Challenges in diagnosis and treatment of Cushing Disease in a 12 years old boy

A. Gjikopulli[1], L. Kollcaku[1], M. Tanka[2], S. Tomori[3], R. Gül Yeşiltepe Mutlu[4]

1.Pediatric Endocrinology Unit, Department of Pediatric, University Hospital Center "Mother Teresa", Albania
2. Radiology and Imaging Department, University Hospital Centre "Mother Teresa", Albania
3. Pediatric Specialty Service Nr.2, Department of Pediatric, University Hospital Centre "Mother Teresa", Albania
4. Division of Pediatric Endocrinology and Diabetes, Koç University, School of Medicine, Koç University Hospital, stanbul, Turkey

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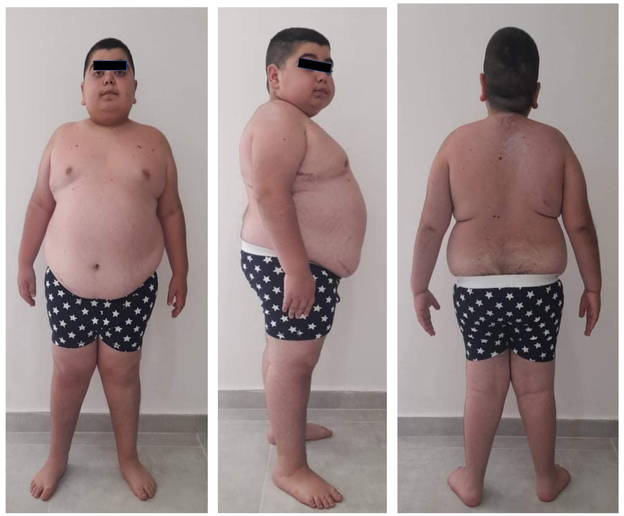
BACKGROUND

Cushing's disease (CD) is caused by an ACTH-secreting pituitary corticotroph adenoma and it is the most common cause of Cushing's syndrome (CS) in pediatric age.
CD is a very rare disease among pediatric ages and most of pediatric endocrinologists have limited experiences in the diagnosis and treatment of children with CD.
Microadenomas are the most of ACTH-secreting pituitary tumors in the pediatric age and the majority of these fail to be detected on MRI because they have a hypo intense signal on this examination and show a normal appearance in about half of the patients.
Therefore, results should be interpreted together with bilateral inferior petrosal sinus sampling (BIPSS) for ACTH.

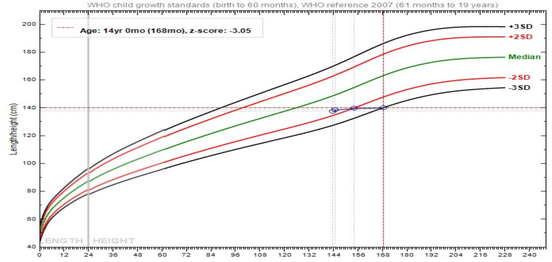
CASE REPORT

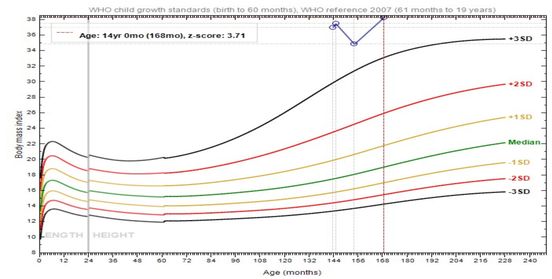
A 12 years old Albanian boy was presented with headache, rapid weight gain during 3 years, stunned height (Patient growth charts 1, 2), increase hair growth and a typical Cushingoid appearance (Patient foto 1, 2, 3).
His investigations there showed the following values: Cortisol: 26.8mcg/dL, ACTH: 95.3pg/dL (8.00 a.m.); Cortisol 30mcg/dL, ACTH: 116.2pg/dL (4.00 p.m.), Salivary cortisol at 11.00 p.m.: 10.55ng/dL, Free cortisol in 24-hour urine: 556mcg/24 hours. Prior to 8 mg dexamethasone suppression test, cortisol level was 13.8mcg/dL and 12.7mcg/dL after the test. DHEAS: 894mcg/dL.
His cranial MRI was unremarkable other than cortical atrophy. Thorax CT and echo cardiogram findings were normal.
The patient was pre-diagnosed with Cushing Syndrome.

PATIENT FOTO



PATIENT GROWTH CHARTS



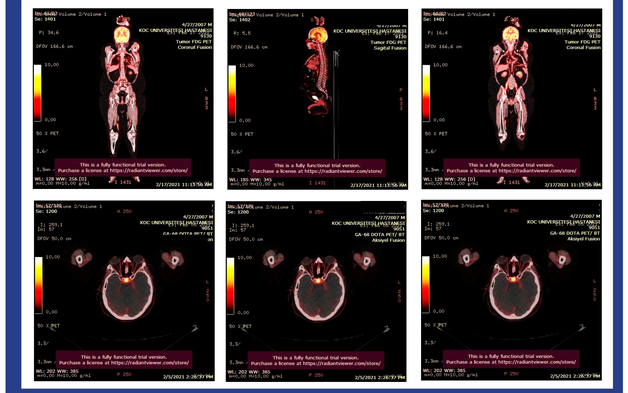


CHALLENGES IN DIAGNOSIS

The patient was admitted to Koç University Hospital, Turkey with the pre-diagnosis: suspicious hypophyseal adenoma.
On 3rd day after admission: an overnight 8 mg dexamethasone suppression test resulted with cortisol level 18.5mcg/dL before the test and 21.9mcg/dL after HDDT. The patient was pre diagnosed with ectopic ACTH-dependent Cushing syndrome.
On 5th day after admission: A thorax CT, abdominal MRI and DOTATATE PET scan were performed. The thorax CT showed a nodular lesion with regular-lobulated sharp contours measuring 16x14x10mm in the right lung lower lobe anterobasal segment. It was suggestive of neuroendocrine neoplasia (carcinoid tumor).
On 11th day after admission: the lower lobe of right lung was resected. It was found out that there was a necrotizing granulomatous focus (more consistent with TBC) rather a bronchial carcinoid. Chromogranin A and ACTH staining results were negative and EZN was positive.
On 13th day after admission: a 1mg dexamethasone was performed in order to reevaluate for hypercortisolism. No suppression on cortisol level was detected. ACTH level was measured as 65pg/mL.
On 17th day after admission: an FDG PET/CT was performed. No ectopic ACTH-depended focus was detected.
On 24th day after admission: it was done an intervention to collect samples from inferior petrosal sinus.
Findings: a left side ACTH-secreting focus (ACTH: 139pg/mL in right petrosal sinus and >2000pg/mL in left petrosal sinus after CRH). The previous hypophyseal MRI images were reviewed and presence of suspicious focus was considered.

Left hemi-hypophysectomy was planned.

PATIENT RADIOLOGIC STUDY



TREATMENT APPROACH

On 24th day after admission: the patient underwent on gamma knife therapy.
After that he started treatment with ketoconazole 2x200mg for medical adrenalectomy and anti-TBC a quadruple medication treatment: oral INH; PRZ; EMB and Rifamycin. for 12 months.

On 33th day after admission he was discharged.

DISCUSSION

Approximately 50% of microadenomas are visible on pituitary MRI [1]. Pituitary image was relatively unhelpful, with a low predictive value of the position of the adenoma as identified at surgery [2].
Therefore, pituitary image using MRI, should be interpreted together with bilateral inferior petrosal sinus sampling (BIPSS) for ACTH. In children, BIPSS contributes to the localization of the microadenoma by demonstrating lateral or midline ACTH secretion. ACTH sampling gives a better prediction of the site of the microadenoma than pituitary imagery [3].

REFERENCE

1. Magiakou MA et al. Cushing's syndrome in children and adolescents. Presentation, diagnosis, and therapy. N Engl J Med. 994;331(10):629–36.
2. Storr HL et al. Factors influencing cure by transsphenoidal selective adenomectomy in paediatric Cushing's disease. Eur J Endocrinol. 2005;152(6):825–33.
3. Storr HL et al. Factors influencing cure by transsphenoidal selective adenomectomy in paediatric Cushing's disease. Eur J Endocrinol. 2005;152(6):825–33.