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SHORT COMMUNICATION

Exacerbation of a Primary Follicular Centre Cutaneous B-cell Lymphoma during Pregnancy and Resolution to Anetoderma After Delivery

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Primary cutaneous follicle centre lymphoma (PCFCL) is an indolent primary cutaneous B-cell lymphoma (PCBCL) originating from the follicle centre cells, composed of a combination of centrocytes and centroblasts (1, 2). Clinically, lesions present as solitary or grouped reddish, violaceous papules, plaques, or nodules ranging in size from 2 to 15 cm, with or without surrounding erythema. Lesions are usually circumscribed and are most frequently found in the head and neck area or in the trunk (3). Histologically, 3 different growth patterns can be identified: follicular, follicular and diffuse, and diffuse (3, 4). Immunophenotypically, neoplastic cells in PCFCL express CD19, CD20, CD22, CD79 and bcl-6 (4). Molecular analysis shows clonal rearrangement of immunoglobulin genes (4). Treatment modalities include surgical excision, radiation therapy, intralesional steroids or combinations of these therapeutic approaches (5). PCFCL has an excellent prognosis, with a 5-year survival rate greater than 95%, and consequently aggressive therapeutic approaches are generally contraindicated (6).

It has been shown that involution and regression of PCBCL may leave areas of anetoderma (7). Anetoderma is a rare condition consisting of well-circumscribed areas of slack skin in which dermal elastic fibres are destroyed or deficient. Anetoderma can be classified as primary or secondary. Secondary anetoderma may be associated with a number of different skin diseases, notably autoimmune disorders, acne, sarcoidosis, skin infections and cutaneous lymphoma (7). We describe here a case of PCFCL that grew rapidly during pregnancy and spontaneously regressed to anetoderma after delivery.

CASE REPORT

A 40-year-old woman at 35 weeks of gestation presented to our unit due to cutaneous lesions that had first appeared 10 years previously. Physical examination revealed numerous erythematous nodules of various sizes on her upper back and shoulders. During the last 2 months the patient had experienced a dramatic increase in nodules over her back. There was no enlargement of the palpable lymph nodes and systemic symptoms were absent. Her past medical history was negative for chronic illnesses except for infertility. The patient had undergone 3 years of infertility therapy, including the use of clomiphene citrate with intrauterine insemination (IUI) and then *in vitro* fertilization (IVF) and embryo transfer resulting in a pregnancy. Complete blood cell count, anti-nuclear antibodies (ANA), liver and kidney function tests were normal.

At the gestational age of 37 weeks, the patient underwent an elective caesarean section delivery and gave birth to a healthy male baby. In the immediate post-partum, biopsy specimens were obtained from lesions on the patient's back. Histopathology revealed neoplastic follicles consisting of small centrocytes with few scattered centroblasts (Fig. 1). Immunohistochemistry showed the following main phenotypical characteristics: $CD20^+$ (Fig. 1), $CD23^+$, $MIB1^+$ 2%, $CD22^+$, $CD79a^+$, $BCL2^+$, $bcl6^+$. Clonal B lymphocyte population was demonstrated by molecular analysis, whereas the translocation t(14;18) was absent. On the basis of the clinical, histological, immunophenotypical and genotypical features a diagnosis of PCFCL was made. Staging investigations, notably complete blood cell counts, blood chemistry analysis, total body computed tomography (CT) scan and bone marrow biopsy, were negative.

After delivery, most lesions gradually regressed leaving areas of anetoderma (Fig. 2). The patient received radiotherapy on the remaining lesions and, at the time of writing, after one year of follow-up, is in complete remission.

DISCUSSION

Several cases of anetoderma secondary to PCBCL have been reported (7–11). Although the pathogenesis of anetoderma remains unclear, many pathogenetic mechanisms could be operative. The destruction of the elastic tissue may be mediated by the release of elastase, metalloproteinases, cytokines, or other sub-

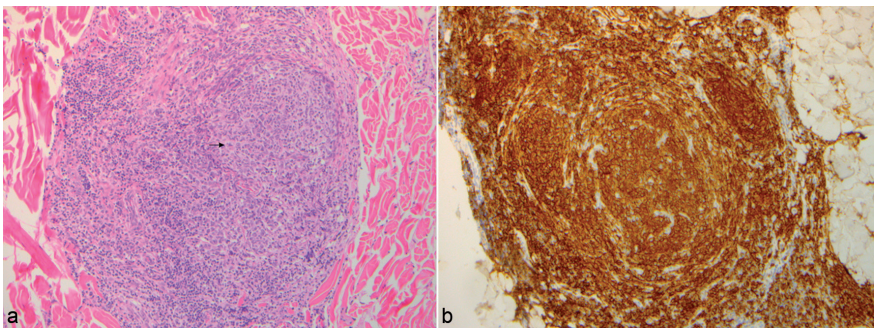

Fig. 1. Skin punch biopsy taken from an erythematous nodule of the upper back of the patient showing (a) small centrocytes with few scattered centroblasts (*arrow*) (haematoxylin and eosin (H&E) stain, original magnification ×20), (b) positive for the pan-B-cell antigen CD20 (immunoperoxidase stain, original magnification ×20).

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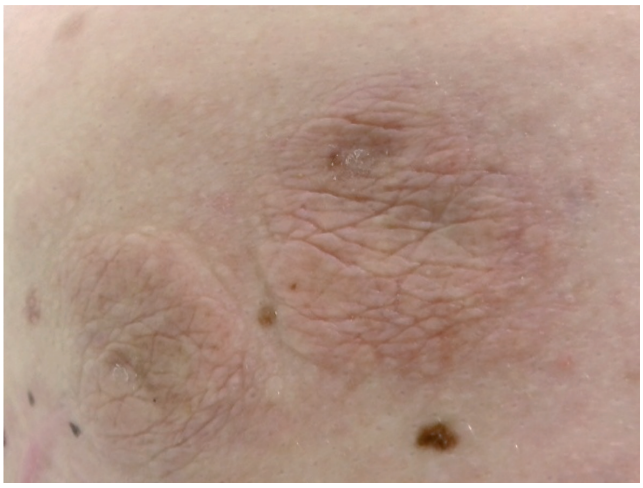

Fig. 2. Areas of anetoderma on the skin of the patient's upper back, previously affected by primary cutaneous follicle centre lymphoma.

stances produced by the inflammatory or tumoural cells. It is known that the degradation of elastic fibres is mediated by elastases, including matrix metalloproteinase (MMP) and it has been suggested that MMP-9 produced by neoplastic cells could be responsible for anetoderma associated with PCBCL (11). An alternative possibility is that interleukin (IL)-6, which induces the final maturation of activated B cells into immunoglobulin-producing cells, may be involved in the elastolytic process observed in anetoderma (8).

To the best of our knowledge, cases of PCBCL exacerbating during pregnancy have not been described previously. The exacerbation could be related to the normal clinical course, although it is more plausible that it could be related to both hormonal and immunological changes occurring over the course of pregnancy. In this regard, successful pregnancy in humans is associated with reduced IL-2, interferon (IFN)-γ and tumour necrosis factor (TNF)-α secretion and consequent impaired anti-tumour activity of cytotoxic cells (12). Moreover, during pregnancy macrophage 1 (M1) activity is decreased and a macrophage 2 (M2) polarization is observed (12). As a consequence of this immunological shift, the anti-cancer activity of M1 macrophages is reduced, whereas the tumour-promotion activity of M2 macrophages is increased (13). This biased immunological phenotype associated with pregnancy could have influenced the clinical course of the cutaneous lymphoma in our patient. On the other hand, restoration of the original immunological homeostasis after delivery may have been responsible for the spontaneous resolution to anetoderma.

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