

# Metastatic adenocarcinoma of the stomach presenting as malignant acanthosis nigricans and tripe palms: a case report

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## Case report

A 46-year-old lady with good past health presented to a tertiary hospital in August 2020 with a 6-month history of chronic cough, epigastric discomfort, and weight loss of 20 kg. She also reported progressive darkening and thickening of skin over both hands, neck, axilla, and groins since March 2020. She had consulted general practitioners and Chinese medicine practitioners and been given topicals and herbal treatment with no improvement. Physical examination revealed velvety hyperkeratosis and hyperpigmentation over both palms (Fig a), nape

(Fig b), bilateral axilla (Fig c), and inguinal regions. The mucosal surfaces were not involved. Physical examination revealed stony dullness to percussion over the right mid-to-lower zone of the lungs and absent breath sounds on auscultation. A non-tender enlarged supraclavicular lymph node of 1 cm was palpable over the left supraclavicular region. Chest radiograph showed moderate right pleural effusion. Therapeutic thoracocentesis drained 2 L of clear straw-coloured fluid. Pleural fluid analysis revealed an exudative pleural effusion with 47.3 g/L fluid protein (70 g/L serum protein) and 224 U/L



FIG. (a) Tripe palms; (b) velvety hyperkeratosis and hyperpigmentation of the nape; and (c) velvety hyperkeratosis and hyperpigmentation over the left axilla of the patient

fluid lactate dehydrogenase (226 U/L serum lactate dehydrogenase). Pleural fluid cytology revealed suspicious cells with high nuclear-to-cytoplasmic ratio, coarse chromatin and enlarged, irregular hyperchromatic nuclei. Other laboratory findings were unremarkable: haemoglobin level 14 g/dL, white blood cell count  $3.62 \times 10^9/L$ , platelet count  $156 \times 10^9/L$ , creatinine level 71  $\mu\text{mol/L}$ , bilirubin level 8  $\mu\text{mol/L}$ , albumin level 28 g/L, alanine aminotransferase level 13 U/mL, and aspartate aminotransferase level 20 U/mL. Tumour markers including carcinoembryonic antigen, cancer antigen (CA) 15-3, CA 19-9, CA-125, and alpha-fetoprotein were all within the normal limits.

A clinical diagnosis of malignant acanthosis nigricans (AN) with tripe palms was made after dermatology review. Upper endoscopy revealed two Forrest class III gastric ulcers in the proximal greater curvature surrounded by abnormal 3-cm mucosal thickening with irregular mucosal surface and microvascular pattern under narrow-band imaging. Biopsy of the gastric ulcers was negative for *Helicobacter pylori* but confirmed poorly differentiated adenocarcinoma on histopathology. Positron emission tomography-computed tomography scan revealed a hypermetabolic focus in the stomach, multiple intra-abdominal lymph nodes, and a large hypermetabolic pelvic tumour. A clinical diagnosis was made of Krukenberg tumour. The patient was referred to medical oncology for palliative chemotherapy. She subsequently developed massive pulmonary embolism and succumbed 3 months after the initial diagnosis.

## Discussion

Acanthosis nigricans is a velvety hyperkeratotic, hyperpigmentation of the skin that occurs most commonly in intertriginous areas such as the back of the neck, axilla, and groins. Eight types of AN have been described and all share a common mechanism. They stimulate receptor tyrosine kinase signalling pathways; epidermal growth factor receptor (EGFR), insulin-like growth factor (IGF-1), and fibroblast growth factor receptors. Increased circulating insulin stimulates keratinocyte IGF receptors, especially IGF-1 and at high concentrations, displaces IGF-1 from IGF-1-binding protein. Increased serum-free IGF-1 in turn stimulates the proliferation of keratinocytes and dermal fibroblasts.<sup>1,2</sup>

Malignant AN is a paraneoplastic phenomenon most commonly associated with gastric adenocarcinoma with an incidence of 55% to 61%, followed by pancreatic cancer, gynaecological malignancies, and lung carcinoma.<sup>2</sup> Increased transforming growth factor alpha (TGF- $\alpha$ ) is postulated to be the underlying mechanism. The TGF- $\alpha$  acts on EGFR, stimulating soft tissue growth.<sup>1</sup>

Amelioration of malignant AN following tumour resection, associated with a reduction in elevated circulating TGF- $\alpha$ , supports the participation of EGFR signalling in malignant AN. Malignant AN can manifest preceding, together, or after diagnosis of an underlying malignancy. Rapid evolution of the velvety hyperpigmentation, tripe palms and signs of Leser-Trélat, a rare finding of sudden eruption of seborrhoeic keratoses, are strongly indicative of malignant AN.<sup>3</sup> Affected patients are typically not obese and may be cachectic because of the underlying malignancies. Histological features are non-specific and commonly include hyperkeratosis, papillomatosis, basal layer hyperpigmentation, and some dermal papillae that project upwards in the form of finger-like projections.<sup>4</sup> Malignant AN may resolve following tumour resection but can recur if there is tumour recurrence.

Krukenberg tumours are defined by the World Health Organization as ovarian carcinomas characterised by the presence of stromal involvement, mucin-producing neoplastic signet ring cells, and ovarian stromal sarcomatoid proliferation. The most common sites of primary malignancies are from the gastrointestinal tract and the breasts. The mean age at diagnosis of Krukenberg tumours is  $49.3 \pm 13.3$  years. The prognosis is generally very poor, probably because of the late stage of diagnosis. The median survival time is  $35.0 \pm 3.5$  months while the 5-year overall survival is around 25%.<sup>5</sup>

This case illustrates the classic presentation of malignant AN and tripe palms that are associated with metastatic gastric adenocarcinoma. Physicians need to be aware of these features since they may be the only presenting symptoms of the underlying malignancies. Full systemic evaluation for underlying malignancies is warranted to enable early diagnosis and timely management.

### Author contributions

Concept or design: CPM Lam.

Acquisition of data: CPM Lam.

Analysis or interpretation of data: CPM Lam.

Drafting of the manuscript: CPM Lam.

Critical revision of the manuscript for important intellectual content: Both authors.

Both authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

### Conflicts of interest

Both authors have disclosed no conflicts of interest.

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### Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. Written informed consent for publication was obtained from the patient's next-of-kin.

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