Pemphigus herpetiformis associated with prostate cancer

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Pemphigus herpetiformis (PH) is a rare entity which combines the clinical features of dermatitis herpetiformis, and the immunological features of pemphigus.[1] In particular, direct immunofluorescence (DIF) study demonstrates deposits of IgG in the epidermal intercellular spaces, and enzyme-linked immunosorbent assay (ELISA) detects antibodies against desmoglein (Dsg) 1 and less frequently against Dsg3 in patient serum.[2]

A 67-year-old man presented because of a one-month duration bullous eruption with intense itching. Numerous erythematous and oedematous skin lesions in an annular arrangement, associated with small-medium size blisters and haematic crusts, were present on the trunk and extensor aspects of the extremities. Bullae were flaccid, on a faintly erythematous base, sometimes arranged in a herpetiform pattern (fig. 1). Routine blood investigations revealed mild anaemia, raised erythrocyte sedimentation rate and prostate-specific antigen (PSA) of 226 ng/ml (normal: <4). Biopsy specimen from a recent skin lesion showed intraepidermal cleavage with marked spongiosis and several eosinophils; a mild perivascular dermal infiltrate consisting of mononuclear cells and eosinophils was also evident (fig. 2). DIF demonstrated the presence of IgG and C3 component of complement in the intercellular spaces of the epidermis. Indirect immunofluorescence (IIF) on monkey oesophagus substrate was positive for IgG circulating antibodies to epithelial cell surfaces, and ELISA on the patient's serum was positive for anti-Dsg1 antibodies with a titer of 104.3 (cut-off <14), as well as for anti-Dsg3 with a titer of 22.8 (cut-off <7). Immunoblot analysis showed a slight reactivity of our patient's serum to an antigen migrating at the same level as the 190 kDa periplakin. However, the band obtained was narrower than the 190 kDa periplakin control band, and the result was considered aspecific. A diagnosis of PH was made, and the patient was given intravenous methylprednisolone 60 mg daily; ten days after, most of the skin lesions were cleared with only post-inflammatory red-brownish macules remaining, and methylprednisolone was kept on at gradually tapering dosages. Furthermore, there was a strong suspect of prostate cancer, and additional exams such as ultrasound studies of the pelvis, total body bone scintigraphy,

and transrectal prostate biopsy were performed. Thus, a diagnosis of prostatic acinar adenocarcinoma with diffuse bone metastases was established, and oncologists proposed androgen ablation with leuprolide acetate and ciproterone acetate. To date, after 13 months of treatment, PSA levels are decreased but not reverted to the normal levels and PH is kept under control with oral methylprednisolone (8 mg daily).

An increased incidence of pemphigus in patients with malignancy has been noticed for decades.[3] A part of these patients are affected by a distinct subtype of pemphigus, the paraneoplastic pemphigus (PNP), defined by a causative autoantibody profile.[4] PH associated with neoplasia is exceptional and, to the best of our knowledge, there have been described three cases associated with lung cancer, and one with oesophageal carcinoma.[5-8] Here, we report the first case of PH in the context of a prostate carcinoma. Prostate cancer is rarely associated to malignancy-driven autoimmune disorders, suggesting that in our patient this association may be coincidental. Nevertheless, among 60 cases of malignancies observed in patients with pemphigus, 9 cases were of prostate cancer,[3] making conceivable a causative link between the two conditions. In cancer-associated pemphigus, tumour antigens should evoke an autoimmune reaction against desmosomal proteins. Within this context, the high expression of Dsg4 transcript in the prostatic gland raises the tantalizing hypothesis that in patients with prostate carcinoma this desmoglein, which shows significant homologies with all the other human cadherins, might favour the production of cross-reacting autoantibodies to Dsgs 1 and 3, and the onset of pemphigus.[9]

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fig. 1 Feston-like, erythematous lesions, with vescicles and bullae at their margins are evident on the back.

fig. 2 Histopathology revealing intraepidermal cleavage with severe spongiosis and some eosinophils, suggestive of pemphigus herpetiformis (hematoxylin-eosin stain, original magnification ×200).