Malignant acanthosis nigricans associated with adenocarcinoma of the prostate

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Abstract

We report a case of malignant acanthosis nigricans, which presented as severe progressive thickening of the skin, tripe palms and cutaneous papillomatosis. The patient did not complain of any other symptoms and it was the nature of the skin involvement that prompted us to hunt for the underlying neoplasm; an adenocarcinoma of the prostate with multiple bone metastases.

The characteristic features of malignant acanthosis nigricans, which help in selecting the patients for further evaluation from the large number of patients who present with acanthosis, are discussed.

Introduction

Benign acanthosis nigricans is a fairly common skin manifestation encountered in Dermatology practice. Malignant acanthosis nigricans is comparatively very rare. It is characterized by onset later in life, rapid progression and extensive involvement of skin and mucous membranes[1].

We report a case of malignant acanthosis nigricans associated with disseminated adenocarcinoma of the prostate. Even though acanthosis nigricans (AN) is most commonly associated with adenocarcinomas[1], coexistence of carcinoma of the prostate with malignant AN is very rare.

Case report

A previously healthy 68-year-old pensioner presented to the Dermatology clinic, NHSL, with a history of yellowish thickening of the palms for one year, and thickening and pigmentation of the face, neck and upper trunk for 2 years. Five years ago he had been diagnosed to have diabetes with nephropathy and hypertension, which were well controlled with medication.

He did not complain of constitutional symptoms like weight loss or loss of appetite. Neither did a detailed history reveal any clue to an underlying malignancy. Gastrointestinal symptoms were absent.

On examination he was an averagely built man with pigmentation and thickening of the skin with prominent skin creases of the face, neck, axillae, upper trunk and the groins. His palms were thickened with accentuation of the palmar creases and roughened thickening of the fingerprints with a yellowish hue (Fig 1). Soles were also involved, but to a lesser extent. He also had discrete, circumscribed 3-5mm sized, rough papillomatous growths over the scalp, hands and the shins (Fig 2). Mucosal surfaces were not affected.

He had a well-defined, hard, 3cm x 7 cm lump over-lying the right 9th rib posterolaterally. Systemic examination including the respiratory system was normal. Digital examination of the rectum revealed a hard, irregular, normal sized prostate with obliteration of the median groove.

On investigation; ESR 10mm, WBC 10,500/cumm with a normal differential, haemoglobin 13.2g/dl, platelet count 194,000/cumm, fasting plasma glucose 135 mg/dl, normal liver function tests and serum calcium. His renal functions were abnormal with serum creatinine 2.1 mg/dl, creatinine clearance 74 ml/min/1.73sqm and 24-hour urinary excretion of 429 mg. These findings were in keeping with diabetic nephropathy.

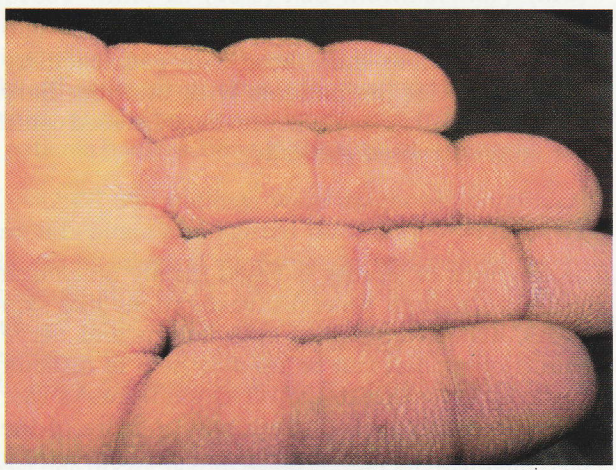

Figure 1. *Palm showing thickening of the fingerprints and accentuation of palmar creases.*

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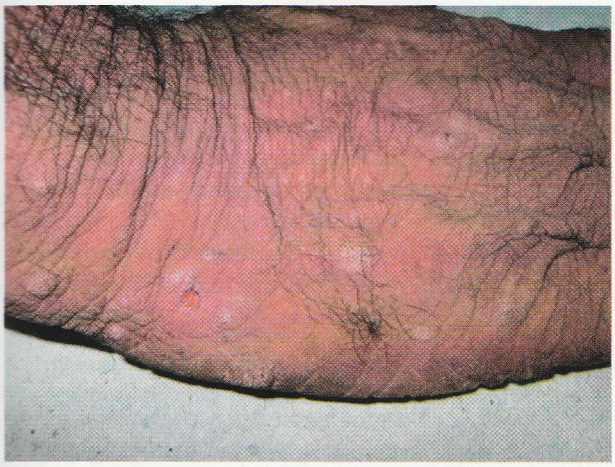

Figure 2. *Discrete papillomatous growths over the dorsum of the hand.*

As gastric adenocarcinoma is the commonest malignancy associated with acanthosis nigricans, upper GI endoscopy was performed. It revealed mild reflux oesophagitis, reduced distensibility and disturbed rugae pattern with multiple healed ulcers. Several biopsies from these sites failed to reveal any evidence of malignant change.

Skin biopsies from several sites showed hyperkeratosis, focal papillomatosis, acanthosis and hypergranulosis consistent with acanthosis nigricans.

CT scan of the abdomen showed that the chest wall lump was a secondary deposit with rib erosion (Fig 3) and the other abdominal organs were normal except for a benign cyst in the left kidney. Trucut biopsy of this lesion showed fragments of bone with multiple deposits consisting of cells with hyperchromatic nuclei with moderate cytoplasm, in keeping with adenocarcinoma deposits (Fig 4).

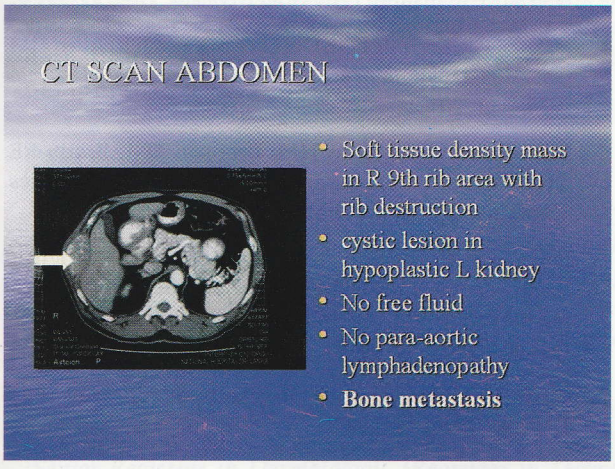

Figure 3. *CT scan abdomen showing the soft tissue mass with erosion of the underlying rib.*

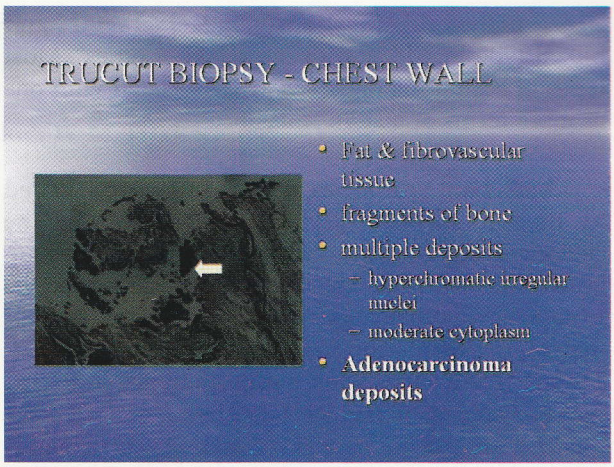

Figure 4. *Soft tissue mass showing fragments of bone and deposits of cells with hyperchromatic nuclei (haematoxylin and eosin x 400).*

Prostate specific antigen was elevated to 30.3/ml (normal 1.1-3.45). Total serum acid phosphates was within normal range (3.6 KAU, normal 1-4) but the tartrate labile fraction showed a twofold increase of 1.5 KAU (normal up to 0.8).

Trans-rectal biopsy of the prostate showed raggedly infiltrating, fused prostatic glands and sheets of cells with hyperchromatic nuclei in a desmoplastic stroma consistent with adenocarcinoma of the prostate. Gleason's sum score was 9. Tc99 bone-scan showed multiple metastases in the thoracic spine, left shoulder, right 9th rib, 3rd lumbar vertebra and right acetabulum. A diagnosis of acanthosis nigricans due to adenocarcinoma of the prostate with multiple bone metastases was made.

The patient was seen by the consultant oncologist, who advised on orchidectomy followed by repeat PSA 3 months post operatively. He underwent bilateral sub capsular orchidectomy in early September 2004. One month after the surgery the bone deposit has regressed in size and the thickness of the skin is also less.

Discussion

Acanthosis nigricans (AN) has been classified into many types. One classification includes six 2 types; namely

1. benign AN
2. syndromic AN
3. pseudoacanthosis (obesity associated)
4. drug induced AN
5. malignant AN
6. naevoid (unilateral) AN.

Another classification includes acral AN and mixed type in addition to the above 6 types[1]. Most types of acanthosis nigricans are associated with one or more forms of insulin resistance[3].

Malignant acanthosis nigricans is characterized by its sudden onset and rapid progression. The cutaneous eruption is in fact induced by the tumour, unlike other forms of AN, which may coexist with the malignancy. 3 other cutaneous markers of malignancy may coexist with acanthosis; namely, sign of Leser-Trelat, florid cutaneous papillomatosis and tripe palms[1]. Our patient had the latter two manifestations.

The majority of patients with acanthosis nigricans are middle-aged. The extent of cutaneous involvement is greater than in the other forms, even becoming generalised[4]. Soft papillomas and warty nodules may occur. There may be localized or generalised pruritus. Striated and brittle nails, longitudinal grooves in nails and leukonychia and alopecia have been described[1].

Involvement of the palms and soles is more prominent in malignant AN. Hyperkeratosis with rugose thickening of the fingerprints, a yellowish hue with prominence of the creases makes up the appearance of tylosis. When the thickening is so prominent to produce a rugose appearance it is called "tripe-palms" a word describing its resemblance of a sheep's stomach[2]. These changes were very prominent in our patient.

Extensive mucosal involvement is also a feature of malignant acanthosis nigricans. Practically any mucosal surface may be affected including the buccal mucosa, lips, tongue, conjunctivae, larynx, oesophagus, anus, vagina and prepuce. Mucosal changes may be absent in less than 50% of patients with malignant AN[2], as was the case with our patient.

The tumours associated with acanthosis nigricans are most commonly adenocarcinomas; most often intra-abdominal. The single most common malignancy occurring together with AN is gastric adenocarcinoma, which constitutes about 70% of intra-abdominal tumours[1]. Other adenocarcinomas include uterine, hepatic, intestinal, ovarian, breast, lung and mediastinal tumours. Other tumours associated with AN include; lymphoma, mycosis fungoides[5], carcinomas of the gall bladder, pancreas, oesophagus, prostate, thyroid, endometrium and parametrium[6]. The underlying neoplasm may be rather indistinct and may take even several years to find[6].

AN is preceded by the malignancy in 17% of patients, occurs simultaneously with the tumour in 61% while it precedes the malignancy in 22%[7], like in our patient. AN is known to regress after successful removal of the tumour, but most malignancies associated with AN run an aggressive course with the majority of patients succumbing to their illness within 1 year of diagnosis.

As AN is a common condition presenting to the clinicians, it has to be borne in mind that progressive, severe AN occurring in a non-obese, post pubertal person should be considered as associated with malignancy, even if the patient does not have any symptoms attributable to an underlying tumour.

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