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Malignant Acanthosis Nigricans in Adrenal Carcinoma

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Adrenal cortex produces three major classes of hormones: glucocorticoids, mineralocorticoids, and androgens. Excesses or deficiencies of glucocorticoids and androgens may have profound cutaneous manifestations. Cushing's disease and adrenal tumors are rare in childhood and adolescence(1). Both disorders occur at any age. However, in general,

adrenal cortisol excess in infancy and early childhood is due to adrenal tumors, whereas after the age of 6 or 7 years Cushing's disease is more likely(2).

We report a case of adrenal carcinoma with a spectrum of dermatologic manifestation including malignant acanthosis nigricans, a cancer clue of high reliability best known for its association with internal malignant neoplasms.

Case Report

A 4 year old girl was brought for increasing abdominal distension for over 9 months. She had pubic and axillary hair, and an enlarged clitoris since the age of 6 months. On examination, she looked plethoric, had central obesity and very fine hair on cheeks. She had advanced physical development with a weight-age of 6.5 years and a height-age of 5 years. Her blood pressure was 140/90 mm Hg. Close observation revealed comedones and papules on ear, nose, central forehead and chin, a velvety brown hyperpigmentation with a finely verrucous dark hyperkeratosis on knuckles, and violaceous striae on the anterior abdominal wall. A well defined, firm right flank

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Received for publication: March 7, 1994;

Accepted: October 31, 1994

intraabdominal mass measuring 20 x 20 cm was discovered on abdominal examination.

Laboratory evaluation revealed a hemoglobin of 11.6 g/dl. Urinalysis and electrolytes were normal. Plain radiograph of abdomen revealed calcification in the right flank. Computerized tomography of abdomen demonstrated a well encapsulated right adrenal mass with areas of necrosis and calcification. Liver, vena cava, and lymph nodes were free from metastasis. (*Fig. 1*). The chest radiograph was normal. Serum testosterone and androstenedione levels were elevated. Basal serum cortisol levels were elevated and a high dose dexamethasone suppression test revealed nonsuppressible cortisol levels. Histological examination of tumor mass showed diffusely arranged pleomorphic tumor cells with abundant acidophilic cytoplasm and hyperchromatic nuclei.

Extensive areas of necrosis were also seen. Histological diagnosis was adrenocortical carcinoma (*Fig. 2*).

Discussion

Acanthosis nigricans is a cutaneous lesion that has in recent years, been of increasing interest to endocrinologists and diabetes specialists. The reason is the recognition that acanthosis nigricans is associated with a number of uncommon, but extremely interesting disorders. The first and best known association is with internal malignant neoplasms(3). This uncommon association most often involves gastrointestinal tract neoplasms but other sites of malignancy have also been associated with acanthosis nigricans.

In acanthosis nigricans a brown pigmented velvety verrucosity or fine papillomatosis appear in the axillae and other body folds. In addition to the flex-

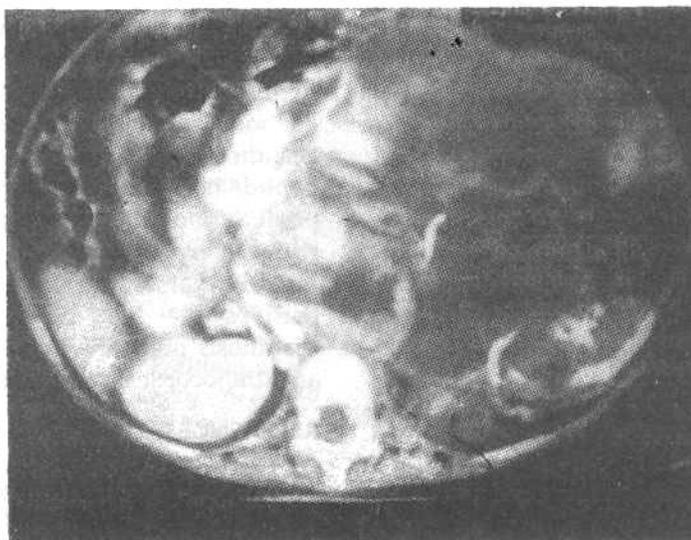


Fig. 1. CT-Scan abdomen showing areas of necrosis and calcification in the region of adrenal gland.

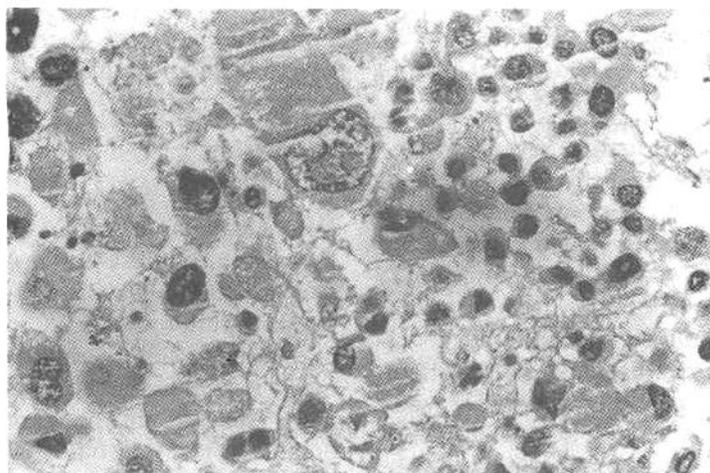


Fig. 2. Histological appearance of adrenocortical carcinoma (x 400).

ural changes, there may be finely verrucous dark hyperkeratosis on the knuckles, as seen in our cases. The basic change appears to be increased epidermal folding over papillary dermal hypertrophy and accompanying increase in epidermal melanization and hyperkeratosis(4). The cases linked with malignancy have been called "malignant" acanthosis nigricans, whereas the other cases have been termed benign. Malignant acanthosis nigricans is most often associated with adenocarcinoma that is generally of the stomach but may appear elsewhere in the gastrointestinal tract. Ovarian, prostatic, breast and lung carcinomas have also been associated, as well as rare instances of lymphomas and squamous cell carcinoma(3).

Curth *et al.*(3) in their review of 42 cases of acanthosis nigricans established an association of this dermatosis with a malignant internal tumor. Among the 42 sections studied by Curth *et al.*, adenocarcinoma were found in 33, several of which were highly anaplastic.

The high degree of malignancy of the cancer associated with malignant acanthosis nigricans was stressed in all cases reported in the literature and was confirmed in almost all cases by Curth *et al.* (3).

There are many speculations about the pathogenesis of acanthosis nigricans. Because of its association with pituitary hypothalamic disturbances and adenocarcinoma a yet to be defined acanthosis nigricans inducing pituitary peptide hormone is believed to stimulate papillary dermal hypertrophy along with hyperpigmentation to produce this rare dermatological lesion(5). Ours is perhaps the first case of malignant acanthosis nigricans in association with an adrenocortical carcinoma.

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Weill-Marchesani Syndrome

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Weill-Marchesani syndrome is a rare systemic connective tissue disease characterized by short stature, brachydactyly, ectopia lentis and spherophakia. This was first reported by Weill in 1932 and subsequently well characterized by Marchesani in 1939(1). Genetically this syndrome often shows autosomal recessive inheritance. Frequent consanguinity between parents support this model. There have been reports suggesting autosomal dominant inheritance(2).

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*Received for publication: December 21,1993;
 Accepted: October 4, 1994*

Gorlin *et al.* reported a family in which a father and two of his three children were affected suggesting genetic heterogeneity or the possibility of pseudodominance(1).

We report six patients with Weill-Marchesani syndrome from 4 sibships, giving an account of family data to help to delineate the mode of inheritance. This is the largest and the first report from India.

Case Reports

The important features noted in our six cases are summarized in *Table I*.

Discussion

In 1932 during research on Marfan syndrome, Weill noted that of the 8 individuals he was studying with presumed Marfan syndrome one was short in stature and had short swollen fingers with limited range of motion(1). Later, in 1939 Marchesani described the association of spherical lenses and brachydactyly in two families and suggested the term of dystrophia mesodermalis hyperplastica which is presently designated as Weill-Marchesani syndrome to distinguish from those with dystrophia mesoder-