Nelson's syndrome after bilateral adrenalectomy for Cushing's disease in pediatric age – report of a case

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INTRODUCTION

Endogenous Cushing's Syndrome is a rare disorder in children and Cushing's disease (CD) caused by an ACTH-secreting pituitary adenoma is responsible for 75–80% of cases. Transsphenoidal surgery is now considered as a first-line therapy in CD but a proportion of pediatric patients who undergo pituitary surgery for CD don't achieve cure or remission. Definitive treatment, such as surgery and/or radiotherapy, rather than long-term medical therapies, is currently recommended for the management of pediatric CD. Nelson's syndrome is a potentially severe complication of bilateral adrenalectomy, more frequent in children than in adults. **We report a case of CD in pediatric age submitted to bilateral adrenalectomy with subsequent Nelson's syndrome.**

CASE REPORT

Nov/2003

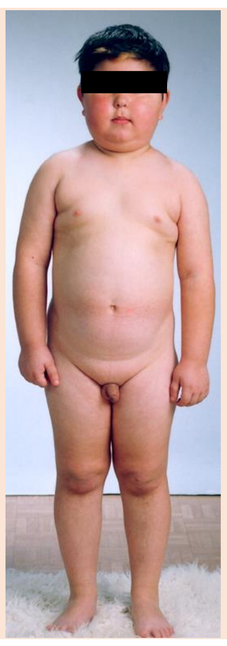
Male, 5-year-old, no significant past medical history or family history

History

- Onset 2 year **rapid weight gain** with associated **growth failure**
- Marked **plethora** and **stretch marks**
- **Mood change/lethargy** for 2-3 months

Physical examination

- **Truncal obesity, "moon" face** with **facial plethora**, marked **purple striae** in the inner thighs and buttocks, **hyperpigmentation of scrotum and penis**



Investigation

Basal cortisol	**85.8 mcg/dL (8.0-17.0)**
Basal ACTH	**59.1 pg/mL (0-46)**
24h urinary free cortisol	**1098 mcg/24H (75-270)**
Cortisol after low dose dexamethasone test	**71 mcg/dL**
Cortisol after high dose dexamethasone test	**50 mcg/dL**
Positive CRH testing with a greater than 40% incremental rise in serum cortisol	

✓ **Brain MRI:** no clear adenoma, enhancement in the right lateral portion of the pituitary
✓ **Abdomen CT and MRI:** hepatic steatosis, no other abnormalities described

Management

Jan/2004
- Ketoconazol 200mg 3 times daily

Feb/2004
- **Liver dysfunction**
- Ketoconazole reduced to 200mg twice daily

April/2004
- Ketoconazole ceased due to **liver dysfunction**
- Development of **hypertension** (BP:155-95 mmHg)
- Propranolol + co-amilozide

Transferred to a specialized center

August/2004
- Persistent elevated cortisol levels
- Metyrapone 250mg 3 times daily → severe **emesis**
- Association of ketoconazole

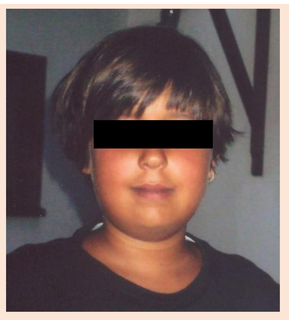
September/2004
- Ketoconazole ceased due to **aggravating liver dysfunction**
- ***Clinically unstable and unfit for pituitary surgery***

Oct/2004
- Persistent elevated cortisol levels
- **Poor nutrition, electrolyte disturbance** and **respiratory compromise**
- Etomidate 3 mg/kg/hr
- **Bilateral adrenalectomy**

Follow-up

- Post-surgical 9am cortisol levels compatible with cure of CD
- **Histology:** bilateral adrenal hyperplasia
- **Started on hydrocortisone and fludrocortisone**
- Regular clinical and MRI surveillance post surgery

2008
- **Significant skin hyperpigmentation**
- **Elevated plasma ACTH (>1250pg/mL)**
- **Brain MRI: 2mm pituitary microadenoma**



Conservative approach decided in order to preserve pituitary function

Nelson's Syndrome

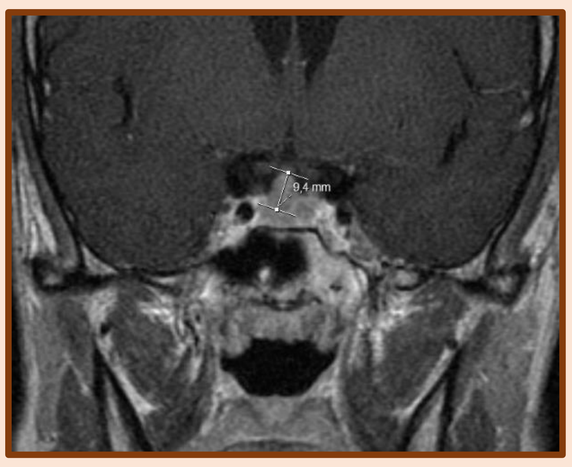
2010
***Brain MRI**: 7 mm microadenoma*

2013
***Brain MRI**: 8-9 mm microadenoma*

2016
***Brain MRI**: Stable, 9 mm pituitary microadenoma*

2017
***Brain MRI**: Stable, 9 mm pituitary microadenoma*

2018
Scheduled for pituitary surgery



Normal growth and pubertal development. No signs and symptoms of CD. No compressive symptoms. No pituitary deficits.

CONCLUSION

Treatment of pediatric CD may be challenging once the aim is to cure hypercortisolism and to preserve pituitary function, in order not to compromise normal development. Once transsphenoidal hypophysectomy is not always possible or available, bilateral adrenalectomy remains a therapeutic option in life-threatening situations. Pituitary surgery should be the first-line treatment option for Nelson's syndrome. Despite surgical intervention, adjuvant radiotherapy may be required in some patients as progression of Nelson's syndrome tumors may occur.

References: (1) Storr HL, Savage MO,.Management of Endocrine Disease - Paediatric Cushing's disease. European Journal of Endocrinology (2015). (2) Barber TM et al. Nelson's syndrome. European Journal of Endocrinology (2010). (3) Klein J et al. Cushing Syndrome. Pediatrics in Review (2014). (4) Richmond EJ et al. Cushing's Disease in Children and Adolescents: Diagnosis and Management. Cushing's Disease (Elsevier, 2017).

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Adrenals and HPA Axis
Ana Leite
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