Pleomorphic T-cell leukaemia in a Caucasian adult: clinical phenotypic and functional characteristics

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Summary: Pleomorphic T-cell leukaemia occurring in an adult Caucasian patient is described. The leukaemia cells expressed both antigenic determinants (T₄ and T₈) normally detected separately on either helper or suppressor cells. They functioned as helper cells and there was evidence of unbridled antibody production. It is possible that a distinctive subtype of pleomorphic T-cell leukaemia occurs in Caucasian patients.

Introduction

At present, there is considerable interest in adult T-cell leukaemia (ATL; Uchiyama *et al.*, 1977), a disease characterized by pleomorphic cells with convoluted nuclei and an association with a specific human retrovirus (HTLV) infection (Kalyanaraman *et al.*, 1981, 1982; Popovic *et al.*, 1982). The disease was first described in Japan, and British cases have been restricted to black West Indian patients (Catovsky *et al.*, 1982). We reported a similar illness occurring in a Caucasian patient, characterized by typical pleomorphic cells which expressed an immature surface phenotype but functioned as helper cells.

Case report

A 58 year old swimming pool supervisor presented with a 2 week history of fever, malaise and shortness of breath, preceded by a fleeting diffuse macular rash. He had previously been well, had never been out of England, and had no known non-white ancestors.

Examination revealed generalized lymphadenopathy and hepatosplenomegaly. There were no skin lesions. His blood count showed $25 \times 10^9/l$ leucocytes (66% lymphocytes) and haemoglobin 11.1 g/dl. The lymphocytes were pleomorphic with some blast cells but a majority of mature forms with varying degrees of

nuclear convolution (Figure 1); some plasmacytoid cells were also present. Lymph node and bone marrow histology showed diffuse infiltration with these cells and a mild vascular proliferation. The serum immunoglobulins were diffusely increased (maximum levels IgG 39.8 g/l, IgA 5.2 g/l, IgM 3.6 g/l). There were sustained high titres of antibodies to toxoplasma, cytomegalovirus, Epstein-Barr virus, autoantibodies to gastric parietal cells, smooth muscle and skeletal muscle, and a transient rheumatoid factor (1/256). After transfusion, antibodies to red cells, white cells and platelets developed. These were associated with transfusion reactions and a steroid-responsive thrombocytopenia. After 8 months the patient developed an anterior and posterior uveitis. Antibody to HTLV was not detected in the serum. The patient did not, at any time, have a raised plasma calcium level.

Using monoclonal antibodies and staining for terminal deoxynucleotidyl transferase the leukaemic cells were shown to have an extraordinary phenotype (OKT 11⁺ 3⁺ 4⁺ 8⁺ 6⁻ TdT⁻). Less than 5% of the circulating lymphocytes were of mature T-cell phenotype (OKT 3⁺ 4⁺ 8⁻ or OKT 3⁺ 8⁺ 4⁻), and less than 2% were B-cells (bearing surface immunoglobulin). The leukaemic cells appear to correspond to a stage of differentiation between the common cortical thymocyte (OKT 11⁺ 4⁺ 8⁺ 6⁺ 3⁻) and the two mature ('helper' and 'suppressor') medullary thymocyte and peripheral T-cell subsets (Reinherz & Schlossman, 1980). Functional analysis of the patient's lymphocytes showed that 2% spontaneously secreted IgG *in vitro*, suggesting polyclonal B-cell activation *in vivo*. Pokeweed mitogen stimulated co-culture experiments revealed that the leukaemic cells

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Figure 1 (a) Typical leukaemia cells by light microscopy, magnification $\times 6,700$ (peripheral blood). (b) Electron microscopy (bone marrow) $\times 16,000$.

provided help for IgM and IgG synthesis by normal B cells.

The patient received aggressive chemotherapy, but it was not possible to eliminate the leukaemic cells and an increasing proportion of blast cells was seen. He died 13 months after presentation; at post-mortem there was hepatosplenomegaly and infiltration of axillary and para-aortic lymph nodes but no thymoma.

Discussion

The clinical and cytological features of this case were similar to those seen in Japanese and black patients with ATL. The phenotype in ATL, however, is generally that of mature T helper/inducer cells (OKT3⁺ 4⁺ 8⁻; Boumsell *et al.*, 1981; Haynes *et al.*, 1981) although the cells paradoxically suppress immunoglobulin synthesis *in vitro* (Hofman *et al.*, 1982; Yamada, 1983). In this case, the phenotype was extremely unusual, in that individual leukaemic cells expressed both helper (T₄) and suppressor (T₈) antigens simultaneously. It may be that the patient's hypergammaglobulinaemia and high titres of a variety of antibodies, including autoantibodies, were attributable to unbridled helper activity by the leukaemic cells.

There is one other published case of leukaemia with this phenotype (Schnitzer *et al.*, 1982). This was also pleomorphic T-cell leukaemia in a Caucasian adult with no HTLV antibodies. These two cases suggest that a type of ATL may occur in Caucasian patients in the absence of HTLV infection. An analogy among B-cell neoplasms is the non-African Burkitt's lymphoma which, in contrast to the African form, is not associated with Epstein-Barr virus infection.

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