HAIRY CELL LEUKEMIA — A RARE CHRONIC LYMPHOPROLIFERATIVE DISORDER

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SYNOPSIS

A 65-year-old Indian man presented with pancytopenia and an enlarged spleen. Peripheral blood and bone marrow examination, including special cytochemistry, showed relative lymphocytosis and the present of typical 'hairy cells'. The clinical features and treatment of this patient with hairy cell leukemia are discussed.

INTRODUCTION

Hairy cell leukemia (HCL) is a rare chronic lymphoproliferative disease characterised by the presence, in the peripheral blood, bone marrow and other tissues, of abnormal mononuclear cells with irregular cytoplasmic projections. The disease accounts for less than 2% of all adult leukemias in most countries and has not previously been reported in this region. It occurs predominantly in middle-aged men. The diagnosis is suspected in the presence of pancytopenia, splenomegaly, recurrent opportunistic life-threatening infections and an absence of lymphadenopathy. We report here the clinical details of a recently diagnosed patient with HCL and discuss the treatment of this disorder.

CASE REPORT

A 65-year-old retired male Indian auditor presented to the National University Hospital with lethargy and malaise two weeks after recovering from an influenza-like illness. He complained of mild anorexia with some loss of weight, but he had no other symptoms. He had been treated for typhoid fever and malaria about 50 years earlier.

On admission his full blood count showed pancytopenia with a hemoglobin concentration of 11.5 g/dl; a total leucocyte count of 2.8 x 10^9/1 (differential count: polymorphs 22%, lymphocytes 72%, monocytes 6%); and a platelet count of 86 x 10^9/1. Careful examination of the lymphocyte population in the peripheral blood film showed that 11% of the mononuclear cells had cytoplasmic projections and slightly indented nucleus, that is typical hairy cells (Figure 1). A bone marrow aspirate and trephine biopsy showed a cellular marrow with diffuse infiltration by similar monocytoid cells (15%) showing the typical features of hairy cells. These cells also demonstrated tartrate — resistant acid phosphatase (TRAP) activity, a distinctive feature of hairy cells (Figure 2). There was increased deposition of reticulin around these cells in the bone marrow trephine. A computed tomographic scan of the abdomen confirmed the splenomegaly, with no evidence of mass lesions and the absence of significant para-aortic or mesenteric lymphadenopathy. The diagnosis of hairy cell leukemia was thus established. The patient was started on recombinant alpha-2b-interferon 3 million units, subcutaneously three times per week, but it is too early, as yet, to gauge his response to treatment.

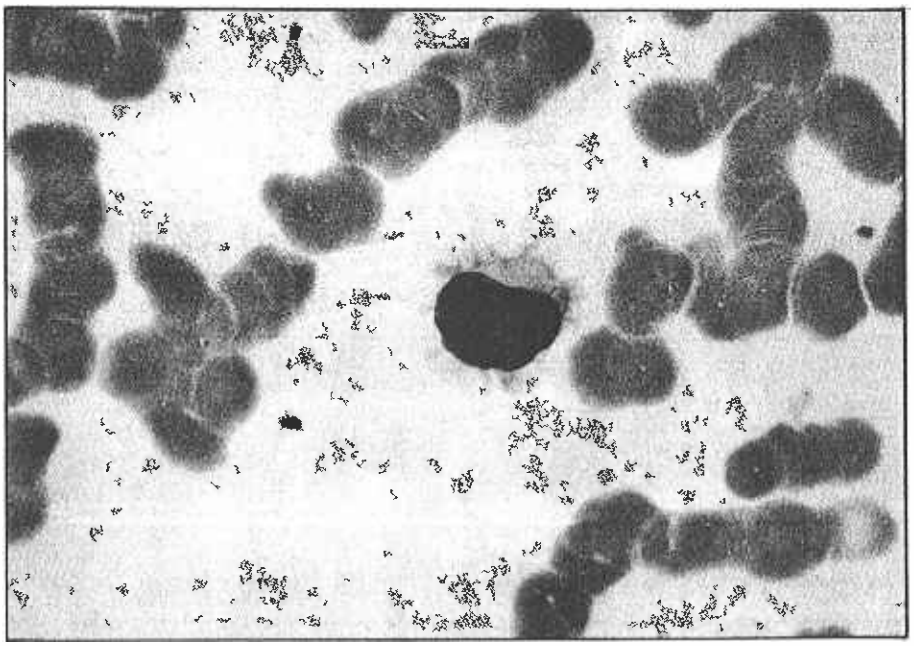

Figure 1. Light microscopy of a typical hairy cell from the peripheral blood of the patient.

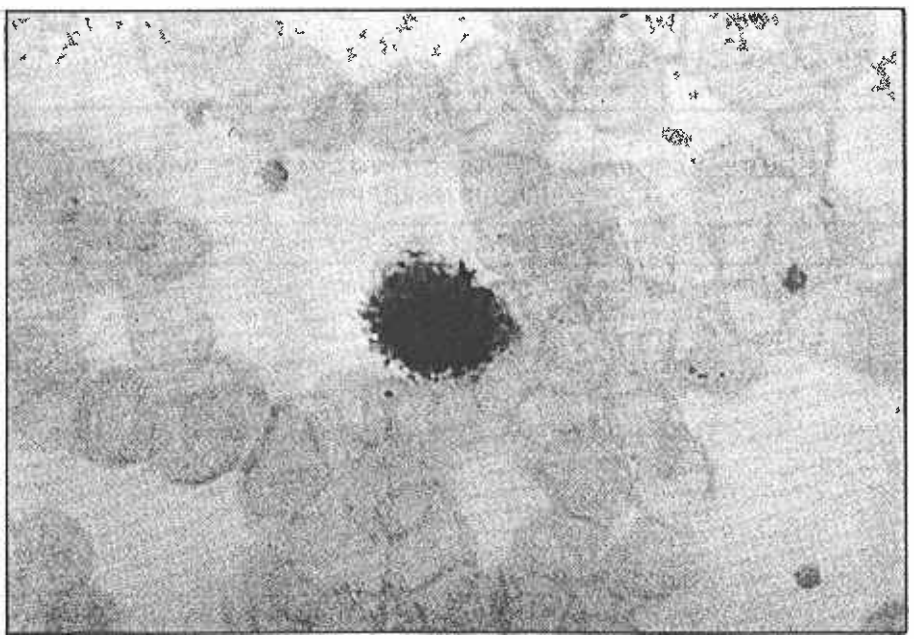

Figure 2. Tartaric-resistant acid phosphatase (TRAP) positivity demonstrated in the hairy cell.

DISCUSSION

Hairy cell leukemia was first described as a distinct clinical entity by Bourancle et al. in 1958 (1). The aetiology of this rare disease is still not clear, although recently the HTLV II retrovirus was isolated from a patient with the T-cell variant of HCL (2). The clinical presentation of our patient is fairly typical of HCL. The clinical characteristics observed in 4 large series are summarized in Table I (3). The age of the patients ranged from 22 to 89 years, with an average age in the early fifties. The male to female sex ratio was approximately 4:1. Non-specific complaints, usually recent infection was sometimes reported. The most striking finding on physical examination was splenomegaly, with minimal or absent hepatomegaly or lymphadenopathy.

At the time of diagnosis, 60 to 70% of patients with HCL have pancytopenia. The haematological findings in 44 patients with no previous treatment are shown in Table 2 (3). The percentage of hairy cells in the peripheral blood varied from 2 to 88% (4).

Hairy cells are white blood cells characterized by the presence of prominent cytoplasmic villi, tartrate-resistant acid phosphatase activity, and inducible phagocytic properties. The lineage derivation of the hairy cell has been the subject of great controversy, and only recently has it been established generally to be of B cell lineage by studies with monoclonal antibody and immunoglobulin gene rearrangement studies. Tumours comprising hairy cells appear to correspond to preplasma cell tumours (5). There is infiltration of the spleen and bone marrow by hairy cells and this leads to pancytopenia by two concurrent mechanisms, i.e. hypersplenism and bone marrow failure secondary to marrow replacement.

Splenectomy has been advocated as the first line treatment of choice, as it corrects the pancytopenia in most patients and improves survival when the spleen is enlarged more than 4 cm below the left costal margin. In a large retrospective multicentre study (6), 225 patients who had undergone splenectomy were compared with 166 non-splenectomized patients. Survival after diagnosis was significantly longer in the splenec-

TABLE 1: CLINICAL CHARACTERISTICS OF HAIRY CELL LEUKAEMIA* (3)

	Golomb et al	Cawley et al	Bouroncle	Jansen et al
Mean age (years)	NP	51	54	52
Youngest/oldest (years)	22/79	NP	22/76	22/89
Sex ratio (M:F)	3.7	3.8	4.5	3.4
Symptoms:†				
Recent infections	38	28	17	NP
Tendency to hemorrhage	34	18	9	NP
Abdominal discomfort	24	10	14	NP
Weakness, weight loss	NP	75	51	NP
Physical findings:*				
Splenomegaly	83	84	93	82
Adenopathy	38	24	23	19
Hepatomegaly	19	40	40	49
Skin rash	14	5	6	NP

† Four large series NP, not published.
* Expressed as the percentage of all patients with symptoms.

TABLE 2: LABORATORY FINDINGS IN 44 PATIENTS WITHOUT PREVIOUS THERAPY*

WBC		PLATELETS		HEMOGLOBIN	
Count ($\times 10^9/l$)	Prevalence (%)	Count ($\times 10^9/l$)	Prevalence (%)	g/dl	Prevalence (%)
$<$ 3	45	$<$ 25	7	3 — 5.9	7
3 — 5	17	25 — 50	14	6 — 8.9	32
5 — 10	17	50 — 100	36	9 — 11.9	43
10 — 25	19	100 — 200	39	12 — 14.9	11
$>$ 25	2	$>$ 200	4	$\geq$ 15	7

* Modified from Golomb et al (3)

tomised group (actuarial survival of 65% at 5 years) in contrast to the non-splenectomized group, if the patients were older than 60 years, if the duration of symptoms were longer than 12 months, if the spleen was enlarged less than 4 cm below the costal margin, or if the haemoglobin level was greater than 12 g/dl, neutrophils greater than $0.5 \times 10^9/1$ and platelets greater than $100 \times 10^9/1$. Splenectomy alone rarely induces complete remission from the disease and disease progression may require institution of cytotoxic therapy. Single agent therapy with chlorambucil, or combination chemotherapy (e.g. CHOP) have been used, with limited success.

New cytotoxic agents are now available for those patients who would not benefit from splenectomy or in whom splenectomy has had short-term benefits only. Prolonged treatment with intramuscular or subcutaneous recombinant alpha interferon appears to be the treatment of choice, leading to normalization of blood counts in most patients after three to six months' treatment, and perhaps to complete remission with treatment lasting more than a year (7). Alternatively, treatment with low dose pentostatin (2'-deoxycoformycin) has been shown to induce complete remission with relatively minor side effects (8). However, its place in the treatment of hairy cell leukaemia has yet to be defined. These drugs may displace splenectomy as the first line treatment in this disease.

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