

In view of clinical, laboratory and imaging findings, presumptive diagnosis of 46 XX DSD due to 21 alpha hydroxylase deficiency CAH was made. Oral Hydrocortisone 15mg/m<sup>2</sup> and Fludrocortisone 0.05 mg were initiated. Therapy was monitored with serum 17(OH)P levels and Androstenedione. Genetic testing for 21 alpha hydroxylase gene however came negative.

This led to further genetic mutational analysis, and there was a homozygous R457H POR gene mutation at exon 12 leading to protein change p.Arg457His (nucleotide change c.1370G>A), confirming PORD. Retrospectively, maternal triple test done during the candidate pregnancy showed low serum estriol,

suggestive of placental aromatase deficiency. Mineralocorticoid supplements were stopped thereafter.

**Conclusions**PORD needs to be considered and differentiated from garden variety of CAH in 46 XX DSD when elevation of 17(OH)P is modest with isolated cortisol deficiency and aromatase deficiency (evidenced by low maternal estriol levels and/or virilization), as its course and follow up are different.

## Neuroendocrinology and Pituitary

### PITUITARY TUMORS II

**Diagnostic Utility of Overnight High Dose Dexamethasone Suppression Test for Differentiating the Etiology of ACTH Dependent Cushing's Syndrome**  
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#### MON-329

Background:

Bilateral inferior petrosal sinus sampling (BIPSS) has been the gold standard in differentiating a pituitary vs. an ectopic source of ACTH in Cushing's syndrome however, it has many limitations. The ON-HDDST being simple to perform and the tests of choice in resource poor setting. The primary aim of our study was to consolidate the present knowledge regarding the diagnostic utility of ON-HDDST in localizing the source of ACTH.

Method:

We retrospectively studied 88 patients with ACTH dependent Cushing syndrome who underwent ONHDDST. Patient were considered as Cushing disease (CD) if either of the 3 criteria were met a) histopathological confirmed b) a central to peripheral gradient >2 was seen in BIPSS or c) pituitary adenoma ≥ 6mm seen in MRI of pituitary. Patient were considered as ectopic ACTH syndrome if the tumor was localized at any peripheral location by imaging or histopathological confirmed after surgery or if BIPSS shown a central to peripheral gradient of <2.

**Result:** Out of total 88 ACTH dependent Cushing syndrome patients, 68 (77.3%) were proven CD and 20 (22.7%) were ectopic. There was no difference in basal serum cortisol however, S. Cortisol after ONHDDST was significantly different between the two with a median of 547.7 nmol/l (341-770) in ectopic vs 273.5 nmol/l (142-689) in CD (p=0.02). A positive response to ONHDDST (≥50% suppression) was seen in about 44 (65%) patients with CD and 5 (25%) patients with ectopic disease (p = 0.002). Among CD

patient, 35 (76.1%) of those with microadenoma, 7 (43.8%) amongst macroadenoma and 2 (33%) patient with no visible tumor on MRI shown positive response to ONHDDST. In ectopic group, cortisol suppressibility was seen in 3 (50%) patient with occult tumor but only in 2(14.3%) patient with. ROC curve plotted for percentage suppression of cortisol after ONHDDST shown as AUC equal to 0.68 (p = 0.01). The best test parameters with sensitivity (65%), specificity (85%) and Accuracy (69%) were seen at 50% cutoff level as were the likelihood ratio for positive test (4.3), AUC (0.75), PPV (93.6%), NPV (41.4%).

**Conclusion:** Our study has shown that ONHDDST has poor diagnostic value in differentiating between CD and ectopic ACTH syndrome whatever be the cutoff level of the cortisol suppression. However, this can still be utilized in setups where no alternative is available. For etiologic confirmation, another test with better sensitivity and specificity is preferable.

## Pediatric Endocrinology

### PEDIATRIC ENDOCRINE CASE REPORTS II

**The First Case in Korea, ZC4H2 Gene Mutation in Wieacker-Wolff Syndrome with Recurrent Hypoglycemia**

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#### MON-068

Wieacker-Wolff syndrome was first described in 1985 and is a rare congenital syndrome cause by ZC4H2 mutation. It is a X-linked recessive disorder characterized by congenital contracture of the feet, mental retardation, progressive neurologic muscular atrophy, scoliosis, and hypoglycemia. 9-years-old boy with brain atrophy, mental retardation, scoliosis, convulsion and exotropia visited our clinic with recurrent hypoglycemia. Hypoglycemia was developed since infant. Physical examination showed dysmorphism and no hepatomegaly. In the 'critical sample', ketoacidosis was present and serum levels of free fatty acid was elevated. Lactate was in the normal range. Hyperinsulinism was excluded with 'critical sample' and glucagon stimulation test. Combined pituitary stimulation showed no deficiency of growth hormone and cortisol, respectively. Fatty acid oxidation was excluded by serum levels of acylcarnitines and urine organic acid test. Due to the presence of multiple anomaly and under the suspicion of glycogen storage type 0, whole exome sequencing was performed and p.P154T mutation on the ZC4H2 was observed. Although Sanger sequencing is in processing yet, clinical features are very similar compare to previous cases. In summary, we reported a first Korean male with a novel ZC4H2 mutation, P154T.

## Adipose Tissue, Appetite, and Obesity

### OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

**The Peculiarity of the Gut Microbiota in Patients with Different Phenotypes of Obesity (Pilot Study)**

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#### MON-594

**Abstract:** Recent studies have shown that obesity is not a homogeneous condition and that there is a subgroup of people with obesity, but without metabolic disturbance. This phenotype of obesity is called “metabolically healthy obesity” (MHO) [1]. More and more data are appearing in the scientific literature, indicating that quantitative and qualitative changes in the gut microbiota (GM) can be a trigger in the development of obesity and metabolic disorders [2]. In order to study the role of GM in the development of various types of obesity, 37 patients were examined, divided into 3 groups: group 1 (n = 11) - healthy people without obesity and overweight (control), group 2 (n = 13) - patients with MHO, group 3 (n = 13) - patients with metabolically unhealthy obesity (MUHO). The basic metabolic parameters were determined for all of them and a quantitative assessment of the condition of the GM was performed using the Real-time PCR method. Results: 1. In people from the control group (group 1) in the GM, compared with formal normative indicators, the number of *Lactobacillus* spp., *Bifidobacterium* spp., *B. thetaiotaomicron* was reduced ( $p < 0.05$ ) and indicators of the total bacterial mass and *Enterobacter* spp./*Citrobacter* spp. were increased ( $p < 0.05$ ). 2. In subjects with MHO (group 2), GM changes similar to group 1 were observed. However, in comparison to group 1, *Klebsiella* spp. and *Proteus* spp. were recorded in feces in quantities exceeding the formal regulatory. In patients with MUHO (group 3), in addition to changes detected in group 2, *C. difficile* was found in feces, as well as a significant ( $p < 0.05$ ) decrease in *F. prausnitzii* and an increase ( $p < 0.05$ ) in the detection frequency of banal *E. coli*, as well as the more diverse composition of the microbiota. Thus, the data obtained as a result of a pilot study certainly indicate changes in the GM in people with different phenotypes of obesity and in healthy ones. Further study of the GM in patients with various types of obesity, but in a larger groups, is required.

**Reference:** 1) Phillips C.M. Metabolically healthy obesity across the life course: epidemiology, determinants and implications. *Ann N.Y. Acad Sci* 2017 Mar;139(1):85-100. doi:10.1111/nyas.13230. 2). Giovanna Muscogiuri, Elena Cantone, Sara Cassarano, Dario Tuccinardi, Luigi Barrea, Silvia Savastano, Annamaria Colao & on behalf of the Obesity Programs of nutrition, Education, Research and Assessment (OPERA) group. Gut microbiota: a new path to treat obesity. *International Journal of Obesity Supplements* 2019 Apr;9(1):10-19. doi: 10.1038/s41367-019-0011-7

## Neuroendocrinology and Pituitary CASE REPORTS IN CLASSICAL AND UNUSUAL CAUSES OF HYPOPITUITARISM II

### *Adenocarcinoma Pituitary Metastasis with Suprasellar Extension*

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#### MON-244

##### Background

Metastasis to the pituitary gland (MP) is an infrequent clinical problem, however, during the last few decades, MPs is increasing in frequency, due both to the improved cancer survival rates and availability of better imaging techniques. Breast cancer, lung cancer and lymphoma are the most common primary sites. MP mimics pituitary adenoma making the diagnosis difficult, especially when clinical evidence of the primary malignancy is absent. We report a case of histologically confirmed pituitary metastasis (adenocarcinoma) from carcinoma of unknown primary, leading to and presenting as panhypopituitarism.

##### Case details

54 year male HBV carrier, asthmatic, non smoker, non alcoholic was seen elsewhere with complaints of increased frequency of micturition associated with nocturia, increased thirst, asthenia and weight loss of 05 kg since 06 months. He also had loss of libido and erectile dysfunction. Patient never experienced headache, vomiting or visual disturbances. There was no personal or family history of malignancy. On physical examination skin was pale, atrophic with fine wrinkles around the eyes. He had BP of 96/60mmHg and PR 100/min but system examination was otherwise unremarkable. Biochemical evaluation confirmed diabetes insipidus, secondary hypothyroidism, adrenal insufficiency and hypogonadism. MRI Brain showed a mass like thickening (11.6 x 11 x 16mm) of the infundibulum and posterior portion of the pituitary gland with upward displacement of optic chiasm. Workup for granulomatous conditions (sarcoidosis/ disseminated Koch's) was negative. He was initiated on desmopressin, thyroxine, hydrocortisone, testosterone and managed elsewhere as hypophysitis.

At presentation to us after 3 months of treatment, visual field examination showed decrease in peripheral vision involving right superior temporal quadrant and an attempt was made to delineate the size and etiology of the lesion. Repeat imaging revealed increase in size of the lesion to 12 x 15 x 18mm. He underwent TSS and the lesion was biopsied. Histopathology showed infiltrative adenocarcinoma with CK20 +, CK7 -, and GATA3 + on IHC. Post procedure WB-PET CT, showed metabolically active residual tumor in suprasellar region and negative for metabolically active disease in other areas. Upper GI Endoscopy, Colonoscopy and Bronchoscopy were also normal. Currently he is on adjuvant radiation therapy for residual suprasellar lesion.

##### Conclusion

Pituitary metastasis may be difficult to differentiate from other lesions in the sellar/parasellar region, presentation as DI and thickened stalk confounded the diagnosis, given that it is a feature of the commoner lesion- hypophysitis. This case reports the rare occurrence of CK20 positive, CK7 negative adenocarcinoma metastasis to pituitary and no evidence of primary.