(DHEAS), androstenedione, testosterone, estrone, estradiol, estriol, insulin and TNF-α were measured by RIA or ELISA. Glycemia and lipid profile were also analyzed. In placental samples, the gene expression of MFS2D2A, CD36, FABP4, SLC27A4, PPARG, LPL and DGAT were determined by quantitative PCR. No differences were observed in sex steroid concentrations and metabolic parameters between groups. On the other hand, the gene expression of MFS2D2A, CD36 and FABP4 were higher in placentas from women with obesity compared to women with normal-weight (P = 0.050, P = 0.037 and P = 0.038, respectively). When distributed according to fetal sex, cholesterol levels were higher in cord blood of women with obesity and female fetuses (P = 0.005), whereas glycemia was lower in women with obesity and male fetuses (P = 0.045). In turn, the gene expression of CD36 and FABP4 were higher (P = 0.024 and P = 0.034, respectively), whereas MFS2D2A tended to be higher (P = 0.092) only in placentas from women with obesity and male fetuses. Moreover, in women with obesity and male fetuses, glycemia was positively correlated with MFS2D2A (r = 0.650; P = 0.02), and in women with obesity and female fetuses FABP4 was inversely correlated with triglyceride levels (r = -0.580; P = 0.048). In conclusion, these data suggest that modifications in placental steroidogenesis do not affect sex steroid serum concentrations in the fetal circulation. On the other hand, metabolic parameters in cord blood of pregnant women with obesity are associated with an abnormal expression of FA transporters in placental tissue.

Tumor Biology
ENDOCRINE NEOPLASIA CASE REPORTS III

Primary Hyperparathyroidism and Meningioma as a Part of Multiple Endocrine Neoplasm Type 1 (MEN Type 1)
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SAT-LB308
Background: Meningioma is a rare association of Multiple endocrine neoplasia type 1 (MEN 1) and very few cases has been reported in literature. Clinical Case: a 75-year-old woman showed severe headache, disturbed consciousness and convulsions. A diagnosis of cerebral meningioma was made and surgical excision was done, histopathological examination confirmed meningioma; patient was transferred to the ICU postoperatively for monitoring. Patient's consciousness was not regained in full and remained in delirium, follow up investigations revealed: serum calcium of 13.2 mg/dl (8.5 to 10.5 mg/dl), serum sodium 141 mmol/L (135-145 mmol/L) and potassium 4.9 mmol/L (3.5-5 mmol/L), serum parathormone of 850 pg/mL (10-65 pg/mL), primary hyperparathyroidism was suspected; further investigations revealed inferior parathyroid adenoma on ultrasound which elicited focal tracer uptake on sesta-mibi parathyroid scintigraphy. Patient did excision of the lesion and was confirmed by histopathological examination to be parathyroid adenoma. Patient recovered well postoperatively, consciousness was regained and no neurological defects were present. Genetic studies where performed and was found positive for MEN type 1 gene. Whole body Ga-DOTATE PET/CT was then done to exclude any associated tumors and no tracer uptake was found. Patient was discharged, family members were offered genetic analysis and were counselled on the importance of screening. Conclusion: MEN type 1 can rarely present with meningiomas with symptoms very similar and easily confused with hypercalcemia and the diagnosis can be missed.

Thyroid
THYROID CANCER CASE REPORTS I

Coexistence of Medullary Thyroid Cancer With Graves Disease: A Case Report
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SUN-LB82
Coexistence of Medullary Thyroid Cancer with Graves Disease: A Case Report
A 59 year old woman presented with enlarged thyroid, weight loss, and hot flushes. She had previously been treated for a thyroid problem in 2013 but was lost to follow up. On exam, she had a diffusely enlarged thyroid gland, without distinct nodule. She had brisk DTR’s and mild tremor. Lab results confirmed hyperthyroidism:TSH <0.01 mIU/L (0.27 to 4.2) FT4 2.4 ng/dL (0.9 to 1.8) FT3 7.95 pg/mL (1.8 to 4.6). TSI was 307 % (<140%). Thyroid ultrasound showed a few sub-centimeter nodules, and 2 clinically significant nodules on the right--1.5 x 1.2 x 1.4 cm, cystic with calcifications; and 1.3 x 0.7 x 1.2 cm hypoechoic. I-123 thyroid uptake/scan showed 61% uptake and 2 right sided cold nodules. FNA biopsy showed medullary thyroid carcinoma (MTC) with staining positive for calcitonin and negative for thyroglobulin. CT thyroid showed no adenopathy. Serum calcitonin was 71 pg/mL (<5), and CEA was elevated 5.4 ng/mL (<2.5). Work up was negative for pheochromocytoma and hyperparathyroidism. After pretreatment with methimazole, she underwent total thyroidectomy with bilateral TE groove dissection. Surgical pathology confirmed MTC pT1b pN1a. She was started on levothyroxine therapy post operatively.

Discussion There are multiple reports of thyroid carcinoma (papillary and follicular) in Graves disease, but rarely MTC. A recent systematic review reports only 21 total cases of MTC in patients with hyperthyroidism, of whom 15 had Graves disease. MTC is derived from C-cells from the thyroid gland rather than from follicular cells. TSI, therefore, should not influence development or growth of MTC. Coexistence of the two conditions is likely coincidental rather than causative.

Conclusion Thyroid nodules in patients with Graves should be worked up as there is a possibility of co-existing thyroid carcinoma. This patient had hyperthyroidism with cold nodules on nuclear scan corresponding to sonographic nodules. Based on these results, she had biopsy leading to diagnosis of MTC. Follow up surgery lead to diagnosis of MTC at earlier stage and provided treatment for both conditions.
References
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Neuroendocrinology and Pituitary TUMORS I
METTL3 Promotes Sparsely Granulated GH-Secreting Pituitary Adenomas to Behavior as Densely Granulated Adenomas
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SAT-LB61
Background: Growth hormone (GH)-secreting pituitary adenomas can be divided into densely and sparsely granulated subtypes, based on electron microscopic studies. The latter are frequently associated with more invasive behavior, and respond worse to somatostatin analogues. The underlying mechanisms are largely unknown. Increasing evidence showed that N6-methyladenosine (m6A) of messenger RNAs (mRNAs) participated in the development of various tumors. We aimed to investigate the role of RNA m6A modification in the classification of GH-secreting pituitary adenomas. Methods: The main components of m6A methyltransferase complex, demethylase, and RNA m6A levels were compared between sparsely and densely GH-secreting tumors. The role of METTL3 was functionally studied. Results: The level of m6A methyltransferases (METTL3, WTAP and METTL14) and demethylase (FTO and ALKBH5) were significantly downregulated in GH adenomas, comparing to the normal pituitary tissues. However, only METTL3 and METTL14 were shown to significantly higher in densely granulated tumors than those in sparsely ones. Consistently, the level of RNA m6A was markedly increased in densely granulated GH adenomas. In addition, the expression of METTL3 was positively correlated with the level of RNA m6A among tumor samples, and METTL3 silencing decreased RNA m6A of GH3 cells. METTL3 was demonstrated to function as a tumor suppressor based on in vivo and in vitro evidence, using patient-derived and GH3 cells. Moreover, the sensitivity of GH3 cells to pasireotide was increased with METTL3 overexpression, but decreased when METTL3 was silenced. Consistently, METTL3 silencing inhibited GH secretory, and decreased the expression of SSTR2 and SSTR5. Conclusions: METTL3 functions as a tumor suppressor in GH secreting adenomas, and enhance tumor cells sensitivity to medical treatment. Our work uncovers the critical roles of METTL3 in the pathogenesis of GH adenomas, since it potentially promotes the transition from sparsely to densely granulated subtypes.

MON-LB48
Title: The genomic landscape of sporadic thyrotrophinomas
Background: Thyrotrophinoma (TSHoma) is rare and knowledge on the genomic landscape of this tumour type is very limited.
Aim: To perform whole-exome sequencing (WES) in a population of TSHomas to identify recurrent somatic genetic events
Method: WES was performed on paired tumour and germline DNA of 7 patients with TSHomas. Three tissue samples were formalin-fixed paraffin-embedded and 4 fresh frozen tumour samples. Fresh blood samples were also collected from each patient. The average of mean depth of coverage amongst all samples was 129X, and 97% of target bases were covered ≥20X.
Results: Four (57%) of the seven patients were male and median age at diagnosis was 52 years. (IQR 46, 60) Six patients (86%) had macroadenomas. Four patients (57%) had central thyrotoxicosis at diagnosis and three patients’ tumour stained positive for TSH on histology examination. Two patients (29%) had growth hormone co-secreting tumours. In total, 69 somatic variants were identified to be of potential interest, averaging 1.4 variants per million base-pair of DNA read. No variants were observed in germline DNA of 7 patients with TSHomas. Three tissue samples were formalin-fixed paraffin-embedded and 4 fresh frozen tumour samples. Fresh blood samples were also collected from each patient. The average of mean depth of coverage amongst all samples was 129X, and 97% of target bases were covered ≥20X.

Neuroendocrinology and Pituitary TUMORS II
Title: The Genomic Landscape of Sporadic Thyrotrophinomas
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Aim: To perform whole-exome sequencing (WES) in a population of TSHomas to identify recurrent somatic genetic events
Method: WES was performed on paired tumour and germline DNA of 7 patients with TSHomas. Three tissue samples were formalin-fixed paraffin-embedded and 4 fresh frozen tumour samples. Fresh blood samples were also collected from each patient. The average of mean depth of coverage amongst all samples was 129X, and 97% of target bases were covered ≥20X.
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