

Paraneoplastic type of *acanthosis nigricans* in patient with hepatocellular carcinoma

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Abstract

Paraneoplastic *acanthosis nigricans* is connected with malignancies in adults in almost 100% of cases. The typical skin changes include: thickening and hyperpigmentation in typical localization with mucocutaneous involvement.

Purpose: The authors report a case of a malignant type of *acanthosis nigricans* in 42-year old female patient with hepatocellular carcinoma.

Case report: First skin lesions appeared in 2000. The patient died within 22 months (of the first appearance of skin symptoms), because of hepatocellular carcinoma.

Herein we report the clinical picture, skin involvement and diagnostic procedures in *acanthosis nigricans*.

Conclusions: Paraneoplastic type of *acanthosis nigricans* – in patient with hepatocellular carcinoma is not frequently reported in the literature. In the aspect of clinical occurrence of skin lesions suggesting *acanthosis nigricans* the diagnostics should be focused on internal malignancies

Key words: *acanthosis nigricans*, hepatocellular carcinoma, paraneoplastic syndromes.

Introduction

Acanthosis nigricans (*acanthosis nigricans*, AN) was firstly described by Pollitzer. It is characterized by eruption of many, symmetric, velvety hyperkeratotic lesions with brownish hyper-

pigmentation. Flexures, skin folds, axills, bend of the elbow, nipples, neck, navel and anogenital regions are predominantly involved.

Acanthosis nigricans appears in the course of the internal malignancies, many systemic disorders, endocrinopathies and dermatological diseases (e.g. atopic dermatitis).

Based on the clinical characteristics *acanthosis nigricans* is divided into 8 types: benign AN, *pseudoacanthosis nigricans* connected with obesity, syndromic AN, paraneoplastic, malignant AN, acral AN, unilateral AN, drug-induced AN and mixed AN. Syndromic type of AN is subdivided into type-A (Hair-AN) with hyperandrogenism, insulin-resistance and typical skin lesions and type-B connected with diabetes and autoimmune disturbances.

Acanthosis nigricans maligna occurs in three abortive clinical subforms as papillomatosis florida cutis verruciformis, tripe palmar syndrome and Leser-Trélat sign. They coexist together or appear consecutively after each other.

Material and methods (Case report)

The authors reported a case of a female patient with diagnosed paraneoplastic type of *acanthosis nigricans* at in the course of hepatocellular carcinoma (clarocellular variant G-2).

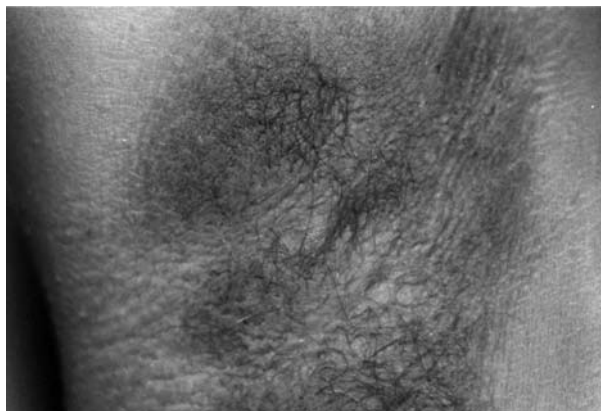
A female patient, 42 years old, engineer of motorways building. She had taken no drugs and never had been treated because of any other serious disorders. At the beginning the patient was hospitalized in the Dermatological Department of Silesian Medical Academy in Katowice in May 2000. Then, papillomatous, hyperpigmented lesions in folds, neck, abdomen and anus were observed (*Fig. 1*). They were symmetrically and quickly widespread as a papillomatous roughly changes on the skin folds, trunk, hands and anus. No changes abnormalities of oral mucosa, nail plates and hair were found. Body mass index (BMI) was 26. The diagnosis of *acanthosis nigricans* was based on histopathological examination. In laboratory tests:

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Figure 1. Skin lesions on neck in paraneoplastic type of acanthosis nigricans



Figure 2. Hyperpigmentation with hyperkeratosis of the axil – “dirty skin”



blood cell count, biochemical parameters in the serum such as electrolytes, uric acid, glucose, aminotransferases, GGTP, LDH, bilirubin, amylase, total protein and electrophoresis were within normal limits. Sedimentation rate – 24/42. X-ray of the chest, upper and lower gastrointestinal tract, and abdominal and thyroid ultrasound examination revealed no neoplastic abnormalities. The patient did not consent for further internal diagnostic tests. Because of skin lesions' progression, within 6 months accompanied by intermittent abdominal pain, the patient was admitted to the Dermatological Department again in October 2000. At this time the dermatological examination revealed skin lesions involving almost all the body. Skin changes were characterized by papillomatous, roughly hyperpigmented and furrowed lesions localized on skin folds, arthral flexures and mucosa of the mouth and anus (Fig. 2). The skin of the dorsum of the hands demonstrated features typical for *acanthosis nigricans* mimicked warts. On the plantar and palmar surfaces exceed hyperkeratosis was found. The skin colour of the whole body was brown – *café au lait* lesions. In laboratory findings ESR 36/84, sideropaenia (8.7 mmol/L N: 10-30.8 mmol/L) and elevated liver parameters (GGTP 43 N: 5-24 IU/L, ALP 96 N: 32-92 IU/L, LDH 689 N: 266-519IU/L) were observed. Other biochemical parameters such as glucose, electrolytes, creatinine, urea, uric acid, CPK, bilirubin, aminotransferases, total protein and total blood count cell and electrophoresis were within normal limits. Urine analysis and coagulation parameters were normal. Markers as CEA, CA 19-9 were within normal limits. CA 125 was increased (47.03 U/ml N: 35 U/ml). Chest X-ray was normal. In abdominal ultrasound and in HRCT examination of abdomen a tumor of the left lobe was found. In liver biopsy no atypical cells were shown.

In November 2000 the patient was diagnosed in Gastroenterology Department. Exploratory laparotomy revealed hepatosplenomegaly with 3 cm sized tumor of the left liver lobe infiltrating the round ligament of the liver. On histopathological biopsy of the tumor, hepatocellular carcinoma (clarocellular variant G-2) was diagnosed. In chest X-ray the right-sided presence of two metastases (2 cm diameter each) was shown. The patient died within 22 months of the first appearance of skin symptoms.

Discussion

The malignant type of *acanthosis nigricans* is characterized by its sudden onset, rapid progression, more expressed hyperkeratosis and hyperpigmentation with coexisting pruritus. Pathological lesions are mainly localized on the mucous membranes and once they appear, the diagnosis of malignancy should always be taken into account.

The occurrence of *acanthosis nigricans* in adults is almost in 100% is connected with internal malignancies. The most often proved malignancies are adenocarcinomas of the stomach, neoplasms of the lungs and breasts, carcinoma of the uterine and bladder and sarcomas and haematological proliferation.

Among 247 cases of *acanthosis nigricans*, mostly cancer of the stomach (112), subsequently lungs (20), liver (19), uterus (18), breast (11) and ovaries (9) were determined. Moreover, the coexistence of *acanthosis nigricans* with malignant neoplasms of the liver and biliary ducts such as adenocarcinoma of bile ducts and gallbladder and also liver carcinoma were reported. *Acanthosis nigricans* has been referred as a sign of liver and bile ducts disturbances, e.g. primary biliary cirrhosis and Wilson's disease.

The occurrence of the abortive clinical forms of *acanthosis nigricans* depends on the type of developing malignancy. This subclinic types are often accompanied by neoplasms of gastrointestinal and respiratory tract.

The frequency of appearance of benign *acanthosis nigricans*, not concerning with malignant neoplasms, has been assessed as 7.1%. In this type involvement of the mucosa is very rare. Both benign and malignant types have similar histologic features. The velvety surface of the skin lesions is the result of papillomatosis. Therefore only clinical progression with subjective complains can suggest malignant type of *acanthosis nigricans*.

Conclusions

Paraneoplastic type of *acanthosis nigricans* – in patient with hepatocellular carcinoma is not frequently reported in the literature.

In the aspect of clinical occurrence of skin lesions suggesting *acanthosis nigricans* the diagnosis should be focused on internal malignancies. Because of the influence of some causative agents another etiopathogenetic factors should also be taken into account.

At presented patient other than neoplastic processes leading to *acanthosis nigricans* were excluded in additional tests.

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