

SHORT COMMUNICATION

Exceptional Association of Syringotropic Mycosis Fungoides with Chronic Lymphocytic Leukaemia

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Mycosis fungoides (MF) is the most common form of cutaneous T-cell lymphoma (CTCL). In very rare cases, prominent infiltration of the eccrine sweat glands is observed; they are designated as syringotropic MF (SMF), a variant of folliculotropic MF, according to the current WHO-EORTC (European Organization for Research and Treatment of Cancer) classification (1). SMF is an extremely rare form of CTCL with only approximately 50 cases reported to date (2–6). We report here an additional case, which is unusual because it occurs in the context of chronic lymphocytic leukaemia and is associated with a very high load of Epstein-Barr virus (EBV).

CASE REPORT

A 72-year-old woman presented with a 6-month history of eruption, prominent in the intertriginous areas. Her medical history was significant for chronic lymphocytic leukaemia (CLL) in remission, treated 2 years earlier with fludarabine, cyclophosphamide and rituximab.

Skin examination revealed punctuate erythematous papules and comedo-like lesions with small milia-like cysts on the trunk. These lesions were prominent on the axillary, inguinal and thoraco-mammary intertriginous areas (Fig. 1a). Inflammatory cystic lesions similar to hidradenitis suppurativa lesions were also observed on the axillary and inguinal regions (Fig. 1b). Patches of alopecia with comedo-like lesions were present on the scalp (Fig. 1c). Biopsy specimen taken from comedo- and cystic-like lesions revealed a dermal infiltrate of atypical lymphocytes with enlarged, hyperchromatic nuclei and irregular nuclear contours, associated with an epidermotropism. The infiltrate was prominent in the follicular epithelium and sweat glands and ducts (Fig. S1¹). The immunohistochemical analysis showed an infiltrate consisting mainly of CD3⁺, CD4⁺ T cells. Study of the T-cell receptor gene failed to reveal a T-cell clone.

Based on the clinical presentation and histological findings, a diagnosis of SMF stage IB (T2 N0Mo) was established.

EBV-encoded small RNAs (EBERs) were detected by *in situ* hybridization in skin biopsy and blood PCR revealed EBV DNA (4.0 log IU/ml).

Treatment with bexarotene was initiated at a dose of 150 mg/m²/day and after 2 months a partial improvement was noted.

DISCUSSION

This case report shows classic clinical features of SMF; i.e. punctuate erythematous papules, follicular and comedo-like lesions and alopecia. Most of the cases previously reported were men (ratio 5:2) with a mean age of 50–55 years (2, 3, 5). The prognosis of SMF appears to follow a benign, chronic evolution (2–4). In our case, as in approximately two-thirds of SMF cases previously reported, a folliculotropism was associated with the syringotropism. Despite the debated link between folliculotropic and syringotropic MF, they appear to be distinct entities with a more favourable prognosis for the latter of adnexotropic MF (3, 5). The absence of monoclonal TCR rearrangement is surprising and led us to discuss a pseudo-MF (reactive lymphoproliferative disorder). However, it is known that true MF may have a polyclonal pattern (7) and after clinical pathological discussion within experts of the French cutaneous lymphoma study group (8), the diagnosis of true MF was confirmed.

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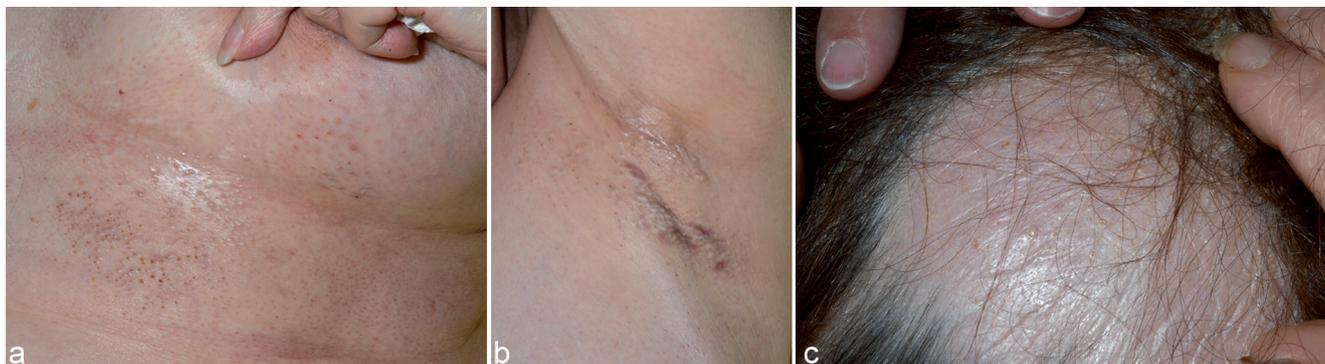


Fig. 1. (a) Punctuate erythematous papules and comedo-like lesions with small milia-like cysts on the trunk, prominent on the thoraco-mammary folds. (b) Cystic lesions and hidradenitis suppurativa-like lesions on the axillary region (also observed on the inguinal regions). (c) Patches of alopecia with comedo-like lesions on the scalp.

Due to the rarity of SMF, there is no guideline regarding the treatment. Radiotherapy seems to be the most effective treatment for focal disease. For the treatment of generalized or multifocal SMF, a variety of treatments have been reported (2, 5): oral retinoids, interferon alpha, systemic chemotherapy, vorinostat, extracorporeal photophoresis (4).

Coexistence in the same patient of MF and B-cell malignancies is unusual (9, 10). A series of 7 cases of cutaneous folliculotropic T-cell associated with low grade B-cell malignancies has been published recently (10), but the association with SMF has never been reported. Various explanations have been proposed for the association of MF with B-cell malignancies (9–11). First, there could be a genetic predisposition for malignancies or lymphoproliferative disorders. Another explanation could be the possible mutagenic effect of cytostatic drug although in most published patients MF is the first malignancy to develop, followed by B-cell malignancies. In our observation, the interval is short (18 months) between the initiation of chemotherapy and the development of MF. Another hypothesis is that both malignancies could originate from the same neoplastic stem cell. One could also assume that the underlying B-cell lymphoma could promote T-cell lymphoproliferation. A further aspect is the role of T cells in the pathogenesis of chronic lymphocytic leukaemia. Data in the literature (12) suggest that the crosstalk between CLL B cells, extracellular components of the microenvironment, and T cells has an important impact on the physiopathology and evolution of the disease, mainly through regulation of CLL B-cell expansion, differentiation, and survival. Conversely, this crosstalk may also induce qualitative and quantitative changes in normal T cells that could impact the fitness of the immune system of CLL patients. The presence of EBV in our patient's blood and skin biopsy is another interesting point; the virus could play a significant role in the outcome of both B-cell malignancy and MF. There is indeed clear evidence for an aetiological role of EBV in certain B-cell lymphoid diseases, including endemic Burkitt lymphoma or lymphomas in the elderly. EBV has also been postulated as a risk factor for non-Hodgkin's lymphoma in the general population, but EBV is not detected in the majority of these tumours. Therefore, a direct role of EBV in an immortalizing transformation of lymphocytes is less likely in these cases and alternative pathways have been hypothesized (13). Moreover, viruses, and especially herpes viruses, are thought to act as persistent chronic antigens in the skin, which could induce or maintain T-cell proliferation and indirectly lead to CTCL (14).

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