CASE REPORT

An atypical case of ectopic ACTH syndrome in an adolescent boy

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Abstract

Ectopic adrenocorticotropic hormone (ACTH) syndrome (EAS) is exceedingly rare in children and scarcely reported. Pancreatic neuroendocrine tumours (NETs) can rarely lead to secretion of ectopic ACTH. A 14-year-old boy presented with hyperpigmentation, hypertension and intermittent abdominal pain, and was diagnosed with endogenous hypercortisolism. An incidental pancreatic mass discovered on routine ultrasonogram (USG) revealed the source of ACTH. He underwent successful excision of the mass with resolution of hypercortisolism. The histopathology revealed a Pancreatic NET and immunohistochemistry was positive for ACTH stain.

INTRODUCTION

Ectopic adrenocorticotropic hormone (ACTH) production is a rare entity in young children, accounting for <1% of the cases. We report the case of an adolescent boy with ectopic ACTH syndrome (EAS) due to Pancreatic neuroendocrine Tumour (NET).

CASE REPORT

14-year-old boy presented with complaints of generalized darkening of skin and intermittent abdominal pain since last 2 months. On examination, he had a lean build and generalized hyperpigmentation. He also had multiple small café au lait spots on abdomen and back with bilateral axillary freckling and large irregular hyperpigmented patches on lower limbs (Fig. 1), his weight was 32 kg (−1.33 SDS), height-143.2 cm (−1.85 SDS) with BMI-15.6 kg/m². He was in Tanner II stage of puberty that was mildly delayed puberty for his age. He was also found to have Stage 1 hypertension BP:130/70 (>95th centile for age and sex).

Owing to the recent onset hyperpigmentation, and hypertension, 8 AM paired serum ACTH and cortisol were done. Serum cortisol came back to be significantly elevated at 49 μg/dl (N:5-25 μg/dl) with inappropriately normal ACTH levels at 26 pg/ml (N:10-46 pg/ml). Venous blood gas (pH-7.38, HCO3-22.4), electrolytes (Na-138, K-4) and plasma blood glucose (86 mg/dl) were normal.

In order to confirm the presence of hypercortisolism, overnight dexamethasone suppression (1 mg) was done, which revealed a non-suppressed cortisol (37 μg/dl: N:<1.8 μg/dl). Twenty-four hours urinary free cortisol (UFC) was very high-2570 mcg/24 h (11–70). Low dose dexamethasone suppression test again revealed a non-suppressed cortisol -18mcg/dl (N<1.8 mcg/dl). Also, there was moderate elevation of serum androstenedione,1.96 ng/ml (0.31–0.65), and serum dehydroepiandrosterone, 201 μg/dl (42–109).

Meanwhile, in view of recurrent abdominal pain, the child underwent USG abdomen, which revealed a left heterogeneously hypoechoic lesion in suprarenal region abutting the tail of pancreas.

Contrast enhanced computed tomography abdomen reported a heterogeneously enhancing mixed solid cystic lesion 6.5 × 6 × 6 cm in the left half of abdomen superiorly abutting...
Ectopic ACTH syndrome in adolescent boy

Figure 1: Clinical photograph of child showing generalized hyperpigmentation and no clinical stigmata of Cushing disease.

Figure 2: CECT Abdomen showing a heterogeneously enhancing pancreatic mass.

The overall incidence of Cushing syndrome is two to five new cases per million people per year, with only 10% of new cases occurring in children yearly [1]. Ectopic ACTH production is a rare entity in young children, accounting for <1% of the cases, as opposed to 10% in adults. Sources of ectopic ACTH include small cell carcinoma of the lung, carcinoid tumours in the bronchus, pancreas or thymus; medullary carcinomas of the thyroid, pheochromocytomas; and other NETs, especially those of the pancreas and gut carcinoids [2].
Understandably, the current experience with this syndrome in children especially is based on only a few case series and individual case reports.

NETs account for 1–3% of pancreatic tumours, NETs that produce ACTH have been reported, despite their lower prevalence than the other types of functional tumours [3].

A recent multicenter retrospective study over a 20-year period identified 10 cases of EAS presenting before the age of 20 years [4]. Out of 10, 8 EAS tumours were NETs with a majority of well-differentiated endocrine lung tumours. The clinical and biological spectrum of presentation of EAS was broad and overlapped with that of pituitary Cushings disease.

Peculiar and extraordinary features in our case were severe biochemical hypercortisolism in our patient without any Cushing stigmata. It was hypothesized that the anabolism due to high IGF1 levels during puberty, the extremely rapid onset of disease, and/or the underlying malignancy lead to masking of features of Cushing syndrome.

The next intriguing aspect of this case was the ACTH levels that being equivocal, and hence it was difficult to delineate an ACTH-dependent v/s independent source, although the un-suppressed level and hyperpigmentation were clues towards an ACTH-dependent Cushings syndrome. Yet, these levels of ACTH did not correlate well with the degree of hyperpigmentation and cortisol excess seen in this child. It can be postulated that precursors of ACTH with melanocyte-stimulating hormone hypersecretion led to hyperpigmentation in our patient.

Pancreatic NET as a source of ectopic ACTH secretion is an extremely rare entity, especially in pediatric population. However, the possibility of EAS should be considered in individuals with ACTH-dependent Cushing’s syndrome even in the absence of extremely increased plasma ACTH concentrations. The broad clinical spectrum of EAS in children may mimic Cushing disease.

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**CONFLICT OF INTEREST STATEMENT**

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ETHICAL APPROVAL
Yes

CONSENT
The authors certify that they have obtained all appropriate patient consent forms. The patients’ parents have given their consent for the patients’ clinical information to be reported in the journal.

GUARANTOR
Dr. Rajesh Joshi.

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