

# Malignant Acanthosis Nigricans: An Early Diagnostic Clue

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## ABSTRACT

Acanthosis nigricans (AN) is characterized by velvety, hyperpigmented, verrucous, symmetric and occasionally pruritic plaques along with papillomatous lesions which have a special predilection for neck, axillae, groin, umbilicu and mucosal regions. Rarely, it presents as a paraneoplastic syndrome and prompts a thorough search for an internal malignancy. We present here a case of malignant acanthosis nigricans seen in an elderly patient who was found to have underlying adenocarcinoma of the lower end of esophagus. After diagnosing associated malignancy, he was referred for further evaluation and subsequent surgical resection of tumour.

**Key words:** *Acanthosis nigricans. Malignant acanthosis nigricans. Paraneoplastic syndrome. Cutaneous marker. Adenocarcinoma. Oesophagus.*

## INTRODUCTION

The term "Acanthosis Nigricans" (AN) is a combination of two words (acanthos, from the Greek for "thorn" and nigricans, from the Latin, "becoming black").<sup>1</sup> Eight different types of disease (benign, obesity-associated, syndromic, malignant, acral, unilateral, medication-induced and mixed type) have been described in literature.<sup>2</sup> It can broadly be categorized into benign and malignant forms. Patients with the benign form mostly have an underlying insulin-resistant state but experience very few complications of their skin lesions.<sup>3</sup> Malignant AN is associated with underlying malignancy which is often an aggressive tumour that generally has a poor prognosis. In contrast to the benign form, which is much more common in people with darker skin pigmentation, there is no racial propensity with malignant AN.<sup>4</sup> Many kinds of cancer have been described in association with AN, but by far, the most common underlying malignancy is a gastric adenocarcinoma. The oral cavity is frequently involved in malignant AN. The tongue and the lips, most commonly, are affected with elongation of the filiform papillae on the dorsal and lateral surfaces of the tongue and multiple papillary lesions appearing on the commissures of the lips.<sup>5</sup> Malignant AN is clinically indistinguishable from the benign forms; however, one must be more suspicious if the lesions arise rapidly, are extensive, or symptomatic or seen in atypical locations. Regression of malignant AN has been seen with treatment of the underlying malignancy and re-appearance may

suggest recurrence or metastasis of the primary tumour.<sup>4,6</sup>

We describe here an elderly male who developed rather rapidly progressing lesions of AN in his body folds including umbilical region along with tripe palms. During the search for any underlying malignancy, he was found to have carcinoma of the lower end of the oesophagus with squamous differentiation.

## CASE REPORT

A gentleman of 64 years, not a known diabetic, presented with 6 months history of gradual onset of pigmentation and thickening of skin of perioral area and axillae. It was associated with postprandial pain in upper abdomen which was non-colicky and non-radiating in character. He had lost nearly 10 lbs of weight during the last 6 months. There was no history of drug intake, fever, vomiting, malaena, cough, pruritus, any urinary or bowel complaints.

On examination, he was a lean but healthy looking elderly gentleman with normal vital signs. Examination of skin showed diffuse velvety thickening of skin of perioral areas especially near angles of mouth (Figure 1a), axillae (Figure 1b), back of neck (Figure 2a), umbilicus (Figure 2b) and groin. There was diffuse thickening of both his palms (Figure 3). Systemic examination including abdominal examination did not reveal any abnormality.

His laboratory workup revealed haemoglobin of 11.2 gm/dl. Histopathological examination showed hyperkeratosis, papillomatosis and irregular acanthosis. There were fingerlike projections of dermal papillae, with occasional thinning of the adjacent epidermis. Pseudohorns were also seen in mid-dermis (Figure 4). Endoscopic examination revealed a small area of nodular thickening of lower oesophageal mucosa. Mucosal biopsy from this area showed diffuse infiltration of mucosa by malignant cells with squamous differentiation. Cords of

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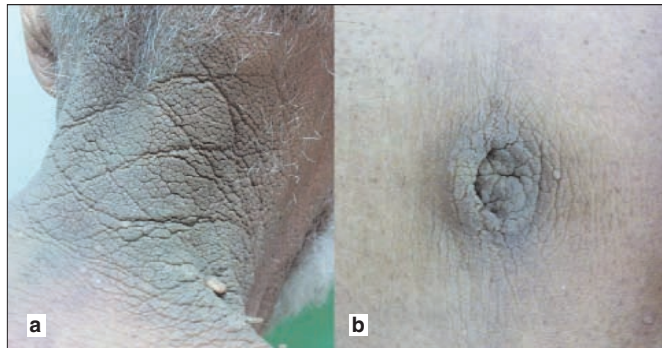
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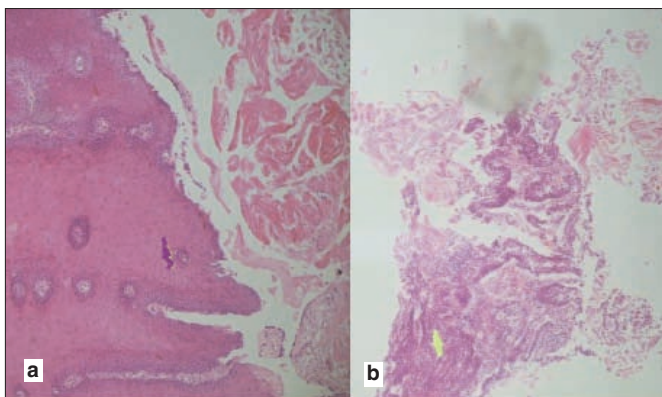
**Figure 1 (a and b):** Gross velvety thickening of perioral skin and thickening of skin of neck and periaxillary area.



**Figure 2 (a and b):** Pigmentation with rugose thickening of nape of neck and velvety pigmentation and thickening of umbilicus.



**Figure 3:** Tripe palms.



**Figure 4 (a and b):** Stromal infiltration by strands of malignant cells of undifferentiated origin.

malignant cells were seen infiltrating the stroma (Figure 4). Computerized tomographic examination of abdomen and chest did not reveal any lymph node or visceral spread. The patient was referred to a gastrointestinal surgeon for resection of the tumour.

### DISCUSSION

Paraneoplastic syndrome is a condition that arises in association with a malignancy elsewhere in the body but, in itself, is not cancerous. Generally, the onset and course of the disease will closely correlate with the malignancy, as described in Curth's original criteria for paraneoplastic syndromes.<sup>7</sup> Malignant Acanthosis Nigricans is a paraneoplastic syndrome which is much less common but more aggressive than the other types of such syndromes.<sup>4,8</sup> AN is caused by factors that stimulate epidermal keratinocyte and dermal fibroblast proliferation. In the benign form, the factor is probably insulin or an insulin like growth factor that incites epidermal cell proliferation.<sup>3</sup> In malignant AN, the stimulating factor is hypothesized to be a substance secreted either by the tumour or in response to the tumour. Transforming growth factor-alpha is structurally similar to epidermal growth factor and is a likely candidate.<sup>9</sup> Malignant AN usually occurs simultaneously with the malignancy but can rarely precede the detection of malignancy by 6-16 years.<sup>7</sup> It is most commonly associated with adenocarcinoma of the stomach and the other reported associations are carcinoma of the pancreas, colon, ovary, prostate, breast and lung.<sup>4,7,6</sup> Malignant AN can coexist with other cutaneous markers of internal malignancy like the sign of Leser-Trelat, hypertrichosis lanuginosa, tripe palms and florid cutaneous papillomatosis.<sup>10</sup>

This patient had the typical cutaneous lesions of malignant Acanthosis Nigricans along with tripe palms and the search for underlying internal malignancy was rewarding as we were able to find out the underlying cause within 2 weeks of detection of the cutaneous marker. It also highlights the fact that malignant Acanthosis Nigricans has more extensive, rapidly progressive and somewhat atypical cutaneous lesions when compared with long standing, slowly progressing, soft velvety lesions of pseudo AN or benign AN.

It is emphasized that any case of unusual AN should vigorously be investigated to look for underlying tumour, as timely diagnosis and appropriate treatment can result in favourable outcome of this potentially fatal paraneoplastic syndrome.

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