Introduction

The occurrence of systemic lupus erythematosus (SLE) and lymphoma in the same patient has been widely reported (1–7), although the pathogenetic mechanisms underlying this association are unclear. Whether such cases are chance occurrences or whether the two diseases share a common etiology is not known; the answer might only be found through large cohort studies. Lymphomas developing in patients with SLE and other autoimmune diseases are virtually always of B-cell origin. To our knowledge this is the first report of a T-cell anaplastic large cell lymphoma in a patient with SLE. This article discusses the association of SLE and lymphoma, with an emphasis on T-lymphoproliferative states.

Key Words: T-cell anaplastic large cell lymphoma; systemic lupus erythematosus; pathogenesis; etiology.

Case Report

ALK-Negative T-Cell Anaplastic Large Cell Lymphoma Associated with Systemic Lupus Erythematosus

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Abstract

Patients with systemic lupus erythematosus (SLE) appear to have an increased risk of developing malignancies, especially lymphomas. We report the development of a systemic ALK-negative T-cell anaplastic large cell lymphoma, stage IIB, in a 53-yr-old Caucasian female with a 12-yr history of stable SLE. The patient responded poorly to chemotherapy and died 2 yr after diagnosis. Lymphomas that develop in patients with SLE and other autoimmune diseases are virtually always of B-cell origin. To our knowledge this is the first report of a T-cell anaplastic large cell lymphoma in a patient with SLE. This article discusses the association of SLE and lymphoma, with an emphasis on T-lymphoproliferative states.

Key Words: T-cell anaplastic large cell lymphoma; systemic lupus erythematosus; pathogenesis; etiology.

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Introduction

The occurrence of systemic lupus erythematosus (SLE) and lymphoma in the same patient has been widely reported (1–7), although the pathogenetic mechanisms underlying this association are unclear. Whether such cases are chance occurrences or whether the two diseases share a common etiology is not known; the answer might only be found through large cohort studies. Lymphomas developing in patients with SLE are generally of B-cell origin, with no obvious predominance of any particular subtype (1). The majority of patients are diagnosed with SLE before lymphoma (8), and the two seem to run independent clinical courses rather than being affected by one another (1).

T-cell lymphomas, however, are very rarely associated with SLE (9–12). This article describes a patient who developed primary systemic T-cell anaplastic large cell lymphoma (T-cell ALCL) after a 12-yr history of SLE.

Case report

A 34-yr-old woman presented with a 4 mo history of intermittent polyarthritis, myalgia, and malaise, and was diagnosed with SLE in March 1988. The diagnosis was based on her symptoms, a pleuropericarditis, blood tests positive for anti nuclear antibodies (ANA) (a 1:128 homogenous pattern) and
anti-DNA antibodies, the presence of LE cells, proteinuria, and a leukopenia (3–3.5 × 10^9/L). Because the patient had mild renal dysfunction (proteinuria, erythrocyturia, granular casts, and hematuria), she was initially treated with oral prednisolone (1 mg/kg/day) and azathioprine (150 mg/day), which resulted in a significant clinical improvement. Her disease course remained stable without any clinical deterioration or increase in serological lupus activity for 10 yr, despite a reduction in drug dosage (to 10 mg of oral prednisolone and 5–25 mg of oral azathioprine daily). During this period the immunological assays gave ANA titers of 1:16–1:32, normal concentrations of C3 and C4 immune complexes, and normal anti-DNA antibodies and anti-smooth muscle antibodies counts. The only complaint was of occasional photosensitivity in the springtime, which was relieved by increasing the daily oral prednisolone to 30 mg over these periods.

In September 1999 she suffered a relapse of polyarthritis with a diffuse photosensitivity of the face and hands, accompanied by an increase in immunological activity (ANA 1:80 with positive anti-DNA antibodies). In addition she developed a mild hepatomegaly accompanied by an increase in the levels of liver transaminases. The azathioprine was stopped and the dose of prednisolone increased to 30 mg. The skin rash unfortunately persisted and so hydroxychloroquine was also introduced, initially at 400 and then at 200 mg/d. When the liver function tests normalized, the prednisolone was once again reduced to 10 mg daily.

In July 2000 she developed painless lymphadenopathy bilaterally with nodes of up to 2 cm in the neck and supraclavicular and axillary regions. Immunological analyses were as follows: ANA titer of 1:80, anti-DNA antibodies of 126 IU/mL (normal < 55), normal levels of CH50, C3, and C4 immune complexes, with a negative ANCA. The prednisolone dosage was once again increased to 30 mg/d, and after an observation period of 6 wk, a biopsy of the persisting lymph nodes was taken.

The histopathology (revealing a diffuse infiltrate of large pleomorphic horseshoe-shaped multinuclear cells invading the lymphoid sinuses) and the immunohistochemistry (showing large neoplastic cells strongly positive for CD30, EMA, HLA-DR, CD3, cytokeratin, and vimentin, and negative for TdT, CD1a, CD20, CD 68, CD 15, CEA, LCA, HMB45, actin, chromogranin A, S-100) were consistent with T-cell ALCL. Additionally, 50% of the tumor cells were strongly positive for the Epstein–Barr virus (EBV) LMP-1 (latent membrane protein-1) antigen, and negative for the ALK protein. The large blastic cells had a high proliferative and apoptotic index. Neurological examination, chest radiography, computed tomography and ultrasonography of the abdomen, endoscopy of the upper and lower gastrointestinal tracts, and bilateral iliac crest biopsies were unremarkable. The serum biochemistry, including LDH, was normal, except for a hypoalbuminemia (32 g/L). Peripheral blood count showed a slight normocytic anemia (107 g/L) and lymphopenia (1.2 × 10^9/L), and the erythrocyte sedimentation rate was raised at 42. IgG antibody to the viral capsid antigen of EBV was positive, while IgM was negative. HIV testing was repeatedly negative. The clinical stage was therefore established as II B according to the Ann Arbor classification with an International Prognostic Index (IPI) of 0. The patient was started on PACEBOM chemotherapy (13), and given four cycles of treatment, but owing to a lack of response, this was changed to the MINE-ESHAP (14) salvage regimen accompanied by field radiotherapy. The patient entered complete remission lasting up until November 2002 when she sustained pathological fractures of the third and fourth lumbar vertebrae. The patient refused any further treatment and died as a result of disease progression later the same month.

There had been no family history of either SLE or hematological malignancy.

**Discussion**

While the association of B-cell malignancy and SLE is well documented in humans (1–7) and in animal models (lupus–NZW/B mice) (15), the occurrence of T-cell lymphomas in the context of SLE is rare. The literature describes five such patients; two with concomitant T-zone lymphoma and SLE (9), one patient in whom SLE preceded a peripheral T-cell lymphoma with a helper-inducer phenotype by 18 y (10), one patient who developed an immunoblastic T-cell lymphoma of the liver expressing the activated helper-inducer T-cell phenotype after a 3 yr history of SLE (11), and a patient who contracted CD4+ lymphoma of the liver after 12-yr