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Case report

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Generalized swelling and convulsions in a 6-year-old boy: Atypical presentation of ectopic Cushing syndrome

*Rahman MA[1], Tarannum A[2], Das D[3], Saad T[4], Islam R[5], Prasad I[6], Nessa L[7]

[1]Md. Ashiqur Rahman, Resident Physician, Department of Medicine, Dhaka Medical College Hospital, Dhaka, Bangladesh; [2]Assade Tarannum, Assistant Registrar, Department of Pediatrics, Dhaka Medical College Hospital, Dhaka, Bangladesh; [3]Debashis Das, Junior Consultant, Department of Thoracic Surgery, Dhaka Medical College Hospital, Dhaka, Bangladesh; [4]Tania Saad, Assistant Professor, Department of Pediatrics, Dhaka Medical College Hospital, Dhaka, Bangladesh; [5]Rumana Islam, Assistant Professor, Department of Pediatrics, Dhaka Medical College Hospital, Dhaka, Bangladesh; [6]Indrajit Prasad, Professor, Department of Endocrinology, Dhaka Medical College Hospital, Dhaka, Bangladesh; [7]Lutfan Nessa, Professor, Department of Pediatrics, Dhaka Medical College Hospital, Dhaka, Bangladesh

Abstract

Ectopic Cushing syndrome is an exceptionally rare condition in the pediatric population, particularly when arising from a thymic carcinoid tumor. We report the case of a six-year-old boy who presented with generalized swelling, moon face, acne, weight gain, hyperpigmentation, hypertension, and seizures. Biochemical evaluation demonstrated elevated cortisol and ACTH levels, unsuppressed by dexamethasone, indicating ACTH-dependent Cushing syndrome. Imaging revealed an anterior mediastinal mass, which was surgically excised and confirmed histologically as a thymic carcinoid tumor. Postoperatively, the patient required corticosteroid replacement, with gradual improvement of clinical features on follow-up. This case underscores the importance of considering ectopic ACTH secretion in children with rapidly progressive hypercortisolism and highlights the need for timely diagnosis and multidisciplinary management for favorable outcomes. *[J Assoc Clin Endocrinol Diabetol Bangladesh,* January 2026; 5(1): *60-65]*

Keywords: Cushing syndrome, Ectopic Cushing syndrome, ACTH-dependent Cushing syndrome, Thymic carcinoid

***Correspondence:** Dr. Md. Ashiqur Rahman, Resident Physician, Department of Medicine, Dhaka Medical College Hospital, Dhaka, Bangladesh; Email: ashiqur19dmc@gmail.com, Phone: 01737392103

Introduction

Cushing syndrome (CS) is caused by exposure to excess glucocorticoids, a rare but clinically important condition in children. In contrast to adults, who typically exhibit classic symptoms like central obesity, thin skin, easy bruising, wide violaceous striae, and proximal muscle weakness, paediatric CS frequently manifests with more subtle features, especially growth failure accompanied by generalized obesity, making the diagnosis challenging. While most pediatric cases arise from pituitary adenomas (Cushing's disease) or adrenal neoplasms, ectopic secretion of adrenocorticotropic hormone (ACTH) is extremely rare in children. Among these, ectopic ACTH production secondary to a thymic carcinoid tumor is particularly uncommon.[1] Although ectopic Cushing syndrome (ECS) is extremely rare in children, when it does occur, it frequently presents with rapidly progressing hypercortisolism, severe metabolic disturbances, and atypical phenotypes like central obesity without classic striae, which can cause significant delays in diagnosis.[2]

Thymic carcinoids, which are neuroendocrine tumors with the potential for aggressive growth and metastasis, represent less than 5% of all carcinoid tumors and are exceedingly rare in the pediatric age group.[3] Their clinical manifestations are often subtle or nonspecific, contributing to diagnostic challenges. When associated with ectopic ACTH production, these tumors may lead to significant metabolic derangements, impaired growth, and rapidly progressive signs of hypercortisolism.[4]

We report a rare case of a 6-year-old boy presenting with features of CS, later diagnosed with ectopic ACTH secretion from a thymic carcinoid tumor. This case highlights the importance of considering ectopic sources in pediatric hypercortisolemia and underscores the diagnostic and therapeutic challenges in managing such an unusual etiology.

Case report

A 6-year-old boy had a history of generalized swelling of the whole body, first noticed as facial puffiness, then the abdomen, without any urinary complaints for about 1 month, and was admitted to the hospital and treated with fluid restriction and diuretics. After 14 days of discharge, he developed swelling again and was treated with homeopathic medicine this time. After 5 days, he developed high-grade fever, several episodes of convulsions, and unconsciousness; he was again admitted to the hospital. A CT scan of the brain was suggestive of the diagnosis of encephalomyelitis. IV methylprednisolone was given, and he made a recovery. However, during his hospital admission, he was noted to have generalized swelling (more prominent centrally), a moon face, plethora, pigmentation of the knuckles, and pressure areas (Fig. 1, 2). His blood pressure was also high (118/82 mm Hg). His height was 106 cm, weight was 17 kg, and BMI was 15.1 kg/m^2. Height Z score was -1.85, weight Z score was -1.57, and BMI Z score was -0.2 (41.9%). Waist circumference was 65 cm. After his steroids had been switched off for almost one week, biochemical tests were done, which revealed hypernatremia, hypokalemia, hypocalcemia, and hypomagnesemia. His serum cortisol was 609 nmol/L, and plasma ACTH was 138 pg/ml (Table I). His 24-hour urine free cortisol level was high. Low-dose dexamethasone suppression test failed to suppress serum cortisol, which points to a diagnosis of CS. As ACTH was high, a diagnosis of ACTH-dependent CS was made. A high-dose dexamethasone suppression test was done, and it also failed to suppress cortisol to 50% of the baseline value (Table I). The CT scan of the abdomen was unremarkable. However, a CT scan of the chest revealed a mediastinal mass suggestive of thymic carcinoid or neuroendocrine tumour (Fig. 3). After medical management of metabolic derangements and high blood pressure, he was sent to cardiothoracic surgery for surgical excision of the mass. Surgery was successfully performed, and the specimen (Fig. 4) was sent to histopathology. On histopathological study, sections made from the specimen showed a tumor composed of oval to spindle-shaped cells with granular cytoplasm and coarse chromatin. The tumor cells were arranged in ribbon and festoon formations, nests, and rosettes, resembling glands with central lumina within a vascular stroma. Occasional mitoses were seen. Adjacent areas showed compressed thymic tissue. All the resection margins were free of tumor. Immunohistochemical analysis revealed tumor cells positive for pancytokeratin (PanCK), synaptophysin,

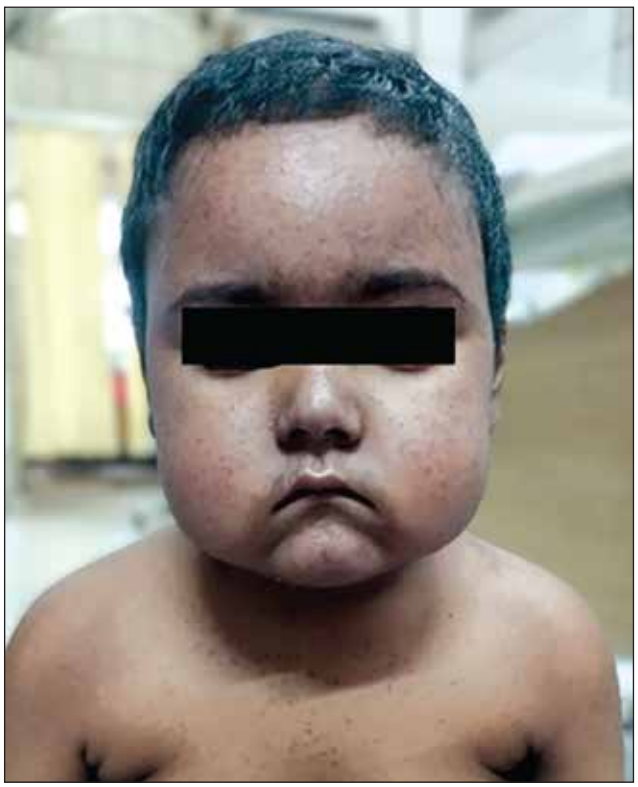


Figure-1: Typical appearance of Cushing syndrome with moon face, central obesity, and acne.

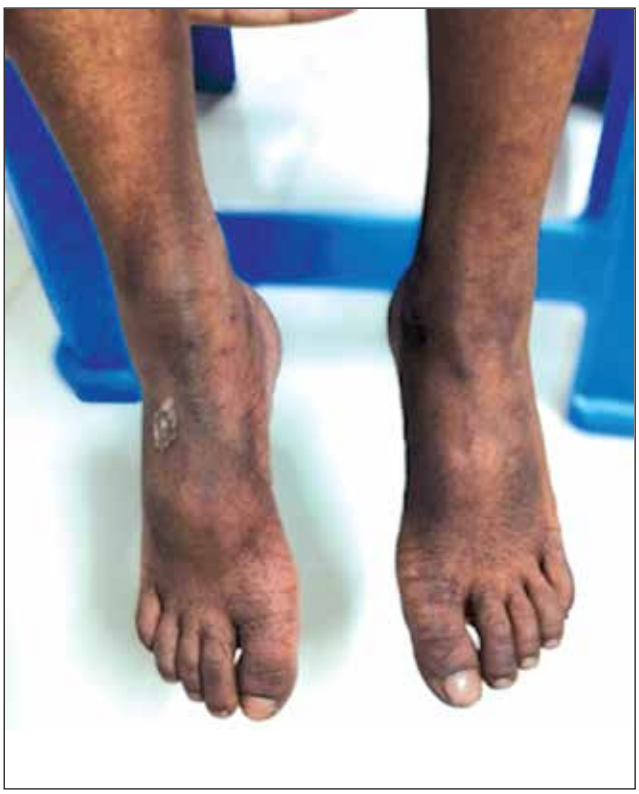


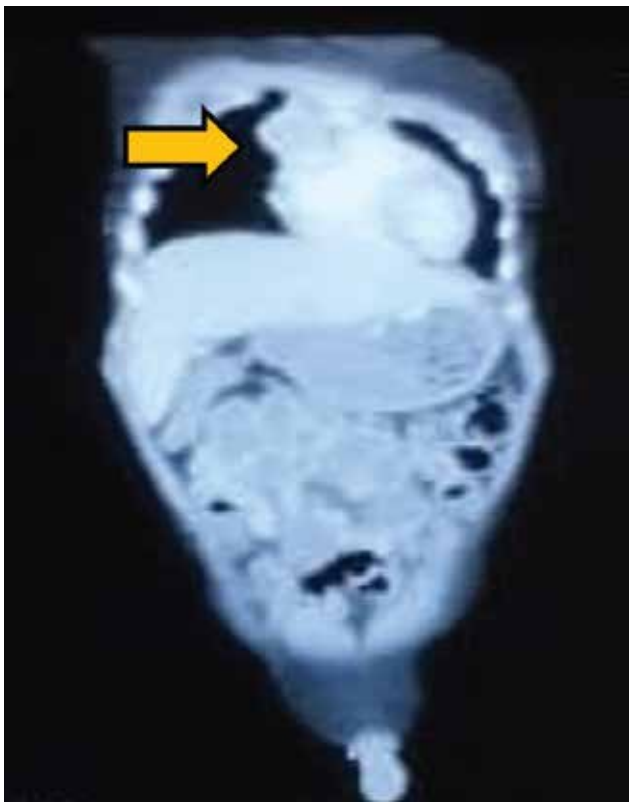
Figure-2: Pigmentation of the legs.

Table-I: Key investigations before and after surgery

Investigation	Before surgery	After surgery	Normal range
Serum Na+ (mmol/L)	148	139	135-144
Serum K+ (mmol/L)	1.7	3.5	3.5-5.5
Serum Cl- (mmol/L)	112	101	96-108
Serum Calcium (mmol/L)	1.60	-	2.12-2.62
Serum Magnesium (mmol/L)	0.42	1.7	0.70-0.91
ACTH (pg/mL)	152.5	12.9	8.3-57.8
Fasting Cortisol (nmol/L)	609	57	101.2-609.0
24hr free urine cortisol (nmol/L)	291	-	4.14-174
Low-dose dexamethasone suppression test (cortisol, nmol/L)	536	-	<50
High-dose dexamethasone suppression test (cortisol, nmol/L)	606	-	-
β-HCG (IU/L)	2.30	-	-
AFP (ng/mL)	0.97	-	<15

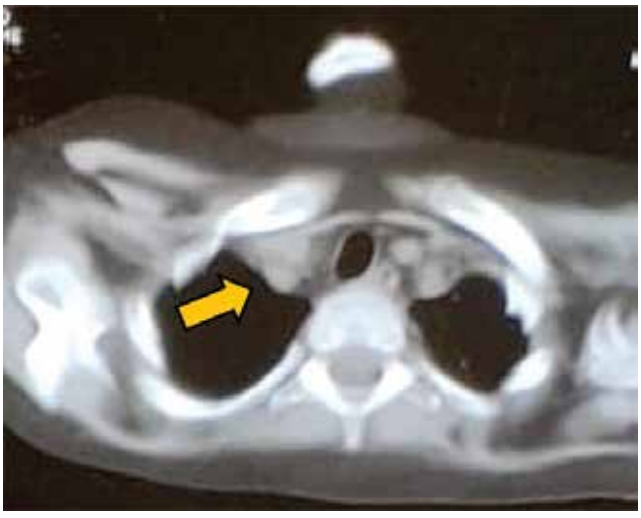
ACTH: Adrenocorticotropic hormone; β-HCG: Beta-Human Chorionic Gonadotropin; AFP: alpha-fetoprotein

chromogranin, and CD56, indicating epithelial origin with neuroendocrine differentiation. Neuron-specific enolase (NSE) showed focal positivity. The proliferative index, assessed by Ki-67, was low at approximately 1%, consistent with a low-grade neuroendocrine neoplasm.



(a)

Overall, the immunohistochemical profile favored the diagnosis of a thymic carcinoid tumor. Post-surgical blood tests revealed low cortisol (57 nmol/L) (Table I). He was started on physiological doses of hydrocortisone. Subsequent follow-up at 3 months revealed that several of the features of Cushing's syndrome, such as weight gain, edema, and high blood pressure, had resolved. The pigmentation was steadily declining as well (Fig. 5). His serum cortisol was 240 nmol/L, suggesting gradual



(b)

Figure-3: CT chest showing a mildly enhancing iso to hypodense lesion at the anterior mediastinum (a) coronal, and (b) transverse view.

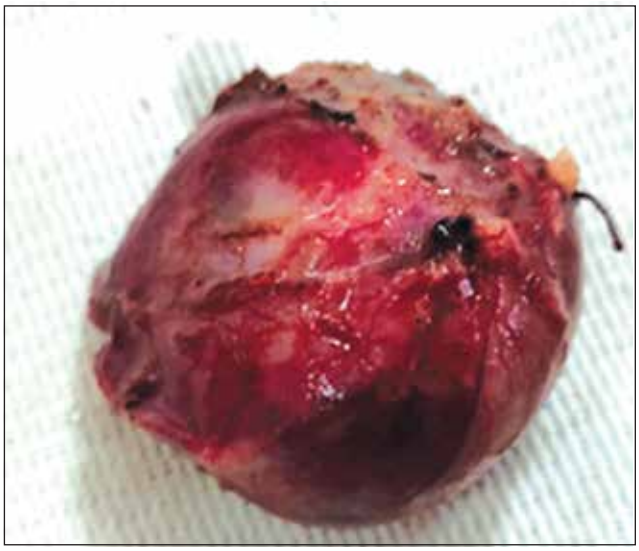
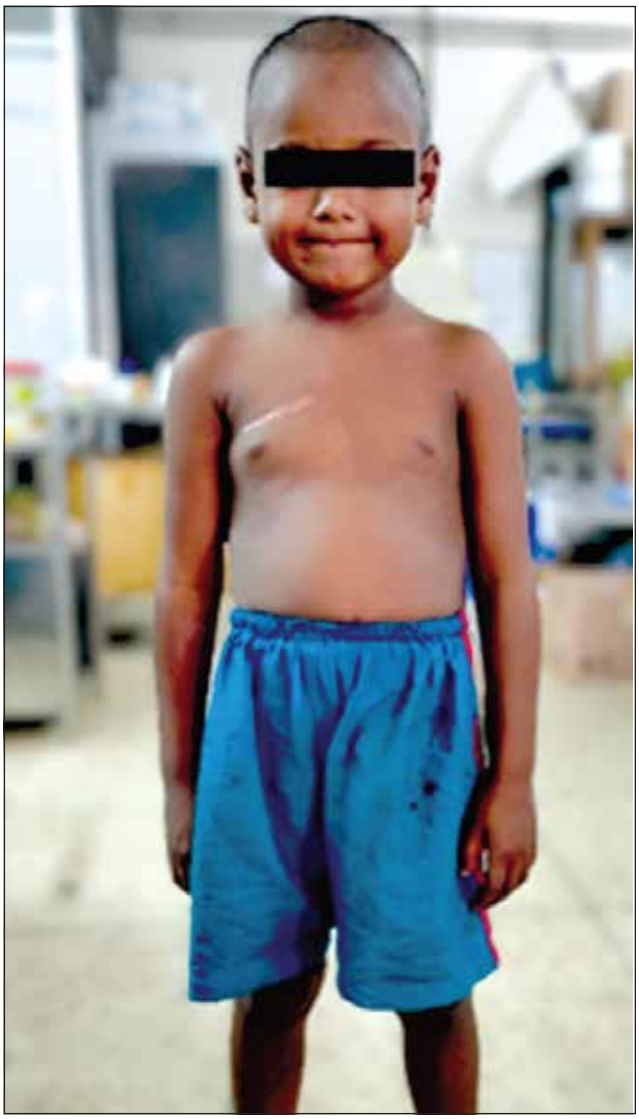


Figure-4: Resected specimen from mediastinal mass.



(a)

(b)

(c)

Figure-5: a: Post-surgical follow-up showing reduction of facial swelling and scar from thoracic surgery, b & c: Reduction of pigmentation after surgery.

recovery of the hypothalamic-pituitary-adrenal (HPA) axis. He is kept under regular supervision for recovery of the HPA axis.

Discussion

ECS in children is an uncommon and diagnostically challenging entity, especially when attributable to a thymic carcinoid tumor. In the pediatric population, most cases of CS arise from exogenous corticosteroid

administration or pituitary adenomas.[5] While the most common cause in children under four years is an adrenal tumor.[6] Ectopic ACTH secretion represents only a small proportion of cases, and within this subset, thymic carcinoid tumors are exceptionally rare.[7] Although it is challenging to determine the exact number, research indicates that a few dozen cases of ectopic Cushing's syndrome caused by thymic carcinoid have been documented. One review from 2001 cited 23 cases, in addition to two new ones, and other studies have reported individual or small cohorts of cases in recent years.[8] In contrast to Cushing's disease, this usually presents with a rapid and severe onset, marked by profound muscle weakness, weight loss, hyperpigmentation, and especially severe hypokalemic metabolic alkalosis due to the extremely high cortisol levels.[9]

Our case describes a 6-year-old boy presenting with rapid weight gain, central obesity, moon face, acne, hyperpigmentation of the knuckles and pressure areas, hypertension, and electrolyte imbalance. Pediatric CS usually presents with generalized obesity and height deceleration. The early manifestations of CS can resemble more common pediatric conditions, such as obesity or metabolic syndrome. According to a study, a significant portion of pediatric CS patients (~31%) do not have obesity (by BMI z-score)[10]. This indicates that pediatric CS may not have classical obesity as seen in adult patients. Nevertheless, growth failure serves as a critical distinguishing feature and should prompt an endocrine assessment in any child who presents with concurrent weight gain and impaired linear growth.[11] The presentation of the boy with normal BMI but central obesity with relatively thin limbs may be explained by the rapid onset of severe hypercortisolism within a short period of time.[12]

His initial presentation with neuropsychiatric manifestations is uncommon, but it is an occasional presentation of CS. While encephalomyelitis is not a common presentation of CS, the condition can cause significant neuropsychiatric symptoms, including cognitive and mood changes, and in some cases, seizures or encephalopathy.[13] Another explanation for this presentation may be the hypocalcemia and hypomagnesemia, which, though uncommon, can occur with severe hypercortisolism.[14] The mineralocorticoid effect of large amounts of glucocorticoids can result in potassium and magnesium wasting, which in turn can cause hypocalcemia (exacerbated by anti-vitamin D effects of glucocorticoids). Rapid progression of symptoms, significant pigmentation, and lack of typical striae, severe hypokalemia, and other electrolyte imbalances lead to a suspicion of ECS.[7]

Biochemical evaluation revealed elevated cortisol levels, which were not suppressed by low-dose dexamethasone and high ACTH levels, strongly suggesting an ACTH-dependent CS. High-dose dexamethasone suppression test failed to suppress cortisol, which is suggestive of ECS. As the clinical picture and investigations were very much suggestive of ECS, a search for ectopic sources was done. Imaging subsequently identified a mass in the anterior mediastinum, and histopathological analysis confirmed it to be a thymic carcinoid tumor-a neuroendocrine tumor capable of secreting ACTH ectopically.

This case is noteworthy due to its presentation at an unusually early age and its rare underlying etiology. Thymic carcinoid tumors in the pediatric population are exceptionally uncommon, often demonstrating aggressive behavior, and may be associated with multiple endocrine neoplasia type 1 (MEN1).[15] In this instance, however, there were no clinical manifestations or family history suggestive of MEN1.

Management in such cases primarily entails complete surgical excision of the tumor, which was accomplished in our patient. In the postoperative period, the child required corticosteroid replacement therapy owing to suppression of the HPA axis, with gradual recovery anticipated over time.[16] Subsequent follow-up showed improvement of pigmentation with reduction of body weight and resolution of swelling. Long-term surveillance is essential to assess potential tumor recurrence, monitor the restoration of HPA axis function, and evaluate catch-up growth.

This case emphasizes the necessity of maintaining a high level of clinical suspicion for ectopic ACTH secretion in pediatric patients presenting with features of CS. It further highlights the value of a multidisciplinary management strategy involving pediatric endocrinologists, oncologists, and thoracic surgeons.

Conclusions

This case underscores the importance of considering rare ectopic sources of ACTH in pediatric CS. Early recognition and surgical excision are crucial for favorable outcomes.

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Disclosure

The authors declare that no conflict of interest could be perceived as prejudicing the impartiality of the research reported.

Financial Disclosure

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Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author upon reasonable request.

Ethical Approval and Consent to Participate

Written informed consent was obtained from the patient's attendant. All methods were performed in accordance with the relevant guidelines and regulations.

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