CO103. PANHIPOPITUITARISMO FAMILIAR POR MUTAÇÃO DO GENE PROP1: 4 DE 7 IRMÃOS AFECTADOS

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Introdução: As mutações no gene PROP1 (Prophet of Pit-1) são a causa genética mais frequente de panhipopituitarismo, uma condição associada à deficiência ou produção inadequada de hormonas da hipófise anterior. O gene PROP1 codifica um factor de transcrição envolvido na ontogênese, diferenciação e função dos somatotrófos, lactotrófos, e tireotrófos. Estas mutações caracterizam-se por uma notável variabilidade clínica, incluindo o início do aparecimento das deficiências hormonais, dimensões hipofisárias e secreção de cortisol.

Caso clínico: Família de pais consanguíneos (primos em segundo grau), composta por 8 irmãos, 4 com o diagnóstico de panhipopituitarismo, seguidos em consulta de Endocrinologia, 3 saudáveis e 1 nado-morto. Dois irmãos do sexo masculino, 41 e 45 anos, com diagnóstico inicial de nanismo aos 9 e 12 anos de idade, respetivamente, tendo sido detetada posteriormente deficiência de TSH, FSH/LH e prolactina, em ambos e também de cortisol no último. As 2 irmãs têm 46 e 50 anos de idade e diagnóstico de panhipopituitarismo, com deficiência de GH, TSH, FSH/LH, prolactina e cortisol, aos 15 e aos 9 anos de idade, respetivamente. Sem história familiar prévia de panhipopituitarismo. Foi efectuado o estudo genético, tendo sido possível detectar nos 4 irmãos uma mutação homozigótica no gene PROP1 (c.301-302delAG).

Discussão: Esta família demontra descreve a variabilidade da expressão clínica e a progressiva alteração funcional hipofisária nomeadamente da secreção de cortisol nos portadores de mutações do gene PROP1.

CO104. CARDIOVASCULAR RISK FACTORS IN ACROMEGALY

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Objective: Cardiovascular (CV) disease is one of the most important causes of death in acromegalic patients (ACR). The aim of this study is to compare these CV risk factors between and a control population and to evaluate the effectiveness of control of the disease.

Methods: 10 ACR with active disease (ACRAct) and 12 with controlled disease (ACRCd) were evaluated for blood pressure (BP), body mass index (BMI), fasting glucose, coagulation status and lipidic profile. A group of 11 subjects with non-functioning pituitary adenomas was used as control population.

Results: ACRAct group had the highest mean BP, and ACRCd group the highest BMI. However, diastolic BP was lowest in ACRCd. Total cholesterol was slightly higher in ACRAct than controls (ns). When compared with ACRCt, the difference was significant (ACRAct having higher levels). HDL-C was higher in ACR, being significantly different between ACRCd and controls. Triglycerides were not significantly different among the three groups. Blood glucose was significantly higher in ACRCd and higher with borderline significance in ACRAct, when compared separately with control group. When categorizing patients as having hyperglycemia, hypertension and hyperlipidemia, higher percentages of all three variables were found in ACR when compared with controls. Significant correlation between those categories and the three studied groups was found only in hyperglycemia ($p = 0.002$). Regarding coagulation status, the fibrinogen levels were significantly higher in ACR when compared with control group. ATIII was significantly higher in ACRAct when compared controls and ACRCd. When considering all ACR, significant positive correlation was found between ATIII and IGF-1 levels ($r = 0.654$; $p = 0.001$) and ATIII and GH levels ($r = 0.498$; $p = 0.013$). A positive, significant correlation was found between glucose levels and BMI ($r = 0.478$;$p = 0.005$) and glucose and SBP ($r = 0.428$; $p = 0.013$). Coagulation factor II levels were slightly higher in ACRAct than in controls and ACRCd (ns). When evaluating correlation among variables in all patients, a positive significant correlation was found between coagulation factor II and IGF-1 levels ($r = 0.569$, $p = 0.004$). A positive significant correlation was found between PAI-1 levels and BMI, coagulation factor VIII, ATIII and Protein C. Positive significant correlation was also found between coagulation factor II levels and fibrinogen and ATIIIT.

Conclusions: There is some reduction in CV risk factors with control of the disease, but possibly without return to basal levels.

CO105. OCCULT ECTOPIC CUSHING'S SYNDROME

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Introduction: Cushing`s Syndrome (CS) can be ACTH-dependent, caused by ACTH-secreting pituitary and ectopic tumors, or ACTH-independent, caused by cortisol-secreting adrenal tumors. The ectopic secretion of ACTH represents around 10% of ACTH-dependent CS and some remain unknown, even with the currently available imaging studies.

Case report: A 41 year-old woman, with a past history of DM, dyslipidemia, polyarthralgias, presented with complaints of weight gain (20 kg), hirsutism and depression. Physical exam showed typical cushingoid appearence. Endocrine studies showed elevated 24-h UFC (522 μg/24h) with basal ACTH 29,2 ng/L, overnight 1 mg dexamethasone suppression test of 29.2 ug/L. She also had non-suppressible cortisol levels in a standard two-day 2 mg test. CRH stimulation test was positive. Pituitary MRI was normal and bilateral Inferior Petrosal Sinus Sampling had no central to peripheral ACTH gradient. Cervico-thoracic MRI scan was normal and abdominal MRI revealed a left adrenal nodule. Octreoscan showed one small left adrenal nodule and an uptake on the right thyroid lobe. FNA of the thyroid nodule showed colloid nature. PET-DOTA-NOC was unremarkable. Considering the severity of the symptoms she was started on methyrapone in increasing dosis and ketoconazole. Six months later she repeated the Octreoscan, showing the thyroid nodule, but failing to reveal the left adrenal nodule. Thoracic CT scans with Mini MIp reconstruction of the "respiratory tree" were normal. 18 months later she was submitted to bilateral laparoscopic adrenalectomy. The pathological exam showed a macroscopic (1.9 cm) adenoma on the right adrenal and microscopic adenoma on the left adrenal.

Conclusions: Despite advances in laboratory and imaging techniques, CS from ectopic ACTH secretion remains a difficult diagnostic and therapeutic challenge. It is essential, however, that patients treated with medication and palliative adrenalectomy pursue imaging studies to locate the tumor because of a small, but real chance of malignancy.