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Systemic lupus erythematosus after acute lymphoblastic leukaemia

SIR, Systemic lupus erythematosus (SLE) is associated with an increased risk of neoplasia of the lymphoreticular system, particularly lymphoma [1, 2]. While non-Hodgkin’s and Hodgkin’s lymphomas are the commonest associated malignancies [3, 4], cases of myeloma [5, 6] and leukaemia [7] have also been documented and there have been reports of SLE occurring after thymectomy or thymomectomy [8] or after chemotherapy and radiotherapy for malignant thymoma [9].

Usually, SLE precedes the onset of lymphoproliferative disease [10–13], but the neoplasia can occur earlier [10] or simultaneously [14]. Single cases have been described of SLE preceding acute lymphoblastic leukaemia (ALL) [15] and of SLE appearing 5 yr after complete remission of ALL induced by mercaptopurine [16]. This report describes the appearance of SLE in a young woman 10 yr after she completed successful treatment for ALL.

The patient presented in 1976 at the age of 2 yr with pancytopenia, lymphadenopathy and hepatosplenomegaly. ALL was diagnosed on a bone marrow biopsy and she was commenced on UKALL V chemotherapy, comprising cycles of prednisolone, vincristine, methotrexate and mercaptopurine. At the onset of treatment she also received cranial irradiation. She completed her last UKALL V cycle in 1979 and subsequently remained in full haematological remission.

In 1989, when the patient was 15 yr old, she developed an intermittent rash and limb pains with a slightly elevated erythrocyte sedimentation rate (ESR) of 22 mm/h. Further investigation for joint pains in 1993 revealed a mild lymphopenia of 1.0 × 10⁹/l and an ESR of 36 mm/h. Antinuclear antibodies (ANA) were detected to a titre of >1:320 and rheumatoid factor to a titre of 1:80, whereas DNA binding activity was within the normal reference range. In 1994 she was referred to the rheumatology clinic with widespread pains and Raynaud’s phenomenon. There was no overt synovitis but she had a mild flexion contracture of her right elbow. Her total white blood cell count was 2.7 × 10⁹/l with a differential of 1.0 lymphocytes and 1.5 neutrophils, and an extractable nuclear antigen screen revealed anti-Sm antibodies. Her platelet count, serum creatinine concentration, urine chemistry and microscopy, liver function tests and serum creatine phosphokinase were normal. She was diagnosed as having mild SLE.

Various mechanisms have been postulated to explain the association between SLE and malignancies of the lymphoreticular system. Hypotheses include a common stimulus, such as a virus infection in a genetically susceptible host, facilitation of the neoplastic process by the autoimmune disorder, and suppression of immune surveillance by cytotoxic therapy. However, the increased susceptibility to malignancy of the lymphoid tissues in lupus appears to be independent of cytotoxic therapy [2, 4, 14]. Another possibility is that oncogene activation in the autoimmune diseases could initiate neoplasia. For instance, lymphocytes from patients with SLE exhibit increased expression of the proto-oncogenes c-myb and c-myc, transcripts of which are found in large amounts in lymphoid tumours [17].

SLE and ALL could simply be different expressions of the same immunological disorder as, although ALL is generally not associated with autoantibody formation, children with ALL have been found with positive test results for ANA in conjunction with clinical features of SLE [18]. Alternatively, the rarity of the association between ALL and lupus may imply that it is no more than a chance occurrence.

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