C/EBPα and C/EBPβ, providing a potential positive feed-forward loop. Notably, we observed that C/EBPα and C/EBPβ mRNA and protein were markedly reduced in *Src-1/-2$^{d/d}$* fetal lungs, compared to WT. Deletion of the *Cebpa* gene in respiratory epithelium of fetal mice caused respiratory failure at birth due to surfactant lipid and protein deficiency. This was associated with increased expression of *TGF-β2*, which inhibits fetal lung maturation. Notably, we observed that expression of TGF-β2 and TGF-β3 were increased in *Src-1/-2$^{d/d}$* fetal lungs. Thus, impaired lung development, surfactant synthesis and delayed parturition in *Src-1/-2$^{d/d}$* fetuses are likely caused by decreased 11β-HSD1 and GR signaling, resulting in decreased *C/EBPα/β* expression and increased TGF-β signaling.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS II

MULTIPLE ENDOCRINE NEOPLASIA TYPE 2A: Familiar Case Report

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MON-906

Introduction: Multiple endocrine neoplasia type 2A (MEN 2A) is a autosomal dominant transmission inherited syndrome which oncogenesis is based on germline mutations with RET proto-oncogene function gain. Patients have medullary thyroid carcinoma (CMT) and some develop unilateral or bilateral pheochromocytoma and/or primary hyperparathyroidism, its frequency depends on the inherited RET mutation. We present a case of a mother and daughter with marfanoid habitus and MEN 2A syndrome confirmed by genetic analysis that identified mutation in the RET gene, codon 634.**Clinical cases:** 35-year-old woman with weight loss, sweating, nausea, hypertensive peaks, syncope episodes and marfanoid habitus, with plasma metanephrines 9.1nmol/L (RV<0.5), bilateral adrenal tumors on MRI (4.7x4.5x3.3 cm left adrenal and 7.4x7.3x6.3 cm) and MIBG scintigraphy high uptake bilateral, with diagnosis of bilateral pheochromocytoma. She also had calcitonin 49.40pg/mL (RV<6.4), calcium 11.9mg/dL (RV 8.6-10.2), PTH 372.7pg/mL (RV15-65) and cervical ultrasound (USG) with solid and hypoechogenic thyroid nodule, diagnosed with CMT and primary hyperparathyroidism with 6 possible parathyroid glands by SPECT CT scintigraphy. Genetic panel by NGS identify germline mutation in RET códon 634 - minsense mutation: c.1900T>C. The patient denied prior family history. In the familiar screening, her 18-year-old daughter has a marfanoid habitus, serum calcitonin 48.8pg /mL (RV<9.8), CEA 3.8ng/mL(RV<3.0), cervical USG shows a thyroid nodule of 0.7x0.5x0.5cm, solid, hypoechoic, with microcalcifications and a central compartiment lymph node, whose puncture calcitonin > 2000pg/mL and 118pg/mL, respectively. She features plasma metanephrines 0.5mmol/L (RV<0.5), normal plasma normetanephrines, MIBG scintigraphy and adrenal MRI without alterations and absence of primary hyperparathyroidism. She has the same mutation as her mother.**Conclusion:** Although rare, it is essential to know the clinical and laboratory changes in MEN 2A in order to enable early diagnosis and treatment. Also, investigate every first-degree relative is important so complications and mortality of this syndrome can be reduced.

Adrenal

ADRENAL - HYPERTENSION

Germline SDHB Exon 1 Deletion Is Associated with Absence of ^{131}I-metaiodobenzylguanidine (MIBG) Uptake in Malignant Paragangliomas

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MON-202

Introduction: Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumors arising from chromaffin cells. More than 30% of patients with PPGLs have a hereditary predisposition. Malignancy in PPGLs is defined by the presence of local invasion or metastasis in nonchromaffin tissues. Germline *SDHB* mutations are found in approximately 40% of malignant PPGLs, mainly paragangliomas (PGLs). However, *SDHB* mutations are not a prognostic factor in malignant PPGLs. To date, no genotype-phenotype correlation has been reported in malignant PPGLs associated with *SDHB* mutations. **Aim:** To investigate clinical and imaging features of patients with malignant PGLs harboring germline *SDHB* exon 1 deletion or splicing site mutation. **Methods:** We retrospectively evaluated 22 unrelated individuals with malignant PPGLs. Six out of 22 (27%) malignant PPGLs harbored germline *SDHB* mutations. Three patients had *SDHB* exon 1 deletion and 3 splicing site mutation (2 with c.201-2A>G and one with c.423 + 1G>A). All *SDHB* defects were classified as likely pathogenic. **Results:** In the exon 1 deletion group, 2 patients had abdominal PGLs (one also had a neck PGL) and one had only head and neck PGLs. In the splicing site mutation group, all 3 patients had abdominal PGLs (one also had a neck PGL). Median age at diagnosis was 26 yrs (16 to 45) and 33 yrs (26 to 53) in the exon 1 deletion and splicing mutation groups, respectively. Two patients (one in each group) had metastasis at diagnosis. All 6 patients had bone metastasis, but liver and/or lung metastasis were more frequent in patients with

SDHB exon 1 deletion (66 *vs.* 33%). Interestingly, metastasis from malignant PGLs harboring *SDHB* splicing site mutations were ^{131}I-metaiodobenzylguanidine (MIBG) avid in all cases, whereas metastatic lesions from malignant PGLs harboring *SDHB* exon 1 deletion did not present any MIBG uptake on diagnostic imaging studies. Therefore, all 3 patients with *SDHB* exon 1 deletion were treated with chemotherapy (cyclophosphamide, vincristine and dacarbazine). In contrast, all 3 patients with splicing site mutations have been treated with MIBG therapy. Median follow-up was 87 months (8 to 360 months). Only one patient (exon 1deletion group) died because of disease progression. **Conclusion:** We first demonstrated here that germline *SDHB* exon 1 deletion is associated with absence of MIBG uptake in malignant PGLs. This finding needs to be confirmed in an expanded cohort of malignant PPGLs.

Bone and Mineral Metabolism

CLINICAL ASPECTS OF OSTEOPOROSIS AND VITAMIN D ACTION

Evaluation of Bone Mass in Transgender Women After Gender Affirming Surgery - a Pilot Study

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MON-393

Estrogen deficiency is classically associated with bone loss in both men and women. In transgender women, after being submitted to gender-affirming surgery (GAS), the main goal of hormone therapy (HT) is to maintain the female phenotype and prevent the consequences of the orchiectomy-related hypogonadal state. The aim of this study was to evaluate the impact of GAS on bone mass in transgender women. A total of 142 trans women attending the outpatient Gender Identity Program were sequentially enrolled. Patients aged < 20 and > 60 years (n=15), with gluteal silicone prosthesis (n=26) and without FSH dosage after surgery (n=9) were excluded. Anthropometric evaluation, laboratory tests and dual-energy X-ray absorptiometry (DXA) were performed in all patients during the follow-up. In women undergoing CAS (CAS-Y), DXA was performed at least 12 months after surgery and with estrogen therapy. In the other women (CAS-N), tests were performed after at least 3 months of standardized treatment (estradiol plus spironolactone or cyproterone acetate). Patients with testosterone values still above the reference for women were not excluded as long as they were on regular HT. Ninety two trans women were included. Among them, 30 had performed CAS, and had DXA assessment performed 37 months (21-78) after surgery. The mean age and BMI were 37 years (33 - 46) and 24.9 kg/m² (23.1 - 27.5) in patients CAS - Y and 30 years (24 - 36) and 24.3 kg/m² (21.5 - 28.5) in patients CAS - N. Trans women CAS-Y were significantly older (p=0.000). No difference was observed regarding estradiol levels between the groups [105.7pmol/L (48.4-207.8) and 147.5 pmol/L (71.9-284.5), p=0.622]. Free androgen index (FAI) was significantly higher [0.45 (0.17 - 1.63) and 4.47 (0.70 - 36.4), p=0.002] and FSH significantly lower [60.4mIU/ml (37.9 - 75.6) and 2.6mIU/ml (0.6 - 4.4), p=0.000] in trans women CAS - N. BMD (g/cm²) and Z-score of lumbar spine, femoral neck and total femur did not differ significantly between the groups. Considering all participants, the lumbar spine BMD was negatively correlated with FSH levels (r=-0.343, p=0.005), which remained significant even after adjustments for FAI. When only CAS - Y trans women were considered, a negative correlation was found between FSH levels and lumbar spine (r=-0.598, p=0.001) and hip (r=-0.404, p=0.033) BMD. In a multiple regression model adjusted for age and surgery, women with FSH > 35 mIU/ml presented a prevalence rate ratio of 11.79 for low bone mass (p=0.040, IC 95% 1.19 - 124.39). The results of this pilot study in trans women show no difference in bone mass according to GAS status. However, long-term elevated FSH levels observed in some post GAS - trans women, even on HT, presented a negative association with bone mass. Further studies with greater sample sizes are needed to confirm the impact of GAS on bone mass and fracture risk.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS II

Low Bone Mineral Density Does Not Equal Osteoporosis: The Finding of XLHR with a Novel Phex Mutation.

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MON-373

Introduction: X-linked Hypophosphatemic rickets (XLHR) is a rare form of rickets that mainly affects children but, in some cases, it can be missed and not diagnosed until later in life. We present a post-menopausal female that was misdiagnosed with osteoporosis for many years until complete work up was done, and she was found to have osteomalacia due to hypophosphatemia. **Clinical case:** A 59-year-old female was evaluated following admission to the hospital for a worsening femur fracture on imaging and had received ORIF. She was diagnosed with osteoporosis at the age of 45 and endorses a history of multiple femur fractures from low impact trauma. Despite previous bisphosphonate therapy, she continued to have recurrent fractures.[RC1] She reported no family history of early osteoporosis, but her mother was diagnosed with rickets as a child. Secondary workup for osteoporosis revealed normal 25OH vitamin D, SPEP, TSH, PTH and serum calcium, endomysial antibodies, and 24-hour urine calcium levels. However, the patient had persistently elevated alkaline phosphatase levels (150-200) and low phosphate levels (1.8-2.4). This raised the possibility of Paget's disease, so a bone scan and lumbar X-ray were obtained which were normal. Given low phosphate levels, fibroblast growth factor (FGF)-23 was obtained and was elevated. This left the differential between tumor-induced osteomalacia (TIO)