Haematology Grand Rounds

Hairy cell leukaemia masquerading as malignant lymphoma

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Summary

Pancytopenia with massive splenomegaly, minimal lymphadenopathy and circulating atypical lymphoid cells with cytoplasmic projections characterize the lymphoproliferative disorder known as hairy cell leukaemia, or leukaemic reticulo-endotheliosis. Many of the features of hairy cell leukaemia are shared with a malignant lymphoma of the B-cell type, from which it can be distinguished on a number of criteria, including histological examination of bone marrow, lymph nodes, liver and spleen. Recognition that this syndrome is not homogeneous is important, since in the B-cell tumour the clinical course is progressive, requiring chemotherapy which is usually effective; the disease is indolent in leukaemic reticulo-endotheliosis and drug treatment may actually shorten survival. The patient presented illustrates the ease with which this diagnostic error can arise, and the features separating these two unusual entities are reviewed.

Case report

A 48-year-old man was completely well until November 1979, when he presented with a slowly resolving influenzal illness. His history was otherwise negative: specifically, there were no symptoms of anaemia and no abdominal discomfort that might be attributed to splenomegaly. The patient was pale and physical findings were limited to a spleen palpable 4 cm below the left costal margin in the midclavicular line. At that time the haemoglobin concentration was 8.5 g/dl, the total white cell count 2.6 x 10⁹/l, the platelet count 62 x 10⁹/l and the ESR 135 mm/1st h (Westergren); the differential count showed 18% neutrophils, 10% band forms, 1% myelocytes, 2% monocytes and 69% lymphocytes. Bone marrow aspiration was unsuccessful in obtaining particles, but a 3 cm trephine biopsy specimen (Fig. 1) showed a diffuse lymphocytic infiltration associated with a marked increase in reticulin fibres (Fig. 2) and mature collagen. Residual haematopoietic tissue was approximately 10% of normal. The marrow was considered to be involved by small-cell malignant lymphoma with associated diffuse fibrosis, and a lymph node biopsy was requested.

Clinical reassessment failed to show any lymph nodes suitable for biopsy, and in view of the pancytopenia with the diagnosis of stage IV disease due to bone marrow involvement by malignant lymphoma, the patient was started on a regimen of bleomycin 30 mg and vincristine 2 mg weekly, and prednisone 30 mg/d orally for 6 weeks. He remained well, requiring repeated blood transfusions, but his pancytopenia was refractory to therapy. During the 6-week period the spleen size increased from 4 to 15 cm below the left costal margin.

The diagnosis was reviewed since it would be unusual in our experience for patients with a malignant lymphoma of this cytological type to not respond, at least initially, to combination cytotoxic chemotherapy, and it was equally unusual for the spleen to increase in size during treatment. It was decided to remove the spleen to exclude the possibility that the lymphoma had undergone initial transformation in this organ, and the same time to reduce any contribution that the splenomegaly
might make to the persisting pancytopenia and the increasing need for blood transfusions. Concern that a diagnostic error may have been made arose with the demonstration of occasional mononuclear cells (Fig. 3) in the blood, having ragged cytoplasm, very weak reaction for surface immunoglobulin and the presence of tartrate-resistant acid phosphatase. Peripheral blood and buffy layers showed hairy cells when examined by electron microscopy (Fig. 4).

The diagnosis was revised to that of leukaemic reticuloendotheliosis, and the patient underwent successful splenectomy 18 months after presentation. Histological, cytochemical and ultrastructural examinations confirmed the diagnostic features in the spleen (Fig. 5). The response to the operation was satisfactory, the platelet count rising and remaining over 200 x 10^9/l, the haemoglobin concentration being above 13 g/dl without any need for transfusions, and the white cell count being 6 x 10^9/l. The persistent abnormality is that of a peripheral blood lymphocytosis, accounting for 70% of the cells and a monocytopenia of 2%.

Discussion

Hairy cell leukaemia or leukaemic reticuloendotheliosis is an unusual lymphoproliferative disorder, and was probably best described in 1958. The name is derived from the presence of abnormal mononuclear cells with exaggerated cytoplasmic processes in the peripheral blood. Although uncommon, the importance of correct clinical diagnosis is that splenectomy rather than radiotherapy or chemotherapy is the optimal form of treatment.

The confusion that may arise between the diagnosis of this entity and that of a malignant B-cell lymphoproliferative disorder with massive splenomegaly, both having inconspicuous lymphadenopathy, pancytopenia, and circulating atypical lymphoid cells, is exemplified by the present case. However, a number of contrasting points exist and emphasize the need for examination of a lymph node or the spleen if the correct diagnosis and appropriate management are to be achieved. The average age in patients with leukaemic reticuloendotheliosis is 50, with the male/female ratio being 4:1, whereas in the B-cell disorders the average age is 66 and the male/female ratio is 1:4.
We give excellent and long-lasting results. Splenectomy is useful in patients who have marked hypersplenism and may greatly improve the quality of life. Over long periods of time spontaneous remissions have been reported, whereas transition to other forms of leukaemia or lymphoma has not.

Two further points are of interest. In patients with B-cell lymphoproliferative disorders surface membrane immunoglobulin markers will usually give a clear reaction, while in leukaemic reticuloendotheliosis fluorescence is either weak or absent and is not clonal. Second, infections occur frequently in patients with leukaemic reticuloendotheliosis and well-marked disturbances have been demonstrated in lymphocyte function.

Our case is a further illustration of the similarity that exists between leukaemic reticuloendotheliosis and a B-cell lymphoma with massive splenomegaly. The features that the two entities share can give rise to diagnostic difficulty which has, in part, contributed to the concept that hairy cell leukaemia is not homogeneous because cellular characterization, natural history and response to therapy are not necessarily invariable. This confusion can be diminished if the differences between similar clinical syndromes are appreciated and attention paid to the trephine biopsy specimen, lymph nodes and histological findings in the spleen, as well as routine light microscopic, cytochemical and ultrastructural findings. The distinction between the two conditions is of more than just academic interest since it has important therapeutic implications for the patient. Those with proven malignant lymphoma can be treated with chemotherapy in anticipation of their having, at least initially, a good response. In contrast, leukaemic reticuloendotheliosis is best managed with splenectomy, and, at least in the early stages, chemotherapy may shorten the patient’s survival period.

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