Indian Journal of Medical Case Reports ISSN: 2319–3832
Online, International Journal, Available at http://www.cibtech.org/jcr.htm
2024 Vol.13, pp. 25-28/Abhinay et al.
Case Report (Open Access)

CUSHING'S SYNDROME IN A 13-YEAR-OLD MALE CHILD

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ABSTRACT
Cushing syndrome is a rare clinical condition, especially in children. The most common cause of Cushing syndrome in children is exogenous or iatrogenic Cushing syndrome. Cushing disease accounts for approximately 75% of all cases of Cushing syndrome in children over 7 years. A 13-year-old male child presented with complaints of short stature, putting on excessive weight, bulging abdomen and puffiness of face. Serum cortisol level was elevated (20.60 μgm/dl). Magnetic resonance imaging with contrast of the brain showed no microadenoma. The child underwent bilateral adrenalectomy and withstood the procedure well. Several treatment options exist in the management of Cushing's disease including trans-sphenoidal surgery, bilateral adrenalectomy, radiotherapy and pharmacotherapy. Following surgery there will be a period of adrenal insufficiency, during which period, glucocorticoids should be replaced at the suggested physiologic replacement dose.

Keywords: *Cushing Syndrome, Pituitary Tumors, Cortisol, Adrenal Cortex, Adrenocortical Hyperplasia*

INTRODUCTION

Cushing syndrome is a rare clinical entity, especially in children (Magiakou *et al.*, 1994). The overall incidence of Cushing syndrome is approximately 2 to 5 new cases per million people per year. Approximately 10% of these new cases occur in children. There is a female-to-male predominance, in children with Cushing syndrome which decreases with younger age. The most common cause of Cushing syndrome in children is exogenous or iatrogenic Cushing syndrome, that results from chronic administration of glucocorticoids or corticotropin (ACTH) for the treatment of many nonendocrine diseases including pulmonary, autoimmune, dermatologic, hematologic, and neoplastic disorders (Stratakis, 2012).

The most common cause of endogenous Cushing syndrome in children is ACTH overproduction from the pituitary called Cushing disease. It is usually caused by an ACTH-secreting pituitary microadenoma and, rarely, a macroadenoma. ACTH secretion occurs in a semiautonomous manner, maintaining some of the feedback of the hypothalamic-pituitary- adrenal (HPA) axis. Cushing disease accounts for approximately 75% of all cases of Cushing syndrome in children over 7 years. In children under 7 years, Cushing disease is less frequent; adrenal causes of Cushing syndrome (adenoma, carcinoma, or bilateral hyperplasia) are the most common causes of the condition in infants and young toddlers.

Autonomous secretion of cortisol from the adrenal glands, or ACTH- independent Cushing syndrome, accounts for approximately 15% of all the cases of Cushing syndrome in childhood. However, although adrenocortical tumors are rare in older children, in younger children they are more frequent. In prepubertal children, adrenocortical lesions are the most frequent cause of Cushing syndrome. Adrenocortical neoplasms account for 0.6% of all childhood tumors; Cushing syndrome is a manifestation of approximately one- third of all adrenal tumors (Tsigos and Chrousos, 1996; Orth, 1995; Stratakis and Kirschner, 1998).

The onset of Cushing syndrome in most children is insidious. The common presenting symptoms include weight gain and lack of height gain consistent with the weight gain (Tsigos and Chrousos, 1996; Orth, 1995; Magiakou and Chrousos, 2002). Other common symptoms that are reported in children include facial plethora, headaches, hypertension, hirsutism, amenorrhea, and delayed sexual development. Pubertal children may present with virilization. Skin manifestations, including acne, violaceous striae, bruising, and acanthosis nigricans are also common (Lodish *et al.,* 2009). Sleep disruption, muscular weakness, and problems with memory is less commonly seen in children as compared to adults.

Documenting hypercortisolism is the first step in the diagnosis of Cushing syndrome (Batista *et al.,* 2007; Bornstein *et al.,* 1999). A 24-hour urinary free cortisol (UFC) excretion is another excellent screening test for diagnosing hypercortisolism (Magiakou *et al.,* 1994). A low- dose dexamethasone suppression test is another baseline test for the establishment of the diagnosis of Cushing syndrome. This test involves giving 1 mg of dexamethasone at 11 and measuring a serum cortisol level the following morning at 8 AM. If the serum cortisol level is greater than 1.8 µg/dL, further evaluation is necessary (Nieman *et al.,* 2008). In this case report, we report a 13-year-old male child who presented with short stature and weight gain and was diagnosed to have Cushing's syndrome.

CASE

A 13-year-old male child presented to a local Pediatrician with complaints of short stature, putting on excessive weight, bulging abdomen and puffiness of face (Figure 1 and 2). The child was diagnosed as a case of Cushing's disease and put on oral Ketoconazole 200 mg twice daily. Serum cortisol level was elevated (20.60 μgm/dl). Rest of the blood biochemistry tests were within normal range. Magnetic resonance imaging with contrast of the brain showed no evidence of micro or macroadenoma within the pituitary gland. Serum ACTH (adrenocorticotrophic hormone) was within normal ranges. Abdominal computed tomogram (CT) showed bilateral adrenals with no focal lesion. The stem of the left adrenal gland measured 12 mm in length and 2.9 mm in width and appeared comparatively thicker than the opposite gland.

In view of the hypercortisolism and the advice of the treating pediatric endocrinologist it was decided to perform bilateral adrenalectomy in this child. The procedure was performed under general anesthesia and the child tolerated the procedure well. The child was put on maintenance corticosteroids and mineralo-corticosteroids. Post-operatively the child recovered well.

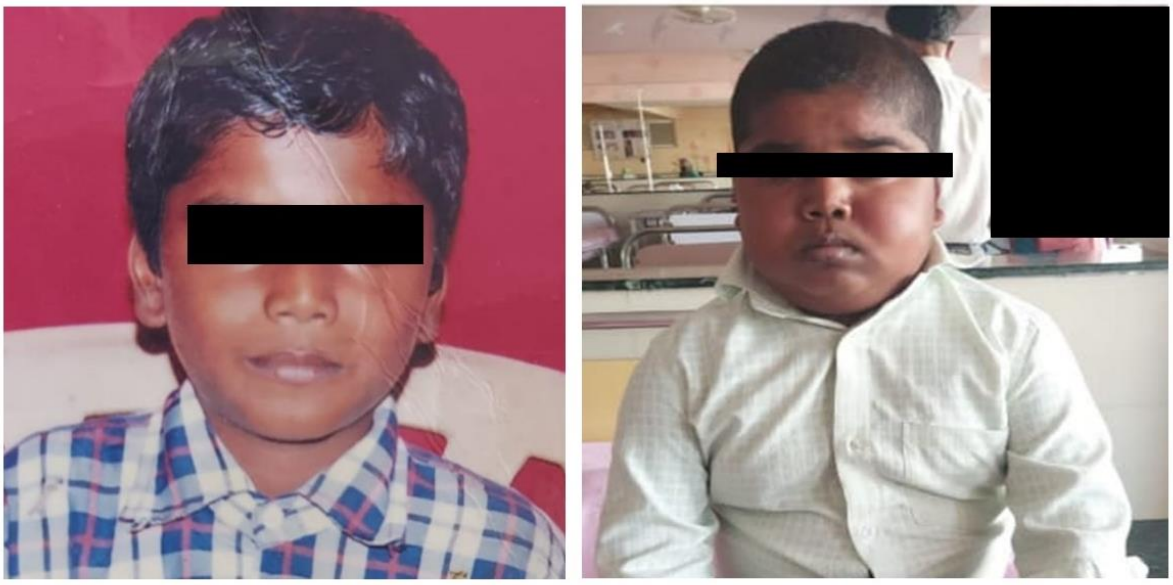

Figure 1a. Shows the child's face one year back. 1b. The child presented with puffiness of face.

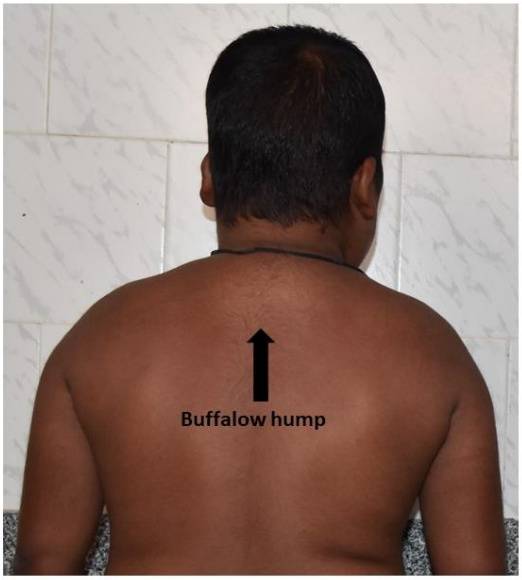

Figure 2: Shows buffalo hump

DISCUSSION

Diagnostic imaging is an important tool in the localization and characterization of Cushing syndrome. The most important initial imaging when Cushing disease is suspected is pituitary magnetic resonance imaging (MRI). The MRI should be done in thin sections with high resolution and always with contrast (gadolinium) (Magiakou *et al.,* 1994; and Stratakis, 2012). The latter is important, since only macroadenomas will be detectable without contrast; after contrast, an otherwise normal-looking pituitary MRI might show a hypo-enhancing lesion, usually a microadenoma. More than 90% of ACTH-producing tumors are hypo-enhancing, whereas only about 5% are hyper-enhancing after contrast infusion. Even with the use of contrast material, pituitary MRI may detect only up to approximately 50% of ACTH-producing pituitary tumors (Batista *et al.,* 2005).

Computed tomography (CT) of the adrenal glands is useful in the distinction between Cushing disease and adrenal causes of Cushing syndrome, mainly unilateral adrenal tumors. The distinction is harder in the presence of bilateral hyperplasia or the rare case of bilateral adrenal carcinoma. Most patients with Cushing disease have ACTH- driven bilateral hyperplasia, and both adrenal glands will appear enlarged and nodular on CT or MRI (Magiakou *et al.,* 1994; Stratakis, 2012; Batista *et al.,* 2005).

The treatment of choice for almost all patients with an ACTH-secreting pituitary adenoma (Cushing disease) is transsphenoidal surgery (TSS). In most specialized centres with experienced neurosurgeons, the success rate of the first TSS is 90% (Batista *et al.,* 2009) or higher. Treatment failures are most commonly the result of a macroadenoma or a small tumor invading the cavernous sinus. Pituitary irradiation is considered an appropriate treatment in patients with Cushing disease following a failed TSS (Stratakis, 2012). Up to 80% of patients will have remission after irradiation of the pituitary gland. Hypopituitarism is the most common adverse effect, and it is more frequent when surgery precedes the radiotherapy. The recommended dosage is 4500/5000 cGy total, usually given over a period of 6 weeks. Newer forms of stereotactic radiotherapy are now available as options for treatment of ACTH-secreting pituitary tumors. Photon knife (computer-assisted linear accelerator) or the gamma knife (cobalt -60) approaches are now available; however, experience with these techniques is limited, especially in children.

The treatment of choice for benign adrenal tumors is surgical resection. This procedure can be done by either transperitoneal or retroperitoneal approaches. Adrenal carcinomas may also be surgically resected, unless at later stages. Solitary metastases should be removed, if possible (Powell *et al.,* 2008). Bilateral total adrenalectomy is usually the treatment of choice in bilateral micronodular or macronodular adrenal disease. In addition, adrenalectomy may be considered as a treatment for those patients with Cushing disease or ectopic ACTH- dependent Cushing syndrome who have either failed

surgery or radiotherapy, or their tumor has not been localized, respectively. Bilateral adrenalectomy can be performed with open, laparoscopic or robot assisted approach (Indupur *et al.*, 2007; Nerli *et al.*, 2011).

Conflict of Interest: The authors declare conflict of interest as None.

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