Letter to the Editor

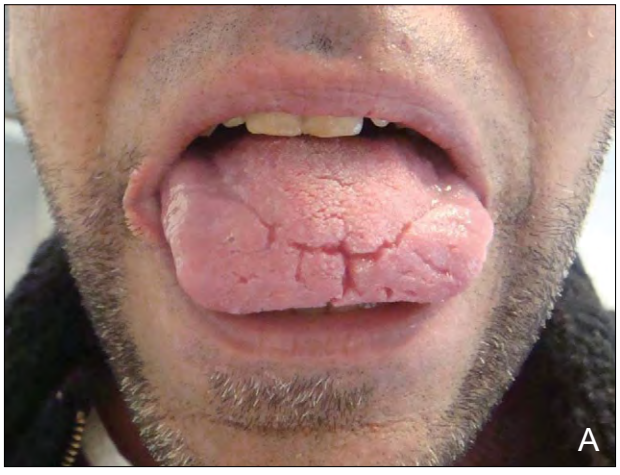
Cutaneous Paraneoplastic Syndrome Presenting With Wartylike Oral Lesions

To the Editor:

An Egyptian 37-year-old man was referred to the Sexually Transmitted Disease Unit at the University of Florence, Italy, for evaluation of a warty lesion of the right labial commissure, which was diagnosed as condyloma acuminatum by the general medicine practitioner. The lesion had been growing for 2 months and was spongy and papillomatous (Figure 1). Mucosa of the tongue appeared warty and thick with deep fissuring (scrotal tongue) (Figure 2A), and the hard palate showed roundish papillomatous growths and accentuated furrows, which gave it a cobblestonelike appearance (Figure 2B).

Complete skin examination revealed velvety skin on the neck with hyperpigmented elevated ridges; the axillae were slightly discolored with numerous skin tags. Familial and personal histories were negative for cutaneous, endocrinologic, and neoplastic diseases. Biochemical profile disclosed normal glycemia and glycated hemoglobin but increased paraneoplastic markers. Histologic examination of the cauliflowerlike lesion from the corner of the mouth described acanthosis, hyperkeratosis, and filiform projections of the dermal papillae, which suggested the clinical diagnosis of acanthosis nigricans.

In a few weeks, the patient showed weight loss, dysphagia, anemia, thrombocytopenia, further increase in paraneoplastic markers, and back pain. Nuclear magnetic resonance imaging and scintigraphy



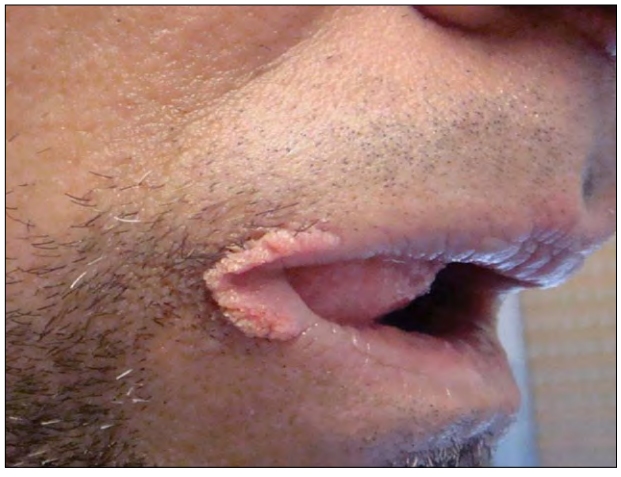


Figure 1. Warty lesion of the right labial commissure that mimicked condyloma.

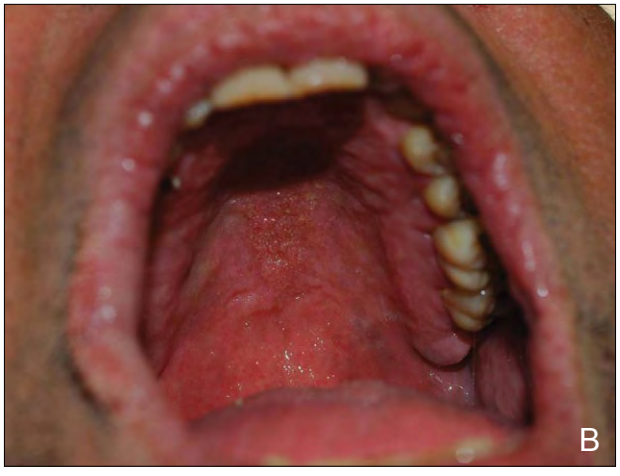


Figure 2. Scrotal tongue (A) accompanied by cobblestonelike features of the hard palate (B).

demonstrated pathologically reactive tissue at the rachis, ribs, pelvis, and nose bridge. Bone marrow biopsy from the pelvis revealed cancerous infiltration.

At that time, hyperpigmented warty lesions appeared in most flexures. The lips became thickened and a new verrucous plaque appeared in the left commissure. The palms and soles were hyperkeratotic; the dorsal skin of the interphalangeal joints of the hand showed villous thickening (Figure 3).

Finally, gastroscopy pointed out the volumetric growth of papillae of Vater and a biopsy revealed atypical glandular structures (cytokeratin 7 positive while cytokeratin 20 negative). Unfortunately, the final diagnosis of cholangiocarcinoma was not confirmed because of sample exiguity and the patient died a week later. For religious reasons, his family did not agree to postmortem examination, hence the primitive neoplasm site remained unknown.

Acanthosis nigricans is a cutaneous disorder characterized by velvety hyperpigmented patches of intertriginous areas. Acanthosis nigricans can be related to many pathological conditions, both benign (congenital or acquired endocrinopathies) and malignant (ANM [acanthosis nigricans malignant])[1-3]; the latter has rapid onset and spread, and typically involves oral mucosa (25%–50%).[2]

Acanthosis nigricans malignant skin signs were completely represented in our patient who showed the typical brownish plaques of intertriginous areas but also the presence of hyperkeratosis with thickening of the fingerprints (tripe palms, pachydermatoglyphia). Moreover, oral manifestations, considered an indicator of tumor progression,[2] were extensive, severe, and progressive in our case, which also displayed lip involvement. The presence of commissural warty lesions in our case is worth reminding for its peculiarity and differential diagnosis with human

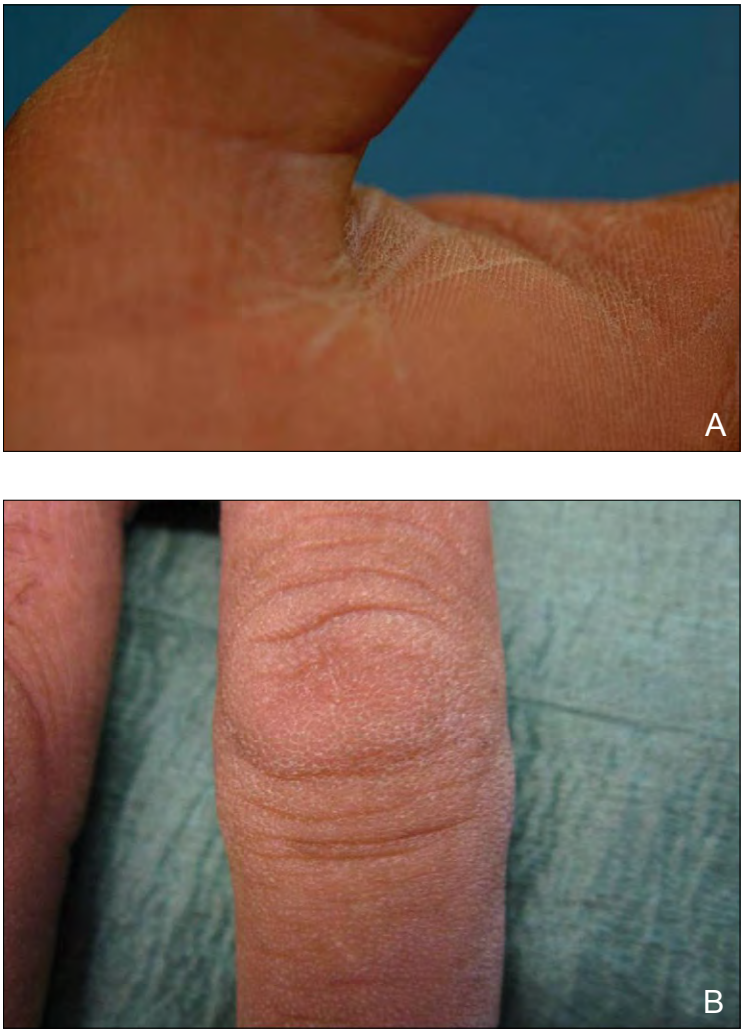


Figure 3. Acral manifestations of acanthosis nigricans malignant including hyperkeratosis of the palms (A) and whitish rough thickened skin above the interphalangeal joints of the hand (B).

papillomavirus–related conditions. This pseudocondyloma actually caused dermatologic advice and heralded paraneoplastic significance in our patient.

At least 26 different tumors have been reported in association with ANM, most commonly gastric adenocarcinoma.[4] In our case, ANM was likely related to biliary duct carcinoma. According to a PubMed search of articles indexed for MEDLINE using the terms *acanthosis nigricans* and *biliary duct carcinoma*, this association has been solely documented in 3 prior cases.[5-7] Despite absence of confirmatory postmortem examination in our case, consistent histologic description and cellular immunophenotype strongly supported the diagnosis of cholangiocarcinoma. As it happens in 61% of cases,[4] ANM occurred simultaneously with the cancer. It emerges from the literature, however, that ANM can predate or follow the diagnosis of malignancy as well.[4]

In conclusion, the case is reported for the unusual association with cholangiocarcinoma and for the peculiar condylomalike buccal lesions, the iceberg tip of a wide clinical picture and fatal disease.

Sincerely,
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The authors report no conflict of interest.

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