Patients with mycosis fungoides (MF) typically have a prolonged clinical course. A small proportion of cases progress over years through patch, plaque and tumour stages, followed by lymph node and visceral involvement (1). Some cases of MF are difficult to distinguish from other skin diseases, such as psoriasis and atopic dermatitis. Currently, tumour necrosis factor (TNF)-α inhibitors, such as infliximab, adalimumab, and etanercept, are widely used for treating patients with moderate to severe psoriasis (2). Blockade of TNF-α, however, is profoundly immunosuppressive, resulting in reactivation of tuberculosis and histoplasmosis, as well as the emergence of malignant lymphomas (3). In fact, some cases with MF manifested by treatment with TNF-α inhibitors have been reported (4–7). We describe here a 60-year-old woman diagnosed with psoriasis who showed exacerbation of MF with large cell transformation during treatment with infliximab.

CASE REPORT

A 60-year-old Japanese woman presented to another hospital with indurated erythema on her face, trunk, and extremities. Eleven years previously, erythema first appeared on her knees, gradually expanding to the whole body. A skin biopsy showed superficial dermal lymphocyte infiltration and psoriasiform acanthosis. She was diagnosed as having psoriasis. Topical corticosteroids, oral etretinate 30 mg/day, and ultraviolet phototherapy improved her skin lesions. After 6 months, the patient stopped taking oral etretinate because of side-effects, such as peeling and severe cheilitis. Cyclosporine 200 mg/day was administered, which slightly worsened the skin lesions. Although etretinate was re-started, side-effects prevented her from taking the medicine constantly. Fourteen months after the diagnosis of psoriasis, she received 2 infusions of infliximab (300 mg, each) at a 2-week interval, which exacerbated her skin lesions. Multiple indurated erythematous plaques appeared on the face, trunk, and extremities (Fig. 1). Several tumours also developed on the forehead. Suspected of having MF, she was referred to our hospital. Histological examination of the tumour showed ulceration and epidermal and dermal infiltration of atypical lymphocytes. Sheet-like infiltration of anaplastic large lymphocytes and infiltration of eosinophils were seen in the upper dermis (Fig. S1). Histological examination of the plaque showed epidermotropism and perivascular infiltration of medium-sized atypical lymphocytes (Fig. S1). Immunohistochemical staining showed that atypical lymphocytes were CD3+, CD4+, CD8+, CD19+, CD20+, and CD56+. Some of the tumour cells expressed CD25. Notably, most anaplastic large cells also expressed CD30. Laboratory examination revealed an elevated serum soluble interleukin-2 receptor level of 1,580 U/ml (normal range, 145–520 U/ml). All other laboratory data, including lactate dehydrogenase, C-reactive protein, and peripheral blood cell count, were normal.

Fig. 1. (a) Clinical presentation before treatment with infliximab. (b) Clinical presentation after the second injection of infliximab. Multiple indurated erythematous plaques on the face, trunk, and extremities and several tumours on the forehead. A written permission from the patient are given to publish these photos.

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Serological examination was negative for anti-human T-cell lymphotropic virus type I antibody. Epstein-Barr virus serology showed previous infection. A computed tomography, a lymph node biopsy from the axillary lymph node, and bone marrow aspirate revealed no evidence of lymphoma other than skin. In the light of these results, she was diagnosed as having MF with large cell transformation (T3N0M0; stage IIB) (8). In addition to topical corticosteroids and ultraviolet therapy, oral etoposide 50 mg/day was intermittently administered. Although the tumours on the forehead disappeared, the slightly indurated erythematous plaques persisted. The patient has shown a stable disease for 12 months since the diagnosis of MF.

**DISCUSSION**

We believe that the skin lesions in the present case were MF from the start. Psoriasiform acanthosis is sometimes seen in other skin diseases, such as MF, atopic dermatitis, and chronic eczema. Epidermotropism and nuclear atypia of infiltrating lymphocytes are characteristic of MF. In some cases, however, they are not noticeable, which could lead to a wrong diagnosis. A high CD4/CD8 ratio of infiltrating lymphocytes, a decrease in, or loss of, CD7 expression, and aberrant expression of CD25 and/or CD30 are helpful for the diagnosis of MF. Detection of clonal T lymphocytes by Southern blotting or PCR is also suggestive of MF.

To the best of our knowledge, 14 cases have been reported in English language publications in which TNF-α inhibitors were associated with the onset or exacerbation of MF (4–7, 9). A review reported that, among 1,298 patients treated with infliximab, one Hodgkin’s lymphoma and 3 non-Hodgkin’s lymphomas were observed (10). The standardized incidence ratio compared with the general population was 6.4 (10). Others postulated that use of infliximab in Crohn’s disease was associated with an increase in lymphoma risk of approximately 5-fold compared with non-immunosuppressive use, and 10-fold compared with the general population (11). Although it is still controversial whether patients treated with TNF-α inhibitors have a higher risk of lymphoma than the general population (9, 12), a pre-existing T-cell lymphoma may well show progression in the context of reduced tumour immunosurveillance. Therefore, we cannot be too careful not to apply TNF-α inhibitors to patients with malignant lymphoma. When MF cannot be ruled out, retinoids and/or ultraviolet phototherapy should be considered because they are effective to both psoriasis and MF. In reviewing the course of the present case, we conclude that we should have taken both psoriasis and MF. In reviewing the course of the present case, we conclude that we should have taken both psoriasis and MF. In reviewing the course of the present case, we conclude that we should have taken both psoriasis and MF.