syndrome usually presents with neurological symptoms such as seizures, tetany, speech impairment, dementia, deterioration of intelligence, involuntary movements. The etiology of Fahr syndrome is mostly associated with endocrine disorders especially hypoparathyroidism either primary or secondary or pseudo hyperparathyroidism; including adult onset neurodegenerative conditions, infectious disease like intrauterine and perinatal infections or inherited congenital causes are also considered.

**Clinical Case**

The authors report a 33-year-old Ethiopian female not known to any medical illness presented with abnormal involuntary left-hand movement, headache and dizziness. Further examination shows positive Chvostek's and Trousseau's signs. In addition, laboratory findings reveal decreased levels of serum calcium (1.227 mmol/L, normal range of 2.2-2.65 mmol/L), serum albumin (33.53 mg/dL, normal range of 35-52 g/L) and parathyroid hormone (0.3pmol/L, normal range of 1.1-8.43 pmol/L), decreased vitamin D serum level (14.52 ng/ml, normal range of 30-75 ng/ml). Interestingly, brain imaging shows bilateral symmetrical subcortical white matter, basal ganglia, cerebellar dentate nuclei calcifications. Thus, Fahr syndrome diagnosis was made. She was promptly treated with calcium and vitamin D replacement. Calcium gluconate was given intravenously with oral calcium carbonate and oral cholecalciferol. The patient recovered with this treatment leading to positive results without any recurring symptoms.
INTERNAL

**Conclusion**

In conclusion, Fahr syndrome is a rare sequel of hypoparathyroidism, mostly presented with neurological symptoms due to hypocalcemia which after correction subdues the occurring manifestation such as in this case presented. Early diagnosis of Fahr syndrome due to hypoparathyroidism is crucial for prompt treatment and reversal of symptoms also to prevent complications.
INTERNAL

# Pediatric Endocrinology

## PEDIATRIC SEXUAL DIFFERENTIATION, PUBERTY, AND BONE BIOLOGY

### *Clinical and Hormonal Features of 37 Families with Central Precocious Puberty Due to MKRN3 Loss-Of -Function Mutations*

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**SUN-085**

**Context:** Loss-of-function mutations in the maternally imprinted Makorin RING-finger 3 (*MKRN3*) gene (15q11.2) are the most prevalent cause of familial central precocious puberty (CPP). **Objectives:** To analyze the phenotypes of a large cohort of children with CPP due to *MKRN3* mutations and to compare them with the phenotypes of idiopathic CPP. **Setting and Participants:** We studied 73 individuals from 37 families with mutations in *MKRN3* originating from nine different countries. The phenotypes of these patients at initial diagnosis were compared to a cohort of 124 patients with idiopathic CPP. Additionally, expression of nine different genes implicated with pubertal timing, including *MKRN3*, was performed in the hypothalamus of female mice in different phases of sexual maturation. **Results:** Nineteen different heterozygous, paternally inherited mutations in *MKRN3* were identified in 73 patients with CPP (48 girls and 25 boys). Six *MKRN3* mutations were frameshifts, one introduced a premature stop codon, 11 were missense mutations predicted to be pathogenic, and one was a deletion in the promoter region. A frameshift mutation affecting codon 161 in the amino terminal region of the protein was the most frequent *MKRN3* defect (46%), representing a hotspot region. Among the cohort with *MKRN3* mutations, first pubertal signs occurred at 6·2 ± 1·2 years in girls and 7·6 ± 1·4 years in boys. Patients harboring severe frameshift/nonsense mutations did not differ significantly in any clinical or hormonal parameters compared to the 20 patients with missense variants. However, when the 48 girls with *MKRN3* mutations were compared with 124 idiopathic CPP girls, some parameters could be considered as possible predictors of the genetic cause: a lower age at first medical appointment (7·1 ± 1·1 in the *MKRN3* group vs. 8·0 ± 2 years in the idiopathic group; p< 0.001) and a shorter time interval between puberty onset and medical assistance (0·8 ± 0·8 vs 2·2 ± 2·1 years; p< 0.001). Interestingly, the other predictor of *MKRN3* mutations was a higher basal FSH level (5·1 ± 2·3 vs 3·9 ± 2·7 IU/L; p = 0.017) at first evaluation, although no cutoff value yielded good accuracy. Patients originating from European/Mediterranean countries were more likely to have missense variants (56% of all mutations) than North American and South American (23%) counterparts (p <0.001). Mouse *Mkrn3* mRNA levels in the arcuate nucleus were highest in the prepubertal phase when compared

with expression of other genes and *Mkrn3* decreased progressively through puberty and adult ages. **Conclusions:** Different types of loss-of-function MKRN3 mutations were associated with premature sexual development in both sexes. Their phenotypes were relatively uniform, regardless of the mutation type. Clinical features of children with *MKRN3* mutations were similar to the idiopathic CPP group.

# Adrenal

## ADRENAL CASE REPORTS I

### *An Adrenal Incidentaloma with Extramedullary Hematopoiesis*

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**SAT-208**

Introduction: Adrenal adenomas are incidentally noted during nonadrenal disease imaging at a rate up to 4%. Frequency of incidentalomas increases with age, most being adrenocortical adenomas. This case highlights an uncommon etiology of such an adrenal mass finding. Case Description: A 37-year-old with a history of hypertension, hypothyroidism, and tobacco use was admitted after post-operative complication. Prior to surgery, she had been experiencing right upper quadrant pain along with 70 lb weight loss and diarrhea. She otherwise had frequent palpitations. Patient had undergone cholecystectomy and common hepatic duct injury was noted. Imaging revealed a 5.3 x 3.5 cm right adrenal mass previously unknown prior to surgery. Hormonal workup was negative for overproduction of aldosterone, cortisol, DHEA-S or metanephrines. Discussion: Patient underwent successful resection of adrenal mass, revealing adrenal adenoma with osseous metaplasia and hematopoiesis. Extramedullary hematopoiesis is a usually discovered incidentally as in this case. Typical sites are the spleen and liver. Cases of adrenal gland manifestations have been reported in the presence of hemoglobinopathies (thalassemia, hereditary spherocytosis) or myelofibrosis. At four-month follow-up, laboratory testing on this patient didn't suggest any erythrocytic or leukocytic disorder. Conclusion: This case highlights an uncommon finding of hematopoiesis in an adrenal incidentaloma without any underlying hematologic defect or disease. References: Motta, I., Boiocchi, L., Delbini, P., Migone De Amicis, M., Cassinerio, E., Dondossola, D., Rossi, G. and Cappellini, M. D. (2016), A giant adrenal myelolipoma in a beta-thalassemia major patient: Does ineffective erythropoiesis play a role?. Am. J. Hematol., 91: 1281-1282. doi:10.1002/ajh.24446. Stewart P, Newell-Price J. (2016). The Adrenal Cortex. In Melmed S, Polonsky K, Larsen P, Kronenberg H, *Williams Textbook of Endocrinology*. (13th ed., pp 489-555). Philadelphia, PA: Elsevier

# Tumor Biology

## ENDOCRINE NEOPLASIA CASE REPORTS II

### *Etomidate - an Under Utilized but Safe and Efficacious Drug to Treat Acute Severe Cushing's Syndrome- Case Reports of Ectopic ACTH Syndrome from Neuroendocrine Malignancies*

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**MON-902**

**Background**: Intravenous etomidate infusion, in non-hypnotic doses, rapidly lowers cortisol levels by blocking 11-beta hydroxylation of deoxycortisol to inhibit cortisol production. It is an underutilized drug due to concerns of excess sedation and ICU monitoring.

**Clinical Case 1**: A 44 year-old female with HTN, diabetes, and recently diagnosed pancreatic neuroendocrine tumor with liver metastases presented with altered mentation. Labs showed severe hypokalemia, metabolic alkalosis, serum AM cortisol >60.2 ug/dL (n 6.7-22.6 ug/dL), ACTH of 698.1 pg/mL (n 7.2-63.3 pg/mL), 24-hour urine free cortisol (UFC) of 5791 ug/24hr (n 5-64 ug/24hr), midnight salivary cortisol of 8.04 ug/dL (n <0.01-0.09), and abnormal low dose (LDDST) and high dose (HDDST) dexamethasone suppression tests each with cortisol >60.2 ug/dL. She developed worsening psychosis, likely secondary to hypercortisolism. After ICU transfer, etomidate infusion was initiated at 2.5 mg/hr and titrated upward, leading to rapid drop in cortisol levels and concomitant improvement in mentation. No respiratory or airway difficulties developed. Ketoconazole and metyrapone were started and etomidate was weaned off. Steroids were added once cortisol levels fell below 10 ug/dL as part of "block and replace." The patient eventually underwent bilateral adrenalectomy with improvement in hemodynamic and blood glucose parameters. She was discharged on physiologic replacement doses of hydrocortisone and fludrocortisone, with no reported issues two months later.

**Clinical Case 2**: A 51 year-old man with one month of hematochezia presented with hypertension, severe hypokalemia, metabolic alkalosis, and QTc prolongation. Colonoscopy was unremarkable; however, labs revealed a cortisol of 43.1 ug/dL, ACTH of 83.6 pg/mL, and 24-hour UFC of 7,494 ug/L, with an abnormally elevated LDDST. Imaging showed a pancreatic mass and multiple hypodense liver lesions. The overall presentation was suggestive of ectopic ACTH syndrome due to metastatic neuroendocrine carcinoma, which was confirmed on biopsy. Chemotherapy, ketoconazole, and metyrapone inadequately lowered cortisol. Etomidate drip was initiated at 3 mg/hr in the ICU, with rapid reduction in cortisol levels to <20 ug/dL without respiratory compromise. Attempts to wean off etomidate were unsuccessful and the patient underwent bilateral adrenalectomy. The surgery was compromised due to extensive liver and pancreatic enlargement, and follow up imaging revealed incomplete resection. 8am cortisol level (off etomidate) was >60.0 ug/dL. Metyrapone and ketoconazole were resumed and hydrocortisone was later initiated for "block and replace". The patient remains in critical condition.

**Conclusion**: Etomidate-in non- hypnotic doses is useful for the rapid lowering of cortisol levels.

# Diabetes Mellitus and Glucose Metabolism

## DIABETES TECHNOLOGY AND ADVANCES IN CLINICAL TRIALS

### *Racial Differences in Technology Use Among Type 1 Diabetes in a Safety-Net Hospital*

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