A Case of Bullous Pemphigoid in a Patient with Dual Cancers, Fortuitous or Paraneoplastic?

Dear Editor,

Bullous pemphigoid (BP) is an autoimmune subepidermal blistering skin condition. It is characterised by the presence of immunoglobulin G (IgG) autoantibodies specific for the hemidesmosomal BP antigens BP230 (BPAg1) and BP 180 (BPAg2). Unlike pemphigus, it is not traditionally recognised as a paraneoplastic phenomenon. As BP becomes increasingly prevalent in our ageing population, it would be important to be on a lookout for paraneoplastic pemphigoid masquerading as BP.

Case Report

An 85-year-old Eurasian female presented with a 2-week history of blisters predominantly over the left ear, hands and thighs. She had a background of diabetes mellitus, ischaemic heart disease, mild renal impairment, gout and hypothyroidism. Further history revealed a loss of appetite and a weight loss of approximately 7 kg over a course of 3 to 4 months. Examination revealed tense intact bullae over the left ear, hands, thighs and haemorrhagic bullae on the buccal mucosa (Fig. 1a). There was no ocular involvement. In addition, a small firm lump measuring approximately 1.5 cm over the upper medial quadrant of the right breast was detected. There were no palpable abdominal masses or lymphadenopathy.

Full blood count showed normochromic normocytic anaemia with a haemoglobin of 10.7 g/dL (range, 11.5 to 15.0). Creatinine was raised at 290 umol/L (range, 50 to 90), consistent with her medical history of chronic renal failure. The liver function test was normal. Besides an elevated CA 19-9 of 41.9 U/ml (range, 0.0 to 30.0), other tumour markers tested such as CA 15-3, CA 125, CEA and alpha fetoprotein were normal.

Skin biopsy from the thigh showed a subepidermal blister associated with lymphocytic and eosinophilic infiltrate in the underlying dermis (Fig. 1b). Direct immunofluorescent showed linear deposition of IgG and C3 along the basement membrane. Indirect immunofluorescent to split skin substrate had a titre of >1/160 with a roof pattern. Ultrasound showed a spiculated 1.3 x 1.5 x 1.6 cm mass in the right upper inner quadrant of the right breast which was highly suspicious for malignancy. Histology of the right breast lump showed Scharff-Bloom-Richardson grade 1 infiltrating ductal carcinoma. This was estrogen receptor positive and

Fig. 1a. A few tense bullae over the fingers.

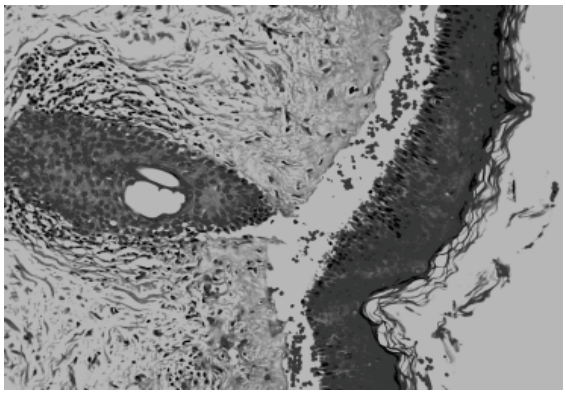

Fig. 1b. Subepidermal blister associated with lymphocytic infiltrate in the underlying dermis (haematoxylin and eosin x400).

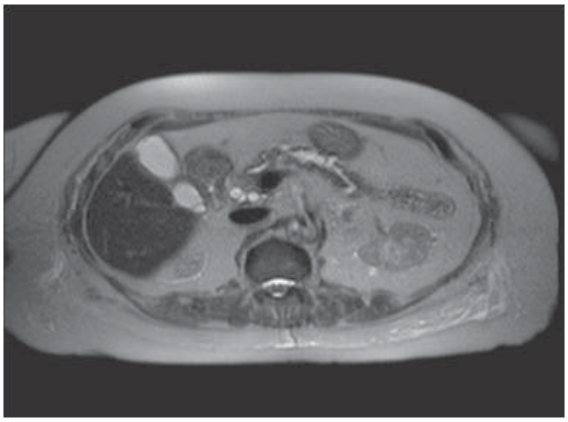

Fig. 1c. Magnetic resonance imaging of the pancreas showing multiple loculated lesions suggestive of intraductal papillary mucinous neoplasms.

progesterone positive. Magnetic resonance imaging of the pancreas showed multiple loculated lesions suggestive of intraductal papillary mucinous neoplasms (Fig. 1c). A bone scan showed no conclusive evidence of metastasis.

Prior to the diagnosis of the malignancies, the patient was started on prednisolone 30 mg once in the morning (0.5 mg/kg/day), in addition to topical steroids with some improvement in the blister count. She was given Tamoxifen for the breast cancer but had elected conservative management for the pancreatic cancer. She did not undergo radiotherapy. The patient was readmitted 2 weeks later for acute-on-chronic renal impairment, during which time, she had no blisters. Prednisolone was tapered over a 2-week period and her pemphigoid remained quiescent. Unfortunately after an almost 2-month stay, the patient passed away from sepsis and worsening renal impairment despite dialysis. She remained blister free at that time.

Discussion

Paraneoplastic pemphigus is a better recognised entity than paraneoplastic BP. However, reports in Asia suggest a higher incidence of malignancies in BP patients compared to age-matched controls. In Japan, 5.8% of 1000 BP patients had malignancies. In China, this was of higher incidence of 6.7% of 104 BP patients. In Taiwan, there was an even a higher incidence of 15.1% of 86 patients with BP who had malignancies.[1]

Less than a handful of case reports have demonstrated a true paraneoplastic phenomenon with the presentation of breast carcinoma. One patient had radical mastectomy for an invasive ductal carcinoma of her right breast and a few months later presented with BP and bone metastasis.[2] Another case report of 3 patients with neoplastic and mastophatic changes in the breast concluded that the treatment failure and appearance of BP during palliative therapy of the breast cancer points to its paraneoplastic character.[3] In our case, the breast carcinoma was diagnosed simultaneously. Pancreatic cancer has been associated with cicatricial pemphioid. One such case with an autopsy showing mucus adenocarcinoma of the head of pancreas had been described previously.[4] Comparatively, our patient had no ocular involvement and biopsy supported the diagnosis of BP.

The actual pathophysiology of this association remains unknown, however, it is postulated that the carcinoma may produce BP 180 antigen or may expose these normally sequestered antigens. The latter is described as the phenomenon of epitope spreading, where the injured mucosa or the carcinoma might expose the BP 180 antigen inducing onset of BP.[5] IgG and C3 have been present at the periphery of the tumour in a patient with BP and adenocarcinoma of the colon.[6] A reduction of titres of BP 180 antibodies after surgical removal and chemotherapy with 5-FU for sigmoid carcinoma with concomitant diagnosis of BP, suggest that the BP is a paraneoplastic process.[7]

Conclusion

In our case, the blisters were only completely resolved after starting Tamoxifen and the patient remained blister-free even after prednisolone was ceased whilst only being on topical steroids. Even so, we recognise that we cannot be certain that the presence of BP with dual malignancies here was indeed a paraneoplastic phenomenon as the underlying tumours were not resected and yet the blisters resolved. Understandably, it can also be argued that BP has a higher incidence in an older age group, which naturally has a higher rate of undiagnosed malignancy. Nevertheless, as BP becomes increasingly prevalent in our aging population, in addition to increasing reports of such a phenomenon, it will be necessary to stay vigilant to cases of paraneoplastic pemphigoid masquerading as BP.

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