

## Malignant Acanthosis Nigricans, Florid Cutaneous and Mucosal Papillomatosis and Tripe Palms in a man with gastric adenocarcinoma\*



### Acantosis nigricans maligna, papilomatosis cutáneo-mucosa florida y paquidermatoglia adquirida en paciente con adenocarcinoma gástrico

We describe the case of a 67-year-old man with a clinical history of smoking, hypertension, and hyperhomocysteinemia. The patient was referred for verrucous lesions on the face that had appeared more than 1 month earlier. A dermatological examination revealed several small, hyperkeratotic lesions on the cheeks and around the mouth (Figure 1A), as well as brownish plaques in the axillary and inguinal folds (Figure 1B). Both hands showed marked accentuation of the dermatoglyphics (Figure 1C). The patient reported that these symptoms had appeared abruptly within a period of less than 2 months. Based on clinical suspicion of a paraneoplastic dermatosis, additional tests were requested to identify the primary tumor.

Analyses revealed a cholestatic pattern with elevated levels of alkaline phosphatase and  $\gamma$ -glutamyl transpeptidase. Tumor marker analysis revealed only a slight increase of  $\alpha$ -fetoprotein levels.

A thoracoabdominopelvic computed tomography scan revealed a lytic lesion in the posterior third of the T12 vertebral body, with slight invasion of the medullary canal, minimal thickening of the antral wall (Figure 2A), and swelling of the periaortic lymph nodes and gastrohepatic ligament lymph nodes (Figure 2B). An upper endoscopy revealed a malignant-looking ulcerated lesion with irregular borders in the area of the gastric incisura, extending towards the gastric body. Biopsy of the

lesion was compatible with poorly differentiated gastric adenocarcinoma.

After treatment with palliative chemotherapy, the patient's basal state worsened and the neoplastic disease progressed with the appearance of multiple pulmonary nodules. One year after diagnosis the patient died following a respiratory infection.

More than 50 types of cutaneous paraneoplastic manifestations have been described, including malignant acanthosis nigricans (MAN), florid cutaneous and mucosal papillomatosis, and acquired pachydermatoglyphia.<sup>1</sup>

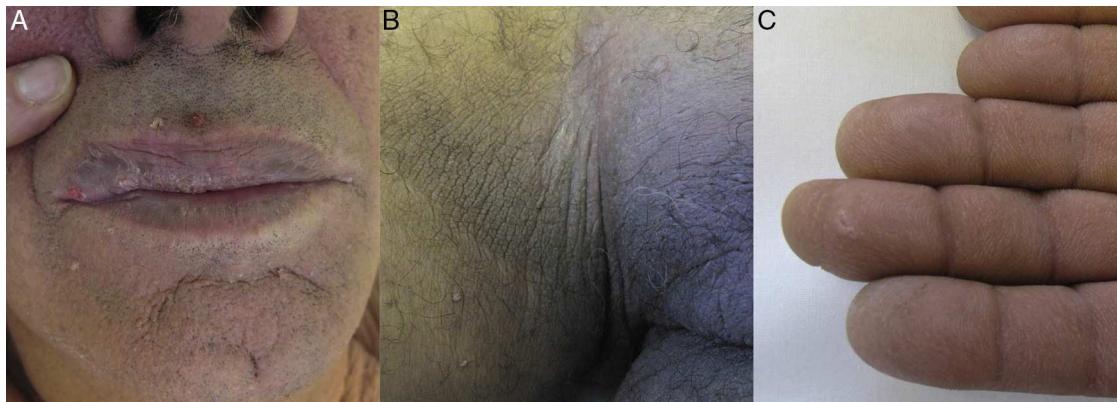
MAN is characterized by the presence of brownish, symmetric, nonpruritic plaques in the skin folds and on the back of the neck that can infiltrate and present as hyperkeratotic plaques. In contrast to the benign form of acanthosis nigricans, the paraneoplastic form is characterized by abrupt onset, rapid progression, and involvement of a large skin surface area. There is a strong correlation between MAN and intra-abdominal tumors, particularly tumors of gastric origin.<sup>2</sup>

Florid cutaneous and mucosal papillomatosis is characterized by the rapid appearance of verrucous papules on the trunk and extremities. The oral or genital mucosa may also be affected. This condition is most strongly correlated with tumors of gastric origin, in particular adenocarcinoma. While these lesions are clinically indistinguishable from viral warts, histologic analysis reveals marked hyperkeratosis with irregular acanthosis and papillomatosis, and no evidence of human papillomavirus infection.<sup>3,4</sup>

Tripe palms is characterized by the enhancement of the epidermal ridges of the palms, which become slightly thickened and acquire a velvety texture, resembling the intestinal villi. In 90% to 95% of cases this condition is associated with the presence of a solid tumor.

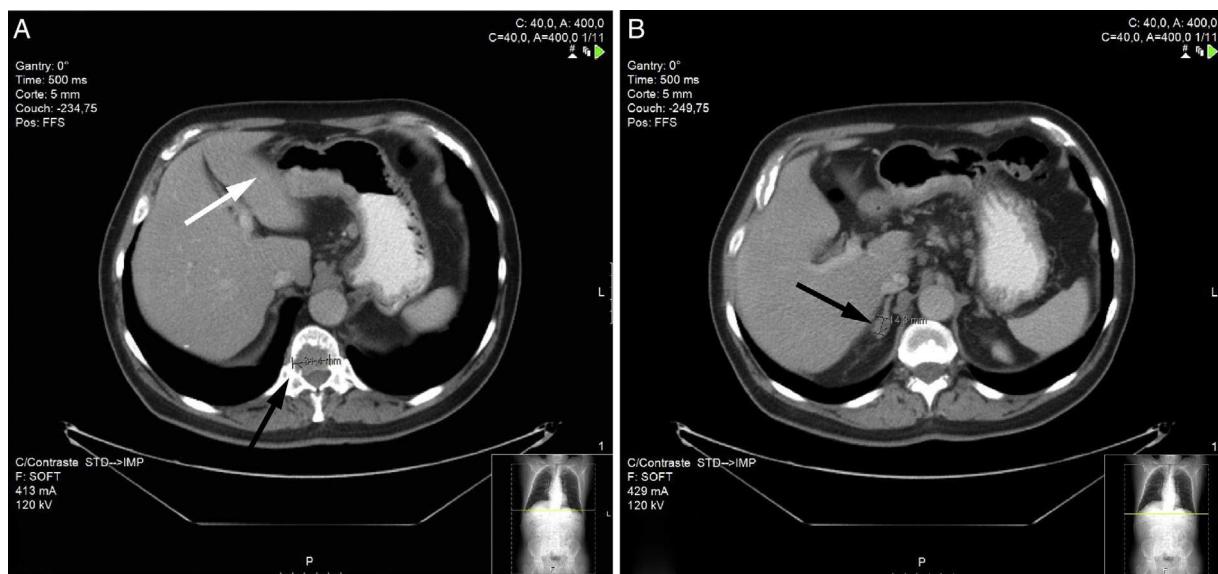
Tripe palms has been associated with many types of cancer, the most common of which are those of the gastrointestinal tract (30%) and lungs (20%).<sup>5,6</sup>

The presence of all 3 of these paraneoplastic dermatoses (MAN, florid cutaneous and mucosal papillomatosis,



**Figure 1** A, Hyperkeratotic papules on the face. B, Inguinal region: brownish plaques with marked thickening of the skin. C, Marked hyperkeratosis on the flexor surface of the fingers with exaggerated dermatoglyphics.

\* Please cite this article as: Vilas-Sueiro A, Suárez-Amor Ó, Monteagudo B, de las Heras C. Acantosis nigricans maligna, papilomatosis cutáneo-mucosa florida y paquidermatoglia adquirida en paciente con adenocarcinoma gástrico. Actas Dermosifiliogr. 2015;106:438–439.



**Figure 2** A, Computed tomography scan with IV contrast: thickening of the posterior gastric wall (white arrow) and lytic lesion of the T12 vertebral body (black arrow). B, Swelling of gastrohepatic ligament lymph nodes (black arrow).

and tripe palms) in the same patient has been previously described in the literature, suggesting potentially common etiological and pathogenic mechanisms. In fact, both tripe palms and florid cutaneous and mucosal papillomatosis are considered by some authors as clinical variants of MAN. Several studies suggest that epidermal growth factor alpha is secreted by the tumor and transported in the blood to the skin surface, where it stimulates the development of keratinocytes by activating tyrosine kinase receptors, which promote widespread mitotic and antiapoptotic cellular activity.<sup>7–10</sup>

Of particular interest in the present case is the association of several distinct paraneoplastic cutaneous manifestations in the same patient. Recognition and identification of these conditions can enable early diagnosis and treatment of associated neoplasms, in some cases resulting in a better long-term prognosis for the patient.

## References

- Silva JA, Mesquita KC, Igreja AC, Lucas IC, Freitas AF, Oliveira SM, et al. Paraneoplastic cutaneous manifestations: Concepts and updates. *An Bras Dermatol.* 2013;88:9–22.
  - Ginarte M, Valdés F, Sánchez-Aguilar D, Peteiro C, Toribio J. Acantosis nigricans, acantosis palmar y papillomatosis cutánea florida asociadas a adenocarcinoma de cuello uterino. *Actas Dermosifiliogr.* 1999;90:37–42.
  - Yang YH, Zhang RZ, Kang DH, Zhu WY. Three paraneoplastic signs in the same patient with gastric adenocarcinoma. *Dermatol Online J.* 2013;19:15.
  - Janniger EJ, Schwartz RA. Florid cutaneous papillomatosis. *J Surg Oncol.* 2010;102:709–12.
  - Fabroni C, Gimma A, Cardinali C, Lo Scocco G. Tripe palms associated with malignant acanthosis nigricans in a patient with gastric adenocarcinoma: A case report and review of the literature. *Dermatol Online J.* 2012;18:15.
  - Pentenero M, Carrozzo M, Pagano M, Gandolfo S. Oral acanthosis nigricans, tripe palms and sign of leser-trélat in a patient with gastric adenocarcinoma. *Int J Dermatol.* 2004;43:530–2.
  - Kleikamp S, Böhm M, Frosch P, Brinkmeier T. Acanthosis nigricans, papillomatosis mucosae and «tripe palms» in a patient with metastasized gastric carcinoma. *Dtsch Med Wochenschr.* 2006;131:1209–13.
  - Stawczyk-Macieja M, Szczerkowska-Dobosz A, Nowicki R, Majewska H, Dubowik M, Sokolowska-Wojdylo M. Malignant acanthosis nigricans, florid cutaneous papillomatosis and tripe palms syndrome associated with gastric adenocarcinoma. *Postepy Dermatol Alergol.* 2014;31:56–8.
  - Koyama S, Ikeda K, Sato M, Shibahara K, Yuhara K, Fukutomi H, et al. Transforming growth factor-alpha (TGF alpha)-producing gastric carcinoma with acanthosis nigricans: An endocrine effect of TGF alpha in the pathogenesis of cutaneous paraneoplastic syndrome and epithelial hyperplasia of the esophagus. *J Gastroenterol.* 1997;32:71–7.
  - Yuste-Chaves M, Unamuno-Pérez P. Cutaneous alerts in systemic malignancy: Part I. *Actas Dermosifiliogr.* 2013;104:285–98.
  - A. Vilas-Sueiro,\* Ó. Suárez-Amor, B. Monteagudo, C. de las Heras
- Servicio de Dermatología, Complejo Hospitalario Universitario de Ferrol, Área Sanitaria de Ferrol, SERGAS, Ferrol, A Coruña, Spain*

\* Corresponding author.

E-mail address: alejandro.vilas.sueiro@sergas.es (A. Vilas-Sueiro).