

Acanthosis Nigricans and Bile Duct Malignancy

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A case of acanthosis nigricans associated with a metastatic adenocarcinoma is presented. To our knowledge this is the first one reported in the literature. The primary tumour is unknown, but it is presumably a cholangiocarcinoma. The skin changes preceded the detection of malignancy by 2 years, during which the skin lesions progressed though the patient was still in good health. If malignant acanthosis nigricans is suspected and the underlying malignancy cannot be found at the initial screening, repeated screenings are necessary because of the time factor. **Key words:** Paraneoplastic syndrome; Tripe palms; Internal malignancy.

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Acanthosis nigricans (AN) is characterized by hyperpigmented, velvety hyperkeratoses with papillomatosis mainly on axillae, neck and groin. AN develops in obese individuals or it may accompany endocrine diseases, often with insulin resistance and hyperinsulinemia, but sometimes AN can be a marker of internal cancer (1). If AN is associated with internal malignancy (MAN), there will often be a diffuse keratoderma of the palms - "tripe palms" - and soles. Esophageal involvement and oral manifestations may be seen in addition to the usual cutaneous findings (2-4). MAN usually appears in persons past 40. The malignant tumour is most frequently an adenocarcinoma of the gastrointestinal tract or a pulmonary carcinoma, and the skin changes may precede, accompany or follow the diagnosis of the underlying neoplasm. Often, however, it will follow an aggressive course (5, 6).

The following case report depicts a patient who developed marked AN in a very short time, the skin changes preceded

the diagnosis of a metastatic adenocarcinoma by 2 years even if screening for internal malignancy was carried out.

CASE REPORT

In the spring of 1990, a 52-year-old obese woman developed skin changes round the neck, in the axillae, under the mammae, and on the abdomen (Fig. 1). The skin was thickened by a papillary overgrowth which was hyperpigmented, almost black, and the affected areas were covered with skin tags (Fig. 2).

On the basis of the characteristic clinical picture and the histological findings, a diagnosis of AN was made. Apart from these severe skin lesions the patient was asymptomatic. A slight hypertension had been treated with hydrochlorthiazid from August 1988 and with atenolol from January 1989. At the same time there was a progressive loss of scalp and body hair, which led to alopecia universalis from September 1989. In the autumn of 1990, another department carried out a thorough evaluation in order to reveal an underlying malignancy, but laboratory findings, x-ray of the chest, thyroid gland scintigraphy, i.v. urography and mammography were all normal. X-ray of colon showed diverticulosis and liver scan only showed cholecystolithiasis. Gastros-

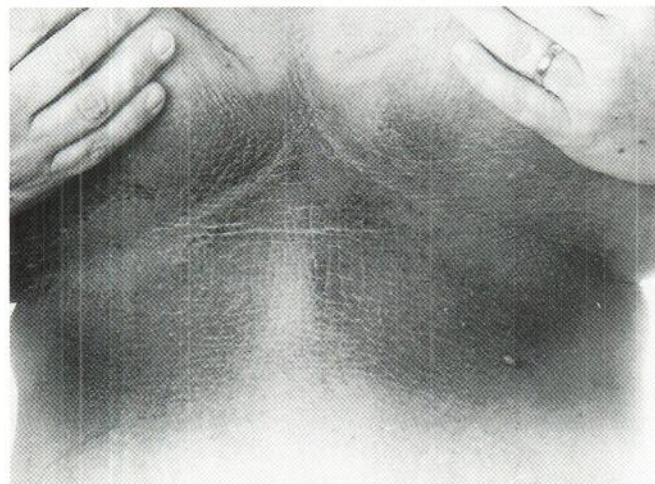


Fig. 1. Skin changes on the abdomen.



Fig. 2. Skin tags covered the affected area.

copy and gynaecological examination also were normal. The patient was referred to our department in the spring of 1992. In the meantime considerable progression of the patient's AN had occurred. Now, there were pronounced tripe palms, and furthermore AN changes had developed periorally and in the cavum nasi (Fig. 3). The patient was still in good health, and except for the skin changes she was quite asymptomatic. Blood levels of insulin and glucose were normal.

A new screening for internal malignancy was commenced. Chest x-ray supplemented with CT scan now revealed multiple, round infiltrates in both lungs, consistent with metastatic disease. Abdominal scan supplemented with CT scan revealed a 12 × 7 cm large mass in the right liver lobe as well as glands around porta hepatis. Liver biopsy guided by ultrasound was performed 3 times before it was successful in getting representative material; at this time light microscopy showed liver tissue with adenocarcinoma, which was most likely a cholangiocarcinoma. It was not possible to operate, and cancer chemotherapy was considered to be of no help and so treatment with etretinate (Neo-Tigason®) was started. The patient remained in good health for another 6 months, but thereafter there was loss of appetite, severe loss of weight and pruritus. The retinoid treatment did not have any effect upon the severe skin lesions.

In the spring of 1993 the tumour in the liver was still growing and alkaline phosphatase was increasing.

DISCUSSION

Previously, 3 cases have been reported of AN associated with adenocarcinoma of the gallbladder, but to our knowledge this is the first one involving cholangiocarcinoma (7).

MAN is a well-known paraneoplastic syndrome. The term is used to describe the indirect effects of cancer that are secondary to the production of biologically active substances in the neoplastic tissue. Because of the fact that many cutaneous paraneoplastic syndromes are proliferative skin disorders, growth factors have been investigated. Ellis et al. (8) hypothesize, from a case report on a patient with a Clark's level II malignant melanoma and skin lesions, that proliferative paraneoplastic skin disorders – such as AN, the sign of Leser-Trélat

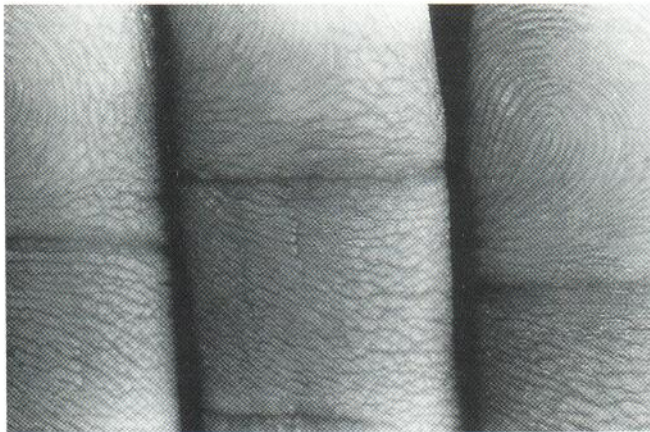


Fig. 3. The patient got tripe palms.

and multiple acrochordons – may have been caused by a production of epidermal growth factor (EGF) or alpha-transforming growth factor (α TGF) by the melanoma. Similarly, androgenic steroids and various peptides have been proposed as causative factors of AN (9).

Tripe palms occur in patients with or without AN. In approximately 90% of the reported cases tripe palms occurred in patients with cancer, most commonly gastric or pulmonary carcinomas (10, 11). It is well-known that the activity of AN often follows the underlying malignancy; AN may regress after radical operation, and it may progress in cases of recurrence or metastases of the tumour (12, 13).

If MAN is suspected, a careful screening for internal malignancy should be carried out, and in case the tumour cannot be found at the initial screening, repeated screenings are necessary because of the time factor. Unfortunately, the malignant disease is often widely advanced when finally detected.

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