Adrenal

ADRENAAL - TUMORS

Advantage and Trustworthiness of Cortisol and Dexamethasone Evaluation in Different Biological Matrices in Patients with Adrenal Masses.

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SAT-166

Advantage and trustworthy of cortisol and dexamethasone evaluation in different biological matrices in patients with adrenal masses.

Biochemical function of adrenal masses is currently based on 1mg post-overnight dexamethasone suppression test (pDST). Several approaches are recently developed, in order to reduce false positive/negative samples, only in retrospective series. They are based on the correlation of some different parameters, i.e. late-night salivary cortisol (LNSC) vs serum and salivary cortisol pDST; LNSC vs serum and salivary cortisol and serum dexamethasone pDST; LNSC and cortisol vs serum cortisol and salivary cortisol and cortisone pDST. Although these findings offer a better diagnostic performance, several conditions are still disappointed. No information is traceable about the harvest time of diurnal salivary and serum samples and no study include neither the levels of salivary nor urinary dexamethasone pDST. Aim of our study is to combine all these strategies in order to avoid the underestimated biases and obtain more precise information about the true “cortisol condition” of the patients.

To reach this purpose we assess both cortisol and dexamethasone concentrations in several samples: saliva at 11PM before the drug administration, diurnal saliva and serum at 8AM and also the urine collection from 11PM to 8AM. Analytes levels are measured using a validated liquid chromatography-tandem mass spectrometry method. In this study we included 20 subjects without morphological adrenal alteration (MRI assessment), dyslipidemia, hypertension and impaired glucose tolerance (healthy controls) and 20 patients with adrenal incidentaloma showing different cortisol levels ranging from normal to ACTH-independent hypercortisolism. In both series, LNSC were similar to salivary cortisol pDST, even if they were greater in the patients with adrenal incidentalomas and subclinical cortisol secretion. Serum dexamethasone levels were in reference ranges, while salivary and urinary dexamethasone found in these matrices require additional sample numbers in order to establish appropriate cut-offs. Our preliminary results suggest that the combination of these findings could represent an improvement to assess the individual cortisol status.

Neuroendocrinology and Pituitary

PITUITARY TUMORS I

Integrated Analysis of Pituitary Adenoma Using Novel Approach of Non-Target Proteomics Along with RNA-Sequencing Analyses

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SAT-309

Objective: To clarify the relationship between proteomic expression and clinical feature of pituitary adenomas. Methods: We have previously developed non-target proteomics analysis, which enables to detect and quantify approximately 7,000 to 9,000 kinds of protein weve, in parallel with RNA-seq analysis, and then subjected to 14 cases of pituitary adenoma surgically removed at Chiba University Hospital. Bioinformatic evaluation including DEGs, heatmap and PCA analyses was performed to reveal underlying their molecular pathogenesis. Results: We successfully identified 789 differentially expressed proteins and 593 DEGs in non-target proteomics and RNA-seq, respectively. Intriguingly, PCA analysis demonstrated that tumors were clearly divided into 3 groups based on protein expression profile; functional pituitary adenomas consisting of two subtypes depending on Pit1 and T-pit lineage, and non-functional tumors consisting of two distinct subtypes, with properties close to functional tumors and unique characteristics of hard tumor difficult to remove by endoscopic surgery. To address the underlying molecular biological functions in each group clustering analysis and heat-map were performed and we found that 3 groups were separated clearly with their own both gene and protein expression profile. Indeed, for instance, GO term of plasma membrane part was significantly enriched in hard tumor group, pathways of GH receptor signaling, GH hormone synthesis as in GH-positive group. Conclusions: We herein demonstrate that pituitary adenoma can be uniquely separated into certain categories through our novel non-target proteomics with coupling to RNA-seq, particularly providing novel group of hard tumor characteristics with enriched expression of both protein and mRNA in plasma membrane part. Thus our method would be beneficial and useful to elucidate underlying molecular pathogenesis for pituitary tumors, while further analysis is required.

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ADRENAAL CASE REPORTS I

A Case of Hypoplastic Left Heart Syndrome and Paraganglioma

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SAT-191

INTRODUCTION:

Cyanotic heart disease and paragangliomas are two rare diagnosis. Co-occurrence of congenital cyanotic heart disease and pheochromocytomas/paragangliomas has been described, but the mechanism is unclear. In those patients where immediate cyanosis resulting from the congenital heart disease happens right after birth there is an association with an earlier detection of tumor compared to those with cyanotic heart disease later in life (26.6 years vs 46.3 years respectively) [1]. The objective of this case is to highlight this association, as a high degree of suspicion needs to be
had when caring for individuals with cyanotic heart disease to pursue evaluation of these tumors. CASE: A 23-year-old man with a chief complaint of diffuse abdominal pain was found to have a 2.6 x 2.8 cm smoothly margined soft tissue mass in the right lower quadrant on abdominal computed tomography. Patient had a known history of hypoplastic left heart syndrome (mitral atresia-aortic atresia) who had undergone a three-stage Norwood repair in childhood. In his adulthood was diagnosed with Central Adrenal Insufficiency, and Type 2 Diabetes Mellitus. At the time of presentation patient was short of breath, tachycardic (heart rate 115), and tender to palpation of his right lower quadrant. Plasma normetanephrines were 3.8 nmol/L (normal < 0.9 nmol/L), 24-hour urinary excretion of normetanephrine was 1117 mcg/24h (normal 103-390 mcg/24h). Plasma metanephrine levels were normal. A nuclear medicine whole body scan with metaiodobenzylguanidine (MIBG) scan confirmed a MIBG avid tumor in the right lower quadrant. Preoperative management was initiated with oral doxazosin. He underwent laparoscopic surgery with removal of a 3 cm pelvis mass resected from the retroperitoneal tissue deep to the peritoneum along the gonadal vein and ureter. Final pathology confirmed the diagnosis of a paraganglioma. Postoperatively, plasma normetanephrines were corrected at 0.86 nmol/L. Patient underwent genetic testing that was negative for FH, MAX, MEN1, NF1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127 and VHL. CONCLUSION: Multidisciplinary approach to these patients is essential given their complex hemodynamics. Long term follow up is necessary to monitor for tumor recurrence, review of case reports may suggest a higher risk of recurrence [1]. Of these case reports there has been no strong genetic association found, the most popular theory is a causal relationship from their cyanotic heart disease.

References:
Zhao B, Zhou Y, Zhao Y et al (2018) Co-occurrence of pheochromocytoma-paraganglioma and cyanotic congenital heart disease: A case report and literature review. Front Endocrinol. https://doi.org/10.3389/fendo.2018.00165

Adrenal
ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

Evaluation of Adrenal Insufficiency and Recovery in Rheumatology Patients on Long-Term Glucocorticoid Therapy
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MON-189
Background
Long-term glucocorticoid (GC) therapy is commonly used to treat rheumatological conditions. This may result in tertiary adrenal insufficiency, as a result of suppression of the HPA axis, when GC doses are weaned/withdrawn. There is little published data about tertiary adrenal insufficiency in this group. This study aims to further evaluate prevalence, characteristics and recovery of adrenal insufficiency in these patients at a large UK teaching hospital.

Methods
We retrospectively identified patients seen in outpatient clinics between January 2014 and September 2019 who had received tapering doses of long-term GC to treat their underlying condition (largely patients with polymyalgia rheumatica, giant cell arteritis or other vasculitis) and had either had a 9am cortisol or short synacthen test (SST). Data were collected using a standardised proforma.

Results
There was a total of 238 patients, median age of 71 years with a female preponderance (75%). Mean duration of glucocorticoid use was 63.3 months. Mean peak dose of glucocorticoid was 29.2 mg.

142 patients had 9am cortisol as the first line test to assess adrenal function. 65% of these were considered sub-optimal based on local protocol (cortisol <350 nmol/L). 38% of these patients went on to have SST, of which 56% continued to show evidence of sub-optimal cortisol production. All patients where baseline 9am cortisol was <100 nmol/L failed to reach stimulated cortisol of >500 nmol/L on SST, whereas 31% failed SST if 9am cortisol was 250-350 nmol/L. In total 138 SSTs were performed of which 51% (n=70) were abnormal (cortisol <500 nmol/L post synacthen). When baseline cortisol was <100 nmol/L on SST, all patients had a suboptimal peak response. However, where baseline cortisol on SST was >350 nmol/L only 3% had a sub-optimal peak cortisol.

32 of these patients with an abnormal baseline SST went on to have a repeat SST within 2 years. 50% (n=16) continued to be suboptimal. Of the 32 patients, 38% (n=12) were switched to hydrocortisone with 33% showing complete adrenal recovery, average time to recovery of 25 months. 62% (n=20) patients did not switch, with 60% demonstrating recovery within the same time period (p=0.05). Mean ACTH levels in patients who had sub-optimal SST were 23.1 ng/L (n=19). ACTH levels were not different between those who recovered and those who did not (p=0.23).

Conclusion
Our study suggests that tertiary adrenal insufficiency is highly prevalent in this cohort of patients with rheumatological conditions requiring long-term glucocorticoid therapy. A 9am cortisol threshold of greater than 350 nmol/L excludes most patients with adrenal insufficiency. These data also suggest no significant difference in adrenal recovery if switched to hydrocortisone versus continuing on prednisolone. ACTH levels were not fully suppressed in patients with adrenal insufficiency and did not predict recovery.

Diabetes Mellitus and Glucose Metabolism
DIABETES DIAGNOSIS, TREATMENT AND COMPLICATIONS

The Risk of Hip and Non-Vertebral Fractures in Diabetes: A Systematic Review and Meta-Analysis Update
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