

# Disseminated granuloma annulare and hepatocellular carcinoma: association or coincidence?

Tiago Mestre, Ana Maria Rodrigues, Jorge Cardoso

Hospital Curry Cabral, Centro Hospitalar Lisboa Central, Lisbon, Portugal

**Correspondence to**  
Dr Tiago Mestre,  
tiago.g.mestre@gmail.com

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## DESCRIPTION

Granuloma annulare is a granulomatous skin disease of unknown aetiology. It is more common in women and has a disseminated form in 10–15% of patients. A small portion of these patients have an associated disease such as diabetes mellitus, viral infection, vaccine reaction or cancer. Haematological neoplasms and adenocarcinomas are those most frequently found.<sup>1</sup>

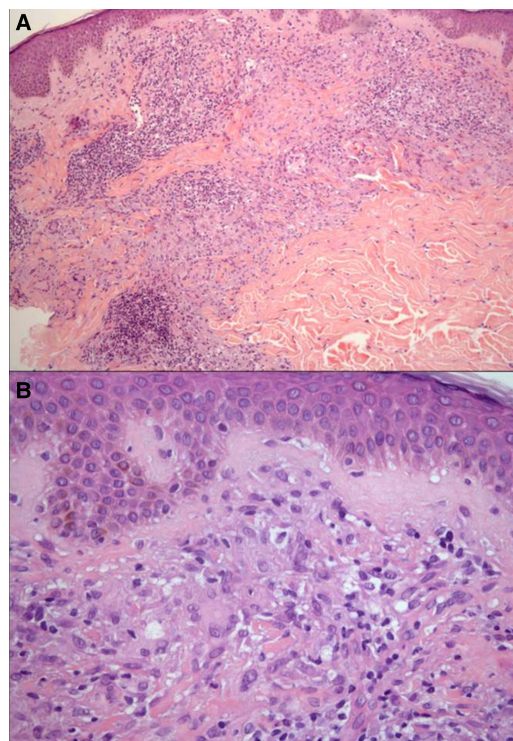
The authors present the case of 68-year-old man with a recent diagnosis of hepatocellular carcinoma (figure 1). Simultaneously with the diagnosis, he referred to the appearance of more than 10 infiltrated erythematous plaques, smooth surfaced and annular shaped (figure 2). Cutaneous histopathological examination of these lesions showed a lymphohistiocytic infiltrate with multinucleated giant cells in a palisade pattern in the papillary and reticular dermis and some foci of granulomatous reaction surrounding foci of altered collagen. This was compatible with the diagnosis of granuloma annulare (figure 3). The patient was treated with topical dipropionate of  $\beta$  methasone twice daily with a slight improvement of the dermatosis. Palliative treatment with chemoembolisation was offered to the patient, but he died some months later.

The pathogenesis of granuloma annulare is unknown. In the cases linked to cancer there is evidence suggesting that the mechanism of pathogenesis is related to a type 1 T helper (Th-1 type) delayed hypersensitivity cross-reaction, in which the tumour antigens act as triggers of the dermatosis.<sup>2</sup> The temporal relationship between the

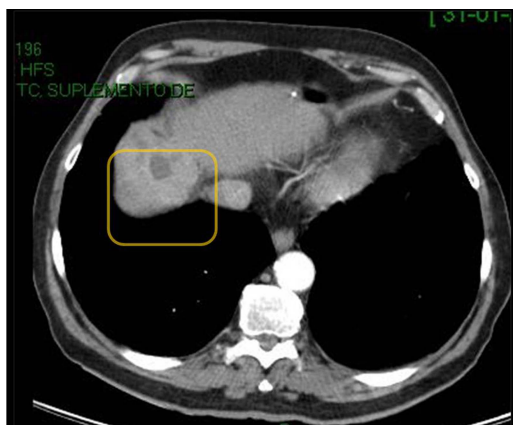


**Figure 2** Erythematous papules forming annular infiltrated plaques on the trunk and limbs.

diagnosis of the neoplasia and granuloma annulare is variable; it may appear before, during or after the first diagnosis (18 months to 7 years). Haematological neoplasms are the most frequently



**Figure 3** Histopathological examination (H&E) (A)  $\times 10$  and (B)  $\times 40$ : lymphohistiocytic infiltrate with histiocytes and multinucleated giant cells in a palisade pattern in the papillary and reticular dermis. Some foci of granulomatous reaction surrounding foci of altered collagen can be observed.



**Figure 1** CT scan: nodule (3.5 cm) in segment VIII with portal thrombus adjacent, highly suggestive of hepatocellular carcinoma,  $\alpha$ -fetoprotein was 38 ng/mL (ref: 0–7 ng/mL).



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observed.<sup>2</sup> Nearly 40 cases of association with neoplasia are reported in published studies, but in only eight cases could a true paraneoplastic nature be proven. Features suggesting association with malignancy are atypical presentation, advanced age, pain and pruritus.<sup>3</sup> In our patient, a true paraneoplastic course was difficult to establish because the patient died a couple of months later.

Therapeutic options for sporadic granuloma annulare include topical and intralesional corticosteroids, CO2 Laser, PUVA, cryotherapy, niacinamide, infliximab, cyclosporine, antimalarics, pentoxifylline, dapsone and topical calcineurin inhibitors. In the cases where a neoplasm is found, treatment of the cancer should be the aim in the treatment of the granuloma annulare.

### Learning points

- ▶ Disseminated granuloma annulare can be associated with hepatocellular carcinoma.
- ▶ Atypical granuloma annulare in elderly patients should alert us to the possibility of an occult neoplasia.

Immunosuppressors should always be balanced against the side effects in the neoplasm outcome.<sup>2</sup>

To the best of our knowledge, this is the first published case of an association between a disseminated granuloma annulare and a hepatocellular carcinoma. Atypical granuloma annulare in uncharacteristic locations in elderly patients should alert us to the possibility of an occult neoplasia.

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**Patient consent** Obtained.

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