocyte size, impaired glucose tolerance, and heavier kidney after 10 weeks of androgenization, which was reversed by both flutamide and exercise intervention. Moreover, DHT exposure increased circulating androgens and donors were completely acyclic. Simultaneous treatment with flutamide reversed the elevated androstenedione, testosterone, and restored estrus cyclicity, indicating that androgen receptor blocker can reverse hyperandrogenemia and reproductive dysfunction, whereas exercise failed to improve these phenotypes. After 6 weeks of exposure or treatment, donor oocytes were superovulated for IVF. Fewer oocytes per donor were found in androgenized + flutamide lineage, but no significant difference was observed in oocyte to two-cell embryo conversion rate after fertilization among all groups. Although the number of live offspring at weaning was similar among all groups, a trend of more F1 male than female offspring was found in both androgenized and androgenized + exercise lineage. Similar results were obtained in the F1 females when generating F2 offspring by IVF, which androgenized + flutamide lineage showed fewer oocytes per donor upon superovulation and more F2 male than female offspring was obtained in androgenized lineage at weaning. We here show that the androgenized donors develop clear PCOS-like phenotypes and give rise to more male than female F1 and F2 offspring. While blocking androgen receptor reverses both metabolic and reproductive disturbance in the donor, it also shows a negative impact on the donor and F1 female oocyte maturation process, although number of offspring via IVF is not affected. Excercise, however, only reverses the metabolic phenotypes in the F0 donor mice with no impact on IVF outcome.

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SAT-381

Background: This is a case of improvement in visual analog scale pain rating and objective functional capacity in juvenile hypophosphatasia (HPP) following treatment with asfotase alfa and adjunct physical therapy (PT) performed in an aquatic environment. Clinical Case: A 45-year-old female with a history of psoriatic arthritis and osteoarthritis was referred for low serum alkaline phosphatase (ALKP) (<10 U/L). Her history of eight fractures over the preceding 25 years including bilateral femur nonunion repaired with rods eight years prior to presentation led to a diagnosis of juvenile HPP, and asfostase alfa was ordered. She is ambulatory only with a rolling walker from a deficit in dynamic standing balance and chronic pain. Referrals were made for both PT and pain management for these symptoms. The initial PT evaluation established reasonable goals to include the performance of in-home exercise, increase strength and range of motion, decrease pain, improve standing balance, and progress from walker to cane. Aquatic therapy was chosen in order to reduce patient's effective weight. The right hip complex, lumbar spine, and left leg were chosen as areas of focus based on pain reports. A four-week follow-up evaluation by the therapist reported patient had been performing at home exercises. Pain scale reports of the lumbar spine, right hip, and left leg were within the moderate range and near or meeting the patient's self-reported least pain experienced. Goniometric measurements of the right hip showed range of motion improvements averaging 9%. The lumbar spine's range of motion increased an average of 18%. Discussion: HPP is capable of creating severe disability, and its rarity has led to a dearth of investigation into appropriate treatment. Recommendations have been made previously for PT in children and infants presenting with juvenile or infantile HPP; this case suggests these recommendations are applicable to adults as well. The mechanisms of these improvements remain unclear; however, evidence exists that weight-bearing exercise may result in increased levels of bone-specific isoforms of ALKP. This endogenous path to increased serum ALKP may play a role in potentiating the effects of asfostase alfa. 1. Shapiro JR, Lewiecki EM. Hypophosphatasia in Adults: Clinical Assessment and Treatment Considerations. Journal of Bone and Mineral Research 2017;32(10):1977–1980. 2. Phillips D, Case LE, Griffin D, Hamilton K, Lara SL, Leiro B, Monfreda J, Westlake E, Kishnani PS. Physical therapy management of infants and children with hypophosphatasia. Molecular Genetics and Metabolism 2016;119(1–2):14–19. 3. Rudberg A, Magnusson P, Larsson L, Joborn H. Serum Isoforms of Bone Alkaline Phosphatase Increase During Physical Exercise in Women. Calcified Tissue International 2000;66(5):342–347.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Adjunct Benefit of Aquatic Therapy in Juvenile Hypophosphatasia Initiated in an Adult

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Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS I

A Case of Adrenal Cushings a Primary Hyperparathyroidism

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