Hairy cell leukaemia: 1986

Hairy cell leukaemia has aroused increasing interest since its first description in 1958 by Bouroncle *et al*.[1] The clinical course and diagnostic criteria of this chronic lymphoproliferative disorder have been further defined in subsequent series.[2-4] It most often affects men aged between 35 and 55, being characterised by pancytopenia, splenomegaly, and a variable number of hairy cells in the peripheral blood. The two main reasons why this uncommon disease has attracted the attention of clinical investigators are the unusual features of the hairy cells (which have prompted many conflicting ideas about their origin) and the impressive clinical responses observed with two drugs—interferon and deoxycoformycin—which had previously been tried with little success in other forms of cancer.

Hairy cells are white blood cells with prominent cytoplasmic villi, distinct tartrate resistant acid phosphatase activity, and inducible phagocytic properties—features which led early investigators to suggest a relation to the so called reticuloendothelial system[5] and to designate the disease accordingly.[1 4] The use of markers for B and T lymphocytes developed in the early 1970s showed that the cells of most patients with hairy cell leukaemia had B cell features.[2 6] Technical advances and in particular the availability of monoclonal antibodies against B cell antigens confirmed the B cell nature of hairy cells,[7 8] which has now been definitively established by the demonstration of rearrangements of the immunoglobulin genes coding for heavy and light chains.[9] This technique has also made it possible to classify hairy cell leukaemia as a monoclonal B cell proliferation. Recent studies have identified hairy cells with B lymphocytes activated in the late stages of their maturation pathway.[9 11] Precise information on the cell of origin of hairy cell leukaemia may be important in interpreting the responses to treatment.

Splenectomy corrects the pancytopenia in most patients[2-4] and improves their survival when the spleen is enlarged more than 5 cm below the costal margin.[12 13] Nevertheless, because the bone marrow is also affected, splenectomy has long-lasting benefits in only a minority of patients.[2 4 13] This and the fact that in 10-20% of patients the spleen is not enlarged lead to about 80% of patients requiring other forms of treatment at some stage. Chlorambucil was formerly popular[14] but has now been superseded by interferon. The beneficial effects of the crude leucocyte interferon first reported by Quesada *et al* only two years ago[15] have now been confirmed and extended by several groups in Europe and the United States with human lymphoblastoid interferon[16] or the various recombinants.[17-20] The effect of interferon has been reported most often in patients who have had their spleens removed, but responses have also been recorded in patients with large spleens.[16] Interferon given daily or three times a week by the intramuscular or subcutaneous route gives a gradual and sustained improvement in the haemoglobin concentration and in the neutrophil, monocyte, and platelet counts and considerably reduces the infiltration of the bone marrow. After three to six months' treatment most patients have normal blood counts. Complete elimination of hairy cells from the bone marrow and correction of the fibrosis require more prolonged periods of treatment (a year or longer); hence few complete remissions have so far been recorded. Unlike other forms of chemotherapy, treatment with interferon confers benefit in close to 100% of cases. The flu-like symptoms due to interferon are only an early feature of treatment. Other minor side effects are easily controlled by reductions in the dose. The clinical condition of patients previously resistant to chlorambucil and with a history of severe infections improves dramatically. Studies are still in progress to determine the optimal duration of treatment with interferon and the need for maintenance treatment. Patients treated for less than a year tend to relapse,[16 19] but prolonged disease free periods may be expected in those treated for longer, especially when the bone marrow has been cleared of hairy cells.

Spiers *et al* have recently reported good results of treatment with the adenosine deaminase inhibitor 2'-deoxycoformycin.[21] At low dosage it induces complete remissions in hairy cell leukaemia without the toxicity caused at the higher dosage used in lymphoblastic leukaemia. At the recent meeting of the American Society of Hematology three groups (Spiers *et al*, Kraut *et al*, and Johnston *et al*) reported complete responses with deoxycoformycin in half the patients with hairy cell leukaemia.[22] In contrast with interferon, the duration of treatment required to obtain complete bone marrow remissions is relatively short and prolonged remissions without maintenance treatment have been recorded in some patients. The appreciable improvement in life expectancy and wellbeing in patients with hairy cell leukaemia as a result of the use of interferon and 2'-deoxycoformycin suggests the need to re-evaluate these agents in other haemopoietic malignancies. The B cell nature of the hairy cell should provide clues to the precise mechanism of action of interferon and 2'-deoxycoformycin, which might be exploited to treat other B cell disorders; hairy cell leukaemia is a good model for their study.

D CATOVSKY

Senior Lecturer in Haematology and Medicine,
Medical Research Council Leukaemia Unit,
Royal Postgraduate Medical School, London W12 0HS

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