Case Report

Acanthosis Nigricans Associated with an Adrenocortical Tumor in a Pediatric Patient

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1. Introduction

Childhood adrenocortical tumors (ACTs) generally present during the first 5 years of life, with a second, smaller peak noted during adolescence [1–4]. Majority of these tumors come to medical attention subsequent to overproduction of adrenal cortical hormones. Virilization is the most common presenting sign (84.3%), either alone (55.1%) or in combination with overproduction of other adrenal hormones including aldosterone or glucocorticoids (29.2%), followed by 5.5% with isolated Cushing's syndrome, and 10.2% with nonfunctional tumors [4].

The diagnosis of ACTs in pediatric patients is generally made within 5–8 months of the first presenting signs and symptoms [2, 4, 5]; however, one-third of pediatric patients have either unresectable or metastatic disease at the time of diagnosis. The remaining two-thirds have disease confined to the adrenals [4]. An elevated blood or urine concentration of adrenocortical hormones and a suprarenal mass generally suggest a preoperative diagnosis of ACT. Imaging studies are necessary for sufficient staging and surgery planning [6]. Surgery is the best treatment plan for those with ACTs, and cisplatin-based chemotherapy with mitotane is indicated for metastatic disease or when complete resection is not possible at presentation [6]. In children with localized ACTs, tumor weight ≤200 g, virilization alone, stage I disease, absence of spillage during surgery, and age ≤3 years are considered important favorable prognostic indicators [4].

Malignant acanthosis nigricans (AN) is a rare paraneoplastic syndrome seen primarily in adults with an underlying diagnosis of gastrointestinal adenocarcinoma. Malignant AN is characterized by hyperpigmentation and velvety hyperplasia of the epidermis. This condition is generally not associated with tumors in pediatric populations or in the adrenal gland. We present a case of malignant AN in a pediatric patient with a nonmalignant, functional adrenocortical tumor.
Table 1: Pre- and postoperative endocrine laboratory values.

| Hormone                        | Preoperative hormone level | Postoperative hormone level | Normal range         |
|--------------------------------|----------------------------|------------------------------|----------------------|
|                                | 4/19/2010                  | 5/11/2010                    | 6/30/2010            | 4/20/2011          | 9/26/2012          |                           |
| Glucose (mg/dL)                | 88                         | 71                           | 127                  | 83                | 78                | 74–127                   |
| Nonfasting insulin (uU/mL)     | 43.7                       | —                            | 30.7                 | —                 | —                 | —                        |
| Hemoglobin A1C (%)             | 4.9                        | —                            | —                    | 4.7               | 4.7               | 3.8–5.9                  |
| Testosterone (ng/dL)           | 150                        | <3.0                         | <3.0                 | <2.5              | <2.5              | Tanner 1 range <3–10     |
| Androstenedione (ng/dL)        | 72                         | <10                          | —                    | <10               | <10               | Tanner 1 range <10–17     |
| Dehydroepiandrosterone sulfate (ug/dL) | 73            | <10                          | —                    | —                 | —                 | Tanner 2 range 31–65     |
| IGF-1/Somatotelin-C serum (ng/mL) | 325                | —                            | 143                  | 101               | 111               | Range for 3–4 years of age 54–178 |
| FSH (mIU/mL)                   | 0.143                      | —                            | —                    | —                 | —                 | Tanner 1 range 0.1–3.0   |
| Luteinizing hormone (mIU/mL)   | 0.010                      | —                            | —                    | —                 | —                 | Tanner 1 range 0.01–0.3  |

Follow-up random cortisol level one year postoperatively was normal at 7.1 mcg/dL (normal range 1.5–9.0 mcg/dL). Pathology review revealed a 12.5-gram encapsulated tumor without hemorrhage, necrosis, or capsular invasion (Figure 1). Tumor cells exhibited rare mitotic figures, favoring the diagnosis of a non-malignant adrenal cortical tumor. He demonstrated marked clinical improvement of all symptoms, including normalization of all laboratory values three weeks after surgery and complete resolution of the acanthosis nigricans three months postoperatively.

3. Discussion

ACT peaks during the first and fourth decades of life [10]. The incidence of ACT varies internationally, with particularly high rates noted in southern Brazil, where the incidence is approximately 10–15 times that observed in the USA [6]. Predisposing genetic factors may be responsible for this increased incidence [6]. ACT in children is exceptionally rare, composing only 0.2% of pediatric cancers [11]. Only 25 new cases are expected to occur annually in the USA, for an estimated annual incidence of 0.2–0.3 cases per million [11].

Acanthosis nigricans (AN), a common cutaneous finding, is characterized by hyperpigmentation and velvety hyperplasia of the epidermis [12]. In general, it affects flexural areas including the neck, antecubital, and popliteal fossa [12]. Benign AN usually presents between birth and puberty and can have a possible genetic component [8]. Benign AN often occurs in individuals exhibiting insulin resistance, such as patients with a diagnosis of diabetes mellitus, obesity, and polycystic ovarian syndrome [12]. Although benign forms of AN are relatively common, malignant AN can occur as a rare paraneoplastic syndrome with approximately 1,000 reported worldwide cases [13]. It is most often seen in adults with an underlying diagnosis of gastrointestinal adenocarcinoma [7, 8]. Malignant AN tends to worsen with progression of the neoplasm, lessen with treatment, and return with tumor finding associated with pediatric tumors. Here, we report the first case of malignant AN in a pediatric patient with a non-malignant, functional ACT at the time of tumor diagnosis.

2. Case Presentation

A previously healthy 33-month-old Caucasian male presented with a three-month history of rapid virilization and a neck rash. Height and weight remained unchanged over the preceding months at the 50th percentile. Blood pressure at the time of diagnosis was 123/65 mmHg and heart rate 112 bpm. Physical examination was notable for coarse facial features, facial acne, anterior and posterior cervical acanthosis nigricans, Tanner 2 pubic hair, and pubertal phallus (8 cm in length and 2 cm in diameter), but prepubertal testes at 3 mL volume bilaterally. Laboratory evaluation revealed an elevated nonfasting insulin level with normal values for glucose, random cortisol 19.6 mcg/dL (normal range 9–22 mcg/dL), ACTH 8.35 pg/mL (normal range 5–46 pg/mL), and hemoglobin A1C 4.7% (normal range 3.8–5.9%). Abnormal laboratory findings for age included elevated testosterone, androstenedione, dehydroepiandrosterone sulfate (DHEAS), all within Tanner 2–3 range. IGF-I level was increased for age. Gonadotropins were Tanner stage 1, confirming a peripheral source for androgen production. Serum electrolytes, beta-HCG, and alpha-fetoprotein levels were all within normal limits. Table 1 is a summary of pertinent laboratory results.

MRI of the abdomen revealed a 2.3 × 3 cm mass within the right adrenal cortex, absent retroperitoneal lymphadenopathy, and lack of tumor thrombus within the IVC. The patient underwent a successful right adrenalectomy and retroperitoneal lymph node dissection without any complications. Postoperative screening morning cortisol was undetectable (<1.0 mcg/dL), indicating suppression of contralateral unaffected adrenal gland. He was treated with stress-dose hydrocortisone and subsequently transitioned to and slowly weaned off of physiologic replacement postoperatively.
Figure 1: (a) Gross photograph of resected adrenal mass. (b) Low power photomicrograph of adrenocortical tumor. The tumor is encapsulated (arrow) and has a pushing border, with compressed normal adrenal cortex on the right. (H&E, 20x). (c) High power photomicrograph of adrenocortical tumor. Arrow is pointing to a thin fibrous capsule. The tumor has similar cytologic features to the normal adrenal seen on the right. Features that have been associated with malignancy (capsular invasion, necrosis, and increased mitotic activity) are not present (H&E, 200x).

Conflict of Interests

No real or perceived conflict of interests exists for the listed authors.

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