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HAIRY CELL LEUKEMIA: A REVERSIBLE DISEASE? A REPORT OF TWO CASES OF SPONTANEOUS REMISSION

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Hairy cell leukemia (HCL) is an uncommon type of leukemia, first described by Bouroncle as « leukemic reticuloendotheliosis »[1], which has been intensively studied in recent years. Most Authors consider it a B-lymphoproliferative disorder[1 2 4 9 15].

The disease has quite a variable course and there is no established form of treatment. Splenectomy has been reported to be the therapy of choice, whereas the effectiveness of other therapeutic approaches (rubidazone, chlorambucil, pentostatin, alpha-interferon, leukapheresis, etc.) is still debated.

Remission following splenectomy alone have been reported by some Authors[2 14]. Moreover, in a series of 82 patients, Bouroncle[1] observed one case of spontaneous remission without any treatment at all.

Between 1967 and 1979 we observed 56 cases of HCL. Twenty patients are still alive and five of them are in good health over ten years after diagnosis. Two out of these five patients never received any specific treatment (including splenectomy). The aim of this brief comunication is to report these two cases of spontaneous remission in HCL.

CASE REPORT

Case 1 - *53-year-old male.* This patient experienced several episodes of upper respiratory tract infections during his early years. Since the age of thirty he attempted periodic anti-inflammatory treatments for rheumatic pains but he never recovered completely. In 1967 he was hospitalized for severe weakness, pallor and persistent headache. He was found to have marked anemia, leukopenia, liver and spleen enlargement. The bone marrow was nearly inaspirable: among the few cells obtained a significant number of atypical lymphoid elements with characteristic hairy-like cytoplasmic projections was detected (Fig. 1a). Surgical bone marrow biopsy revealed massive replacement by a population of the same type of cells and a diffuse stromal reaction with large amounts of reticulin (Fig. 1b, 1c). This condition was diagnosed as « lymphoid myelofibrosis » after Duhamel (successively confirmed as typical HCL) and the patient was treated with blood transfusions, androgens and prednisone at low doses (0.1-0.3 mg/kg/die) for his moderate thrombocytopenia. In the following three years he had several hospital admissions due to recurrent infections, such as bronchitis, cystitis and cholecystitis, and to persistent mild anemia. Afterwards, he showed progressive reduction of the hepatosplenomegaly and an improvement of the haematologic picture so that no further treatment was given. Subsequently the patient resumed work and was followed up with periodic blood counts. In 1980 he underwent transurethral prostatectomy for prostatic hypertrophy. In December 1983 the patient was admitted for a re-evaluation of the case. Spleen and liver were no longer palpable; a trephine bone marrow biopsy revealed complete disappearance of lymphoid replacement and absence of fibrosis (Fig. 1d). In December 1984 he was still doing well without treatment 17 years after the diagnosis of HCL.

The results of the tests performed at onset and at the reappraisal time are shown in Table I.

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KEY WORDS: Hairy cell leukemia, spontaneous remission, interferon.

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TABLE I.
Clinical and haematological features in two cases of spontaneous remission.

	Case 1		Case 2	
	1967	1983	1971	1983
Hb (g/dl)	6.4	15.9	8.2	17.3
WBC ($\times 10^3$/l)	1.0	4.7	1.0.	4.6
Neutrophil count ($\times 10^9$/l)	0.38	3.66	0.22	2.62
Hairy cell count ($\times 10^9$/l)	0.01	0	0.24	0
Platelet count ($\times 10^9$/l)	44.0	180.0	80.0	143.0
Bone marrow §	80	0	90	10
Spleen *	6.0	0	12.0	0
Liver *	2.0	0	6.0	0

§ percentage of hairy cell i,nfiltration.
* centimetres below costal margin.

Case 2 - 61-year-old male - This patient has been treated for peptic ulcer for a total of above ten years since 1940. He was well until 1971 when he was hospitalized for dyspnea and pain in the upper left quadrant of the abdomen; the admission was preceeded by fatigue, pallor and a persistent mild fever. The blood counts revealed pancytopenia with a significant percentage (24% at the differential) of atypical lymphoid cells with thin cytoplasmic projections. The bone marrow aspiration showed quite a number of such atypical cells (Fig. 2a); bone marrow trephine biopsy indicated an almost complete replacement by the same cell population and a marked increase of the reti-

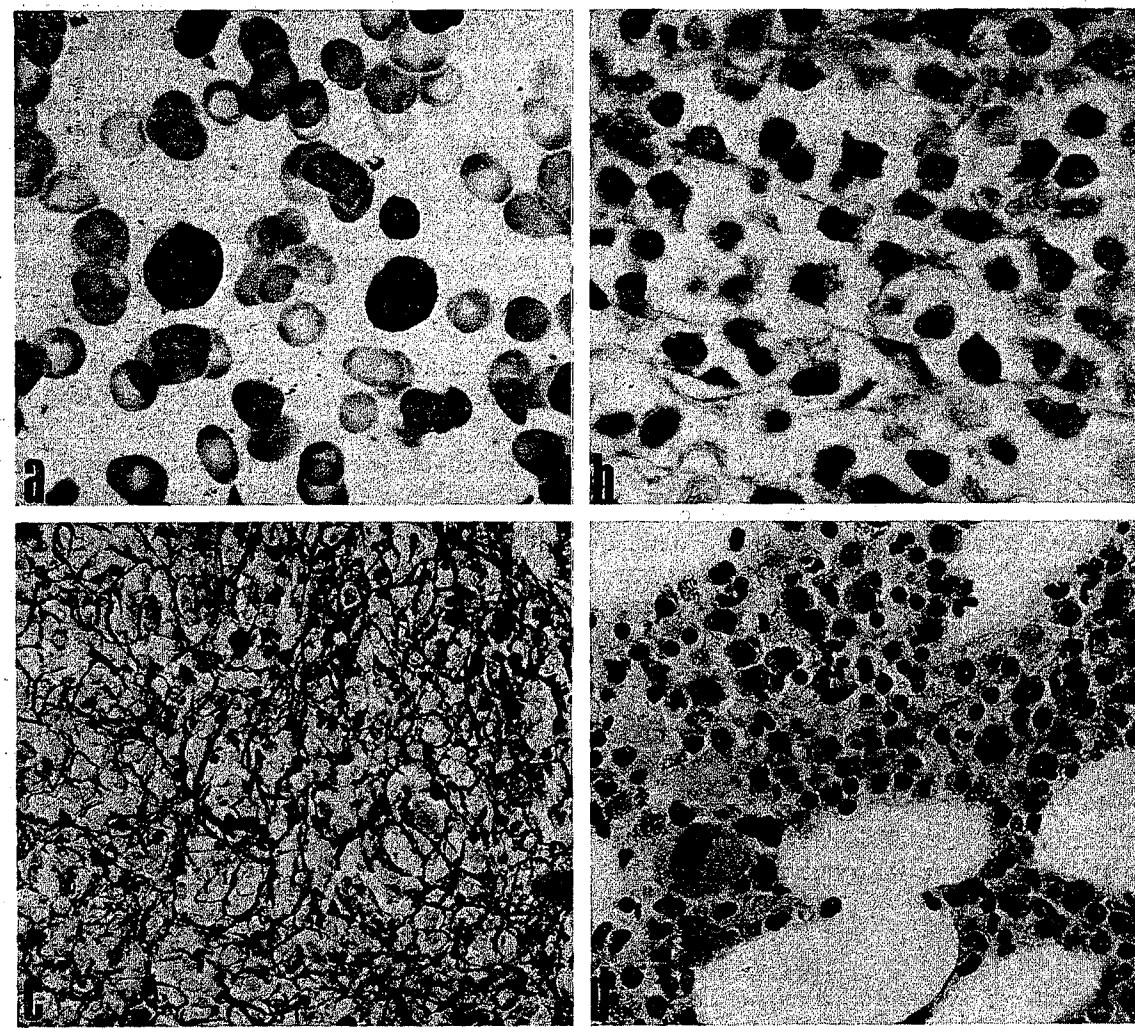

Fig. 1.
Case 1. a) Bone marrow aspiration (onset, 1967): two typical hairy cells. MGG, 630×. b) Bone marrow surgical biopsy (1967): neoplastic mononuclear cells with hairy-like cytoplasmic projections. Some of them show a bilobed nuclear shape, HE, 630X. c) Bone marrow surgical biopsy (1967): slightly condensed reticulin network. Gomori, 250X. d) Bone marrow trephine biopsy (1983): normal appearance of myelopoiesis. HE, 400X.

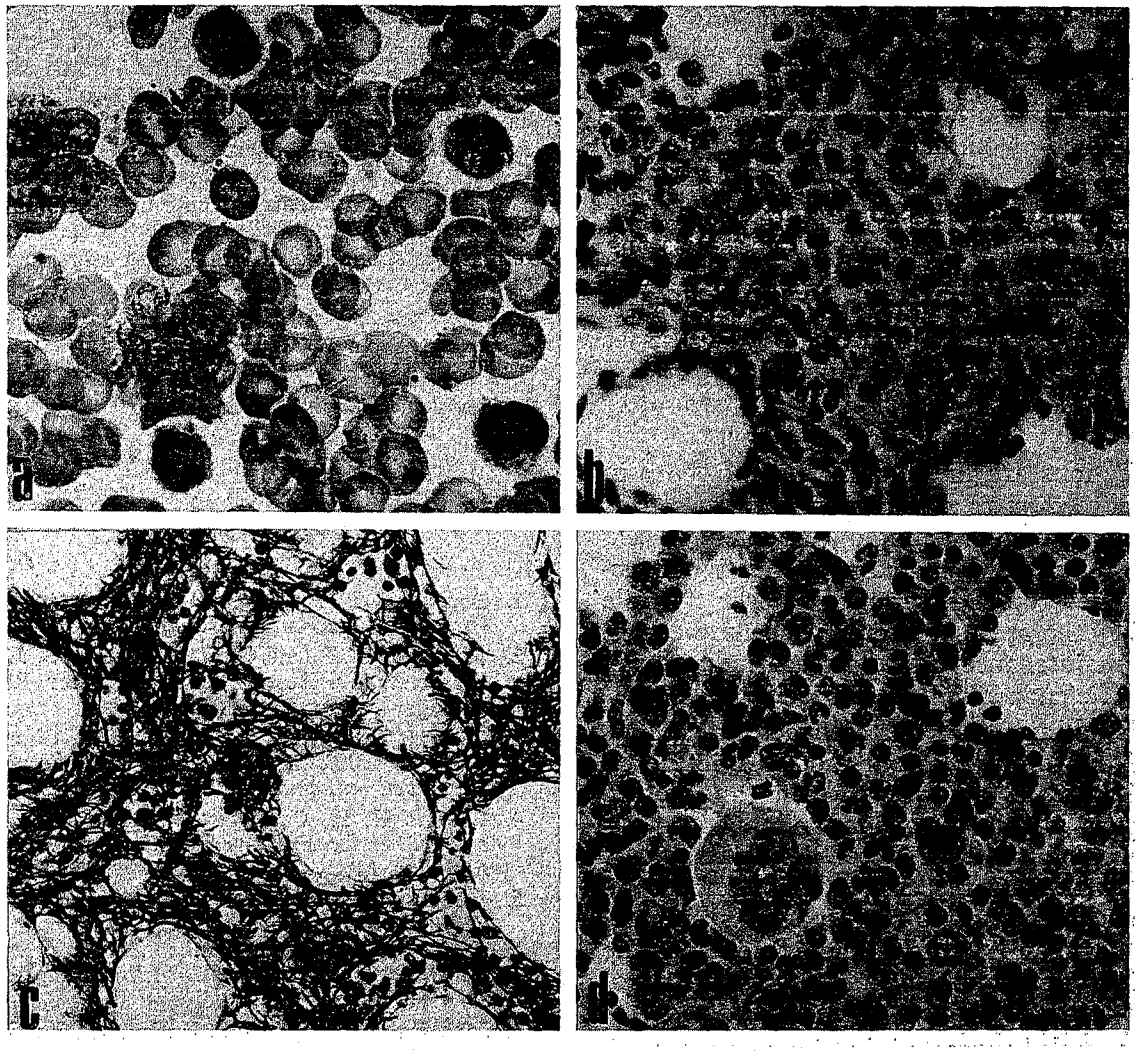

Fig. 2.

Case 2. a) Bone marrow aspiration (onset, 1971): four typical hairy cells. MGG, 630X. b) Bone marrow trephine biopsy (1971): monomorphic, loose infiltration of mononuclear cells. HE, 400X. c) Bone marrow trephine biopsy (1971): a strongly condensed reticulin network is present in the haemopoietic cords. Gomori, 250X. d) Bone marrow trephine biopsy (1983): re-expansion of normal haemopoiesis. HE, 400X.

culin network (Fig. 2b, c). The physical examination revealed extreme liver and spleen enlargement; lymph nodes were not palpable. A diagnosis of « leukemic reticuloendotheliosis » was made (also this case was subsequently confirmed as typical HCL). The patient was treated with steroids (0.2-0.3 mg/kg/die), antibiotics and blood transfusions. In the following two years he received transfusions at intervals for a moderate anemia.

Afterwards, he had four hospital admissions for severe infections (erysipelas, pleuritis, bronchopulmonary infections) which regressed with antibiotic therapy. Subsequently, his physical and haematologic conditions slowly improved, the splenomegaly disappeared and he received no further specific treatment. A group of laboratory tests (performed once a year) displayed progressive return to normal rates.

A trephine bone marrow biopsy, performed in December 1983, revealed a sharp reduction in hairy cell infiltration with reversal of marrow fibrosis (Fig. 2d). The patient was still in good health in December 1984, 13 years after the diagnosis of HCL. The clinical and haematologic features at onset and at the follow-up are summarized on Table I.

Discussion

HCL shows, in the majority of cases, a chronic progression. Most deaths occur within 36

months of diagnosis regardless of any therapeutic approach [2 16]. Some Authors have suggested that patients surviving more than three years from diagnosis have an overall life expectancy which is similar to a normal control group [13 16].

HCL, usually after splenectomy, may display prolonged clinical and haematologic remissions, even if quite a number of hairy cells is still present in the bone marrow. To this regard, Westbrook, Groopman and Golde [17], in a series of 31 cases, reported four patients alive and in good health with their disease ten years after diagnosis.

Infections are the major cause of death in HCL; according to some investigators [3 6 11] this could be actually attributed to a defect in cell-mediated immunity, including ineffective monocyte or neutrophil function. However the role played by therapy (splenectomy, chemotherapy) in the maintenance of the disease induced immunodeficiency is still undefined.

It is not easy to give a satisfactory explanation of the favourable course of HCL in the reported cases. In fact the treatment (antibiotics, androgens, blood transfusions and low-dose corticosteroids) unlikely affected the leukemic clone anyway. Similar occasional spontaneous remissions in low grade non-Hodgkin's lymphomas other than HCL [10] and in chronic idiopathic myelofibrosis (even including regression of marrow fibrosis) have also been reported [8].

Bouroncle [1] suggested that improvement might be correlated with successfully treated infections. In fact, both of our patients experienced recurrent infections during the progress of the disease (as in the majority of cases of HCL).

Could infections sometimes activate an immune response against leukemia? Viral infections may be accompanied by production and release of Interferon which has been shown to produce complete remission in HCL [5 7 12]. Thus, if patients survive the infections they might benefit by Interferon and obtain a remission of the underlying disease.

HAIRY CELL LEUKEMIA: UNA MALATTIA REVERSIBILE? SEGNALAZIONE DI DUE CASI DI REMISSIONE SPONTANEA

Vengono riportati due casi di remissione spontanea in corso di Hairy cell leukemia (HCL). Entrambi i pazienti hanno presentato all'esordio un quadro clinico simile: grave pancitopenia e marcata splenomegalia. Il decorso della malattia è stato contrassegnato da frequenti episodi infettivi risoltisi con antibiotico-terapia. Nessun altro trattamento, come, ad es., splenectomia o chemioterapia antiblastica, fu instaurato. I pazienti sono tuttora vivi ed in buona salute a distanza rispettivamente di 17 e 13 anni dalla diagnosi. A quanto ci risulta finora solo un caso di remissione spontanea di HCL è stato segnalato in letteratura.

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