

Malignant Acanthosis Nigricans and Tripe Palms Associated With Pancreatic Adenocarcinoma

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Malignant acanthosis nigricans is a disease that has an abrupt onset and is most commonly associated with gastric adenocarcinoma. It also has occurred as a paraneoplastic phenomenon in other carcinomas. Malignant acanthosis nigricans can occur simultaneously, before, or after the onset of internal malignancy. Malignant acanthosis on the palms is referred to as tripe palms. We describe a rare association of oral malignant acanthosis nigricans and tripe palms secondary to an underlying pancreatic adenocarcinoma.

Cutis. 2006;78:37-40.

Malignant acanthosis nigricans was first described in 1890.¹ Acanthosis nigricans commonly presents with velvety hyperpigmented plaques on the sides and nape of the neck, axillae, inframammary folds, groin, antecubital and popliteal fossa, and periumbilical areas. The following 8 types of acanthosis nigricans have been described in the literature: acral, benign, malignancy associated, medication induced, mixed type, obesity associated, syndromic, and unilateral.²

Malignant acanthosis nigricans is a disease of abrupt onset most commonly associated with gastric adenocarcinoma. Rigel and Jacobs³ found malignant acanthosis nigricans to be associated with carcinomas of the ovary, endometrium, cervix, breast, testicle, lung, kidney, pancreas, liver, esophagus, prostate, thyroid, and pharynx, as well as lymphoma, adenocarcinoma of the gallbladder, osteogenic sarcoma, lymphosarcoma, and fibrosarcoma. Associations with other internal malignancies include mycosis fungoides,⁴ cholangiocarcinoma,⁵

rectal carcinoid,⁶ and laryngeal cancer.⁷ Most of the internal malignancies associated with malignant acanthosis nigricans are adenocarcinomas.

Tripe palms are malignant acanthosis nigricans of the palms.⁸ This condition was first described by Clarke⁹ and later by Breathnach and Wells.¹⁰ Except for rare cases, tripe palms occur in patients with an internal malignancy¹¹ and can precede the underlying cancer by as much as 15 months.⁸

Brown and Winkelmann¹² found oral mucous membrane involvement in 6 (35%) of 17 patients with malignant acanthosis nigricans. It is especially common on the tongue and lips.¹³ We present a case of a rare association of oral mucous membrane malignant acanthosis nigricans and tripe palms secondary to pancreatic adenocarcinoma.

Case Report

An 81-year-old white woman was referred to the University of Virginia's Dermatology Department for a biopsy, which showed changes consistent with viral papilloma with fungal superinfection on her lip. Human papilloma virus typing subsequently was performed and was found to be negative for the presence of human papilloma virus DNA.

Burning and soreness of the mouth was first noted in February 2003 after a course of moxifloxacin for bronchitis. The burning and soreness was followed by the development of verrucous papillomatous papules and plaques on the patient's upper and lower lip. The oral mucosa, including the gingiva, had a diffuse cobblestoned appearance. She was treated with nystatin for presumed oral candidiasis secondary to the moxifloxacin, but the lesions did not improve.

The patient was first evaluated at the University of Virginia on October 22, 2003. She had lost 7 pounds in 4 months and was having gastrointestinal upset. She denied abdominal pain, hematemesis, melena, or hematochezia. Her medications included atenolol, hydrochlorothiazide, and lisinopril. She

Accepted for publication May 6, 2005.

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The authors report no conflict of interest.

Reprints not available from the authors.



Figure 1. Diffuse verrucous papillomatous papules and plaques on the upper and lower vermillion.

denied a history of diabetes mellitus but did have hypertension and bronchitis. On physical examination, there were diffuse verrucous papillomatous papules and plaques on her upper and lower vermillion, buccal mucosa, and tongue (Figure 1). The palms showed accentuation of the dermatoglyphics bilaterally, consistent with tripe palms (Figures 2 and 3). Malignant acanthosis nigricans was not present on the neck, axillae, antecubital fossa, periumbilical areas, or groin.

The patient was clinically diagnosed with malignant acanthosis nigricans and referred to her primary care provider for a complete malignancy workup. A computed tomography scan of the abdomen on October 30, 2003, showed a mass adjacent to the head of the pancreas and adenopathy. A fine needle aspirate of the mass was performed and revealed pancreatic adenocarcinoma. The patient subsequently underwent treatment with gemcitabine. She had a good response to the treatment with rapid improvement and clearance of her malignant acanthosis nigricans.

Comment

Malignant acanthosis nigricans is most commonly associated with gastric adenocarcinoma but can be a paraneoplastic phenomenon secondary to many different internal malignancies.¹⁴ Our case presents the rare association of pancreatic adenocarcinoma with malignant acanthosis nigricans and tripe palms. Malignant acanthosis nigricans can present on and within the oral mucosa as well as the most common sites for acanthosis nigricans.¹⁴ Malignant acanthosis

nigricans occurs more often with an internal malignancy but can occur before or after the malignancy has developed. It also can coexist with other paraneoplastic cutaneous entities including the Leser-Trélat sign,^{15,16} florid cutaneous papillomatosis,^{17,18} and tylosis of the palms and sole.¹⁰ Histologically, acanthosis, hyperkeratosis, and papillomatosis are seen. Hyperpigmentation usually is not seen histologically.

Tripe palms are most commonly associated with internal malignancy.¹¹ Cohen et al¹¹ found that tripe palms is associated with internal malignancy in 69 (90%) of 77 cases. Acanthosis nigricans and tripe palms are present together in 57 (77%) of 74 cases. Pulmonary carcinoma (9 [53%] of 17 cases) is most commonly seen with tripe palms alone, and gastric adenocarcinoma (20 [35%] of 57 cases) or pulmonary carcinoma (6 [11%] of 57 cases) presented when tripe palms and acanthosis nigricans occurred together.¹¹ Clinically, exaggeration of the dermatoglyphics on the ventral surface of the hands resembling tripe, or cow stomach, is seen.

The pathogenesis of malignant acanthosis nigricans is unknown. The current theory suggests that transforming growth factor- α being secreted by tumors and stimulating epidermal growth factor receptor leads to epidermal hyperproliferation and differentiation.^{19,20} The binding of epidermal growth factor receptor by transforming growth factor- α activates the mitogen-activated protein kinase pathway and leads to the hyperproliferation and differentiation of the keratinocytes.²¹ It also has been proposed that insulin resistance might produce malignant acanthosis nigricans.²² Elevations



Figure 2. Tripe palms consistent with malignant acanthosis nigricans of the palms bilaterally.



Figure 3. Accentuation of the dermatoglyphics resembling tripe, or cow stomach, consistent with tripe palms.

of other hormones, including thyroid stimulating hormone, human growth hormone, melanocortin-stimulating hormone, and male sexual hormones, have been reported with malignant acanthosis nigricans and could play an etiologic role.²³

The treatment of malignant acanthosis nigricans is for the underlying malignancy, whereby the clinical lesions may improve or completely resolve. The mechanism for this resolution possibly is related to decreased production of substances from the tumor.

Conclusion

Our case demonstrates a rare association of malignant acanthosis nigricans and pancreatic adenocarcinoma.

Chemotherapy with gemcitabine led to the resolution of the cutaneous lesions. An evaluation for malignancy should be performed in any individual with a possible diagnosis of malignant acanthosis nigricans.

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Malignant Acanthosis Nigricans and Tripe Palms

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