Cushing's Disease in an 11-month-old Child

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Cushing's disease (Pituitary tumor causing bilateral adrenal hyperplasia) is very rare in children and more so in infants. Cushing's syndrome in pediatric patients is usually due to adrenal tumors. We report a case of an 11-month-old child with Cushing's disease caused by a Pituitary macroadenoma.

Keywords: *Cushing, Pituitary gland, Macroadenoma.*

Cushing's disease is bilateral adrenocortical hyperplasia secondary to excessive secretion of ACTH by the pituitary gland and is very rare in children(1,2). Very few cases have been reported in Indian and world literature(3). Cushing's syndrome in pediatric patients is usually caused by adrenal tumors(4), as opposed to this pituitary tumors causing Cushing's disease are extremely rare under the age of 7 years and more so in infancy(3). We report a case of an 11-month-o1d child with Cushing's disease caused by a Pituitary macroadenoma.

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Case Report

An 11-month-old female child, first issue of non-consanguineous marriage was referred for obesity. On examination the patient was 77cms long (97th centile Agarwal charts) and weighed 14 Kgs (above 97th centile Agarwal charts). She had generalized obesity, blood pressure was 140/110 mm of Hg using a mercury sphygmomanometer, moon facies, edema, hirsuitism, clitoral hypertrophy and dark pigmentation. Within 3 weeks patient started showing visual inattention though the fundoscopic examination was normal.

Investigations showed a raised midnight Adrenocorticotrophic hormone (ACTH) (122 pgm/ml), serum Prolactin (100 ngm/ml), and plasma Cortisol (88 mcg/dL) and post prandial glucose of 72 mg%. Thyroid stimulating hormone was 3U/ml (0.4-5 U/mL), Thyroxine was 10 microgm/dL (5-12 microg/dL), Triiodothyronine was 120 ng/dL(70-190 ng/dL), serum sodium was 141 (136-152 meq/lit), serum potassium was 2.3 (3.5- 5.6 meq/lit). An MRI of the brain showed the presence of a large pituitary macroadenoma measuring 3 × 2.5 × 2.5 cm (*Fig. 1*) elevating the optic chiasma. No calcification was seen. Both the adrenal glands were well visualized on CT scan of the abdomen suggesting bilateral adrenal hyperplasia. On the basis of physical examination, endocrine and neuro-radiologic assessment, diagnosis of Cushing's disease was made. Since neurosurgical experience in Pituitary macroadenomas in infancy is limited it was decided to manage the patient medically with Cyproheptidine and Bromocriptine. After three weeks of medical therapy patient developed visual inattention and hence immediate surgery was planned. As sphenoid sinuses are not developed at this age transsphenoidal surgery was not possible. Transcranial surgery was performed. The tumour was successfully removed however, despite

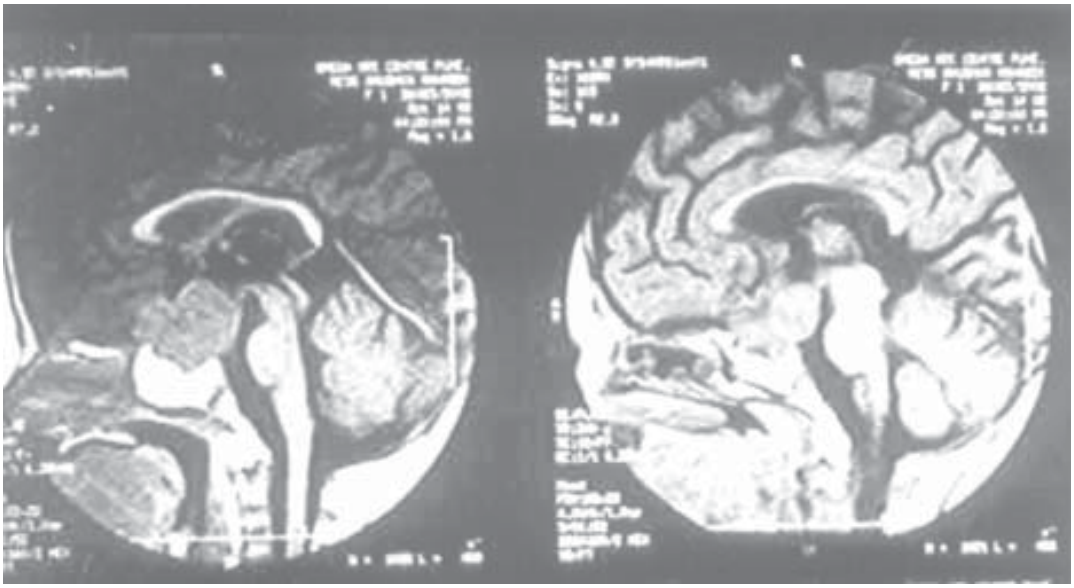

Fig. 1. MRI showing large pituitory macroadenoma.

careful monitoring and Pediatric ICU care patient succumbed due to severe electrolyte imbalance in the immediate post-operative period.

Discussion

The term Cushing's disease is currently used for condition in which bilateral adrenocortical hyperplasia is secondary to excessive secretion of ACTH by the pituitary gland. The adrenals may be slightly or greatly enlarged. Reviews of literature reveal that Cushing's disease is extremely rare in infancy(3). Pituitary Cushing's may be caused by a pituitary adenoma though macro-adenomas are rarely found in children (5). Most adenomas found in children are under one cm and do not extend outside the pituitary fossa. When the pituitary adenoma extends outside the fossa it grows upwards into the suprasellar recess and compresses the optic chiasma as happened in our patient.

The signs and symptoms of Cushing's disease are due to cortisol excess and to pressure symptoms caused by the pituitary adenoma. Frequent clinical findings include weight gain, truncal obesity, straie, hyper-tension, glucose intolerance and infections. Progressive obesity is often the first symptom as was seen in our patient.

The evaluation of patients with suspected Cushing's disease and syndrome requires an understanding of the proper use and limitations of the tests commonly included in the diagnostic work-up. Estimation of urinary free cortisol, study of circadian rhythm, low dose and high dose Dexamethasone suppression test may be required for a definitive diagnosis and for locating the tumour. For neuroimaging Magnetic Resonance Imaging with enhancement is the diagnostic investigation of choice. Surgical excision of an ACTH-producing pituitary tumour is the optimal therapy for Cushing's disease. However, medical therapy may have either a primary or adjunctive role if the

patient cannot safely undergo surgery. The medications work through three broad mechanisms. "Neuromodulatory" compounds modulate corticotropin (ACTH) release from a pituitary tumor *e.g.*, Bromocriptine and Cyproheptidine, steroidogenesis inhibitors reduce cortisol levels by adrenolytic activity *e.g.*, Mitotane, Metyrapone, Ketoconazole, and Aminoglutethimide, glucocorticoid antagonists block cortisol action at its receptor *e.g.*, Ketoconazole(6). In the past, attempts have been made to manage Cushing's disease by medical therapy *viz*., Cyproheptidine and Bromocriptine without much long term success(3). Cyproheptadine and bromocriptine have been reported to be therapeutic in suppressing ACTH levels in Cushing's disease.

Surgery is the treatment of choice in all patients with pituitary tumors and the transsphenoidal removal of the tumor is the treatment of choice. However in infants as the sphenoidal cells are not formed and the pnematization is only complete by 4 years(5), this option is not available. Death in the immediate post-operative period as was seen in our patient is also reported in a similar case(7).

This extremely rare case demonstrates that though a pituitary macroadenoma is extremely rare at this age it should still be considered as a cause for Cushing's syndrome in infancy although the commonest cause at this age is adrenal tumors.

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