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Hairycellleukemia About a Case

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Abstract

Hairy cell leukaemia is a rare chronic lymph proliferative disorder characterized by the absence of peripheral lymphadenopathy and the presence of isolated splenomegaly in 75% of cases. The patients are most often neutropenic and monocytopenic and the evolution is dominated by the infectious risk in the untreated subjects. Diagnosis is made by evidence of diffuse infiltration of the spleen and bone marrow by lymphoid B cells: hairy cells. These are particular cells by their hairy appearance with extension towards the peripheral blood. Treatment is by cladribine first, but several other molecules are recommended. Splenectomise remains a last resort with special and limited indications. We report the case of a 35-year-old patient, whose diagnosis was difficult because of the absence of neutropenia and monocytopenia at the beginning of the pathology, as well as inconclusive reports of blood smear and sternal puncture due to non-characteristic morphological appearance of tumour cells. It is the osteomedullary biopsy that guided the diagnosis, which will be confirmed after histological study of the spleen. The management was complicated by clinical-biological worsening even with interferon Alfa treatment, hence the indication for splenectomise, which is rarely performed in hairy cell leukaemia today.

Keywords : Tricoleucocyte leukaemia, hairy cells, splenomegaly, splenectomise

Introduction

Hairy cell leukemia (HCL) is a rare malignant disease of mature B cells, classified as indolent (non-malignant) non-Hodgkin's lymphoma, and more frequently observed in humans starting in the fifth decade[1,2].It is revealed by an alteration of the general state, a very frequent voluminous splenomegaly and also frequently pancytopenia with neutropenia and monocytopenia associated with anemia and thrombocytopenia [3]. The diagnosis is based on the identification of the tumor cells: the hairy cells (HC) in the blood, the marrow and / or the spleen

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[2,4]. these cells are B-hairy lymphoid not expressing the CD5 membrane molecule but expressing CD11c, CD19, CD20, CD22, CD25, CD103, DBA-44 and CD123[1]. There are no specific clonally and recurrent chromosomal abnormalities [1,2].
However, the diagnosis of HC sometimes pose difficulties: the morphology of HC is not always characteristic, the blood cell tumor sample is in low percentage, the bone marrow samples difficult to achieve by the presence of myelofibrosis [1].

OBSERVATION

This is a 35-year-old patient with no notable pathological history who consulted a gastroenterologist for asthenia with pain in the left hypochondria 5 years ago.
During the interrogation, an alteration of the general state and a weight loss of 5 kg in the year were found.
Clinical examination showed splenomegaly 5 cm from the costal margin without hepatomegaly or lymphadenopathy.
A Complete Blood Count (CBC) showed the following results:
Hemoglobin (Hb) 10.2 g / dL; MCV fl 90; MCHC 32%; leukocytes: 4.60 G / L; platelets 124 G / L; reticulocytes 74.5 G / L (N 25-90).The leukocyte formula showed: 34% PNN, 58% lymphocytes, 6% monocytes and 1% eosinophils.
The patient is then sent to the hematology department where he was hospitalized for the management of bicytopenia with splenomegaly.
The blood test showed: absence of inflammatory syndrome with CRP <3 (N 0-5); ESR: 26 mm (N, 0-15); also absence of hemolytic: total bilirubin, LDH, haptoglobin were normal. Serum total protein : 74 g / L with normal electrophoresis. Hepatic, renal and thyroid blood test were normal. Antinuclear auto antibodies were negative.
A blood smear was performed and found morphologically atypical lymphocytes with rare circulating erythroblasts.
A bone marrow study was indicated but could not be performed and the patient was lost to follow-up.
Hematology consultation 2 years later found enlarged splenomegaly with pancytopenia and monocytosis
The blood smear showed a 45% peripheral invasion by atypical lymphoid cells with sometimes a round nucleus, sometimes a deiform nucleus, an irregular chromatin, a clear cytoplasm with a poorly defined outline. The appearance was not specific but the lymphoid population was monomorphic suggestive of a lymphoproliferative syndrome.
A sternal puncture made found a diluted medullar specimen but confirmed the lymphoproliferative syndrome with 52% medullar invasion by the same lymphoid elements found at the level of the peripheral blood suspecting HC.
The assessment was then completed by the osteomedullary biopsy showing diffuse medullar infiltration by large B-type lymphocytes with rounded nucleus and clear cytoplasm, without condensation of the reticulinic bundle, which had allowed, with the clinical data, to guide the diagnosis to lymph proliferative B syndrome with strong suspicion of HC.

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Immunophenotyping was not as helpful, showed atypical circulating lymphoid elements with immunologic profile: CD20 +; CD5 -; CD10-; CD79b-.
The diagnosis of leukemia with tricholeukocyte being retained, treatment with cladribine continuous 5-day intravenous treatment has been prescribed. But the patient was again lost sight of.
Hospitalization Oncology done after 3 years for chemotherapy called for a review of clinical and biological data which showed a renewed increase in the size of spleen arriving at the umbilicus and CBC: Hb 9.1 g / dL ;MCV fl 84; MCHC 31%; leukocytes: 1.94 G / L; platelets 48 G / L; leukocyte formula: PNN(18.6%), lymphocytes (66.9%), monocots (13.1%) and eosinophilic PN(1.4%).
Treatment with interferon alfa was started because of the worsening of the clinical state and the lack of means of the patient, with the protocol of 3 injections a week. After 6 weeks, a reassessment made in the face of the clinical aggravation reported by the patient and the appearance of an infectious syndrome, found a further increase in the size of the spleen became gigantic occupying almost the entire abdomen and driving the rest organs (confirmed on abdominal ultrasound) even under treatment, with aggravation of pancytopenia.
Blood smear: presence of HC at 70% (Figure 1, 2).
A medical staff asked for a splenectomy that was performed urgently because of the risk of splenic rupture. CBC done 3 days after the procedure: Hb 10.8 g / dL; MCV 80 fl; MCHC 32.3%; leukocytes: 5.8 G / L; platelets 76 G / L; leukocyte formula: PNN (82.2%), lymphocytes(12.4%),monocots (5.2%) and eosinophilic PN(0.2%).
Blood smear Presence of rare HC with many circulating erythroblasts.
The patient died on D5 post-operatively following hyperkalemia.
The operative specimen was a huge spleen that was 28/18/9 cm, and 2.7Kg in weight.
The anatomopathological study of this part revealed a massive invasion of the spleen by a low-grade lymphomatous temporal process composed of lymphoid cells with small round nuclei, weakly nucleated, with light scant cytoplasm. This proliferation colonizes the sinuses of the red pulp without persistence of white pulp. Reticulum staining revealed discrete fibrosis. This aspect was compatible with HC (Figures 5, 6).

DISCUSSION

HC leukemia (HCL) is a rare malignant pathology of mature B cells, accounting for 2% of all leukemia's [1, 2, 5]. The median age at the time of diagnosis between 50 and 55 [1]. Men are affected four to five times more often than women [1, 2].
Our patient was 35 years old, this young age of the disease is described in the literature but rare.
The classic HCT develops extremely slowly, in 15% of cases are diagnosed following a routine blood count [1,4,7]. The most common symptoms are fatigue, left hypochondria pain, fever and bleeding [2, 4, 8]. Splenomegaly is the most common sign, we can also see hepatomegaly, repeated infections. rarely are vacuities, haemorrhagic syndrome, neurological disorders, bone invasion or immune disorders [8,9].

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The biological assessment of HCT begins with the hologram, which shows pancytopenia, sometimes only neutropenia. The presence of monocytopenia contrasts with the analysis of automata that identify tricoleukocytes(TL) as monocots, thrombocytopenia or anemia often slightly macrocytic (unusual anemia at diagnosis, is due to significant fibrosis) [2, 4, 9]. Careful examination of the blood smear can identify the presence ofTL, even if the number of abnormal cells can be very rare [2, 4]. These are large cells with an extensive, weakly and irregularly basophilic cytoplasm with fine cytoplasm projections. cytoplasm inclusions "Granulo-lamellar"with the appearance of discrete basophilic rods with a clear central area are sometimes detected. The nucleo-cytoplasmic ratio is low and the core often off-center oval or rounded, it can be sometimes deiform. Nuclear chromatin has a finely dispersed appearance and the nucleolus with little or no visible appearance is small and often unique. It can contain many micro vacuoles [1, 2, 4].
In 10% of cases, there is a leukocytosis greater than 10 G / L, consisting essentially of TL [9].
The positivity of these cells for tartrate-resistant acid phosphatase confirms the diagnosis, but cytochemistry is no longer practiced in favor of immunophenotyping [2,9].
Medullar involvement is constant with more or less infiltration by tumor cells [1,7].
For our patient, the TL was found in the blood smear at an advanced stage of the disease.
The osteomedullary biopsy (OMB) shows a constant densification of the reticulinic network and a diffuse cellular infiltration with variable conservation of zones of hematopoietic. On section, the TL are rather characteristic by a clear and extensive cytoplasm, spacing the nuclei and giving the cut a clear appearance very different from the infiltration present in the other chronic lymphoid hemopathies.The TL are labeled with the DBA44 antibody [2, 4, 9].
In our situation, the OMB was not conclusive, but the association with the clinical picture the diagnosis of HCL seemed the most obvious.
The splendid involvement in HCL is characterized by the presence of an infiltration of the red pulp, with deletion of the white pulp, formation of splendid pseudo-sinuses with enlargement of the pulp cords. Splenectomy is not justified to assert the diagnosis of HCL; The splendid homing of tumor cells can be explained by the interactions of vitronectin with the αVβ3 receptor [2,10].
It is the pathological study of the operative specimen after splenectomy for our patient that confirmed the diagnosis with certainty.

Immunophenotyping shows that TLs are mature B cells, expressing surface immunoglobulin's (IgG3), CD19, CD20 (moderate to strong expression), CD22 (strong expression) and CD79b, but do not express CD5 molecule or CD23 and CD24 molecules. The expression of CD27 a memory B cell marker, is negative. The expression of CD10 is positive in 10% of cases [2,11]. The expression of CD11c is strong and CD25 (IL2-R) moderate to intense, with a characteristic positivity of CD103, DBA44 / CD72 (used in histology), and CD123.The most specific marker is annexing a1 which is characteristic of LT (also used in histology) [11]. TL do not express BCL6 germinal center marker, or CD38 [12].An immunological score, such as the Matte score used in chronic lymphocytic leukemia (CLL), was developed for the diagnosis of LT. This score is based on the expression of four markers: CD103, CD11c, CD25 and CD123.A point is given for a positive expression and 0 points for a negative expression. Ninety-eight percent of HCL cases

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have a score of 3 or 4, in contrast to the variant form of LT or villous lymphocyte splendid lymphoma (SLVL) where the score is usually 0 or 1 [11, 12].
The immunological study of blood tumor cells for our patient was incomplete and inconclusive. But allowed us, with the histological aspect, to confirm the B character of the lymphoid proliferation and to eliminate the CD3 + and / or CD5 + and / or CD10 + and / or CD79b + lymphomas that could pose a differential diagnosis with the HCL in our case.
The cerotype does not reveal specific abnormalities. It is not practiced [1, 2].
Apart from treatment, the general condition of patients with HCL is fairly well preserved except in case of complications. The media survivalist 52 months [7].
Complications of HCL are: progressive amplification of bone marrow failure with worsening of neutropenia, thrombocytopenia and anemia, which may be due in part to splendid sequestration [13]. Infections are the most common and serious complications responsible for the majority of deaths [7,14]. Haemorrhage is directly related to the severity of thrombocytopenia [7]. The increased incidence of solid or hematopoietic secondary tumors (2.5 to 10% according to the series of the literature) [6,7].
Other complications more rarely: Vacuities lesions, osteolytic lesions, splendid rupture [7,8].Before 1984, the only treatment for HCL was splenectomy. Currently, it is no longer regularly indicated except in very rare cases where the patient presents from the start a very large splenomegaly and a deep pancytopenia and patients who are refractory to treatments by purine analogues or patients whose diagnosis is doubtful [2, 5].
Interferon alpha is a historical treatment, now replaced by purine analogues.

CONCLUSION

This observation allowed us to review the diagnosis and management of HCL in its usual form, which may pose come problems by atypical clinical, biological or immunehistological signs or by the way of evolution or inappropriate treatment response.
We can deduce that circulating TLs are difficult to identify, we must know how to think about them in any bi or pancytopenia, especially when there is a monocytopenia. Monocytopenia may not appear if TLs are confused with monocytes and may be missing in early forms, so the laboratory must thoroughly examine the blood smear before performing sterna puncture or OMB because the diagnosis of TL leukemia is now on the examination of the blood smear confirmed by immunophenotyping including markers CD25 and CD103 which are added to the panel at the request of the cytologist.

Conflicts of interest:
The authors do not declare any conflict of interest

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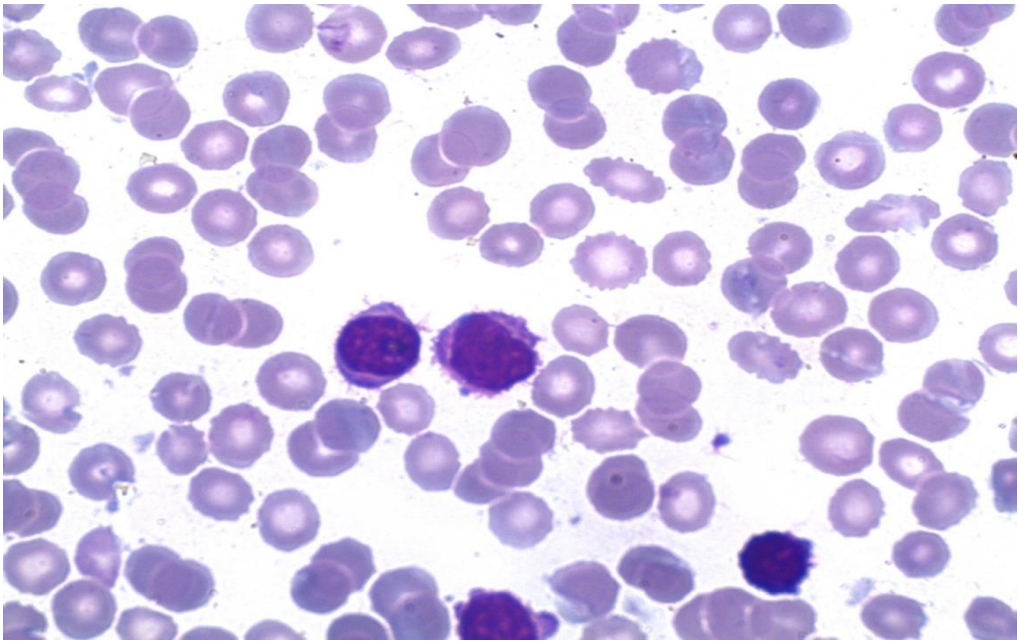

Figure 1: Blood smear stained with MGG showing hairy cells (MHA hematology laboratory)

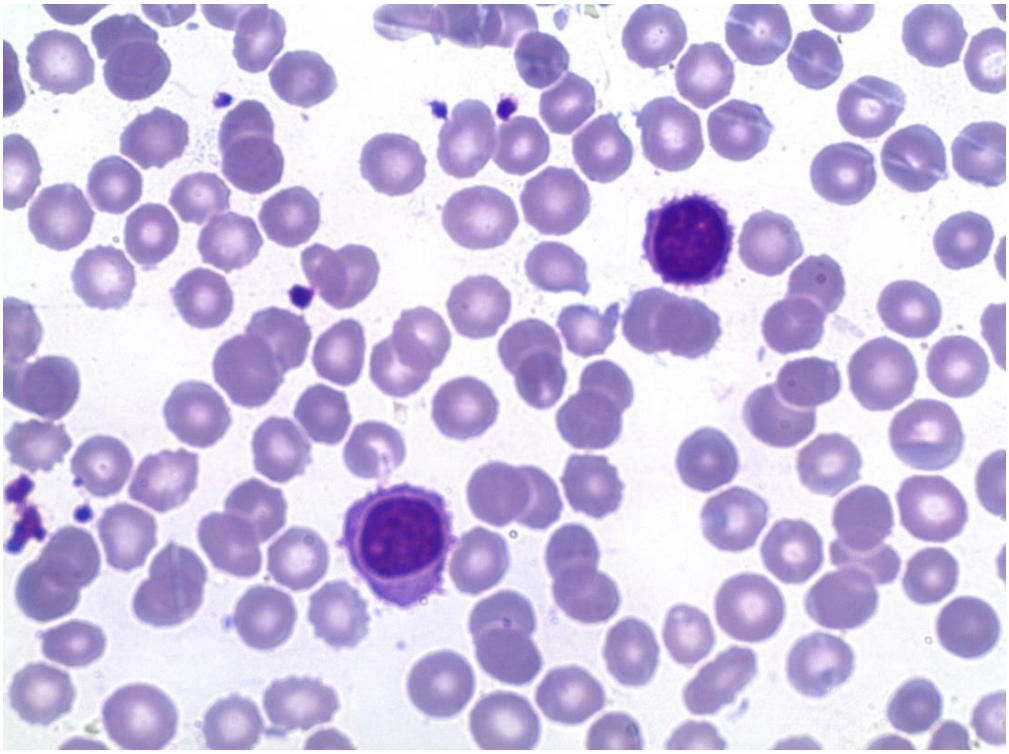

Figure 2: MGG-stained blood smear showing hairy cells (hematology laboratory: MHA)

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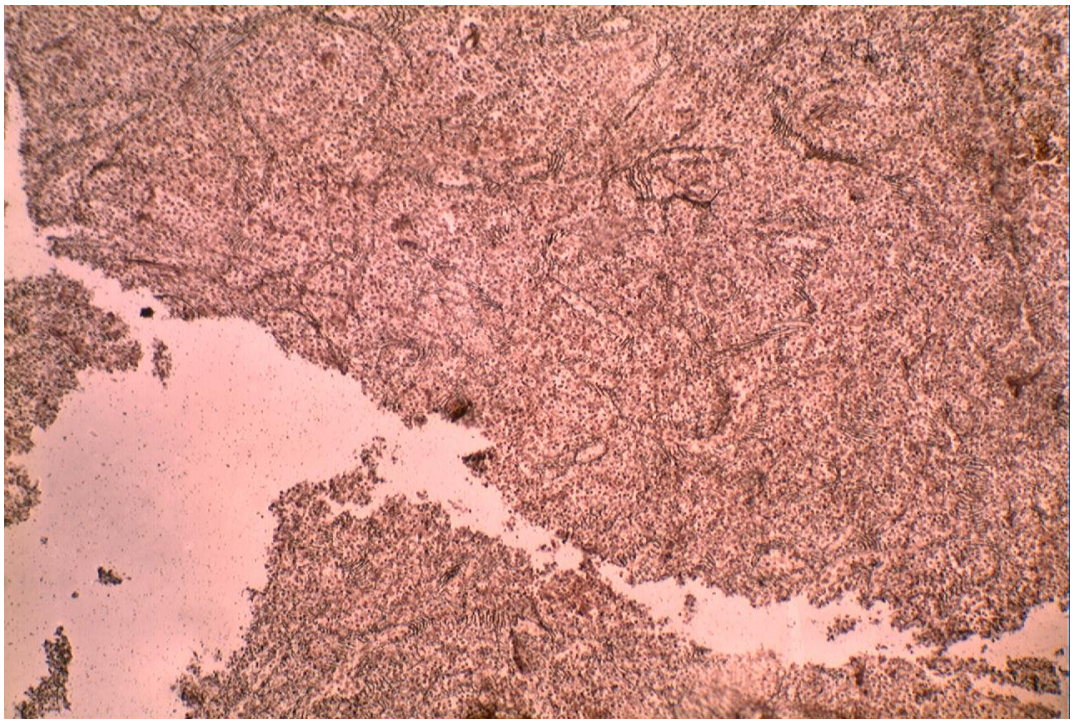

Figure 3: photomicrograph showing moderate interstitial fibrosis: silver impregnation (Pathology Anatomy Lab: MHA)

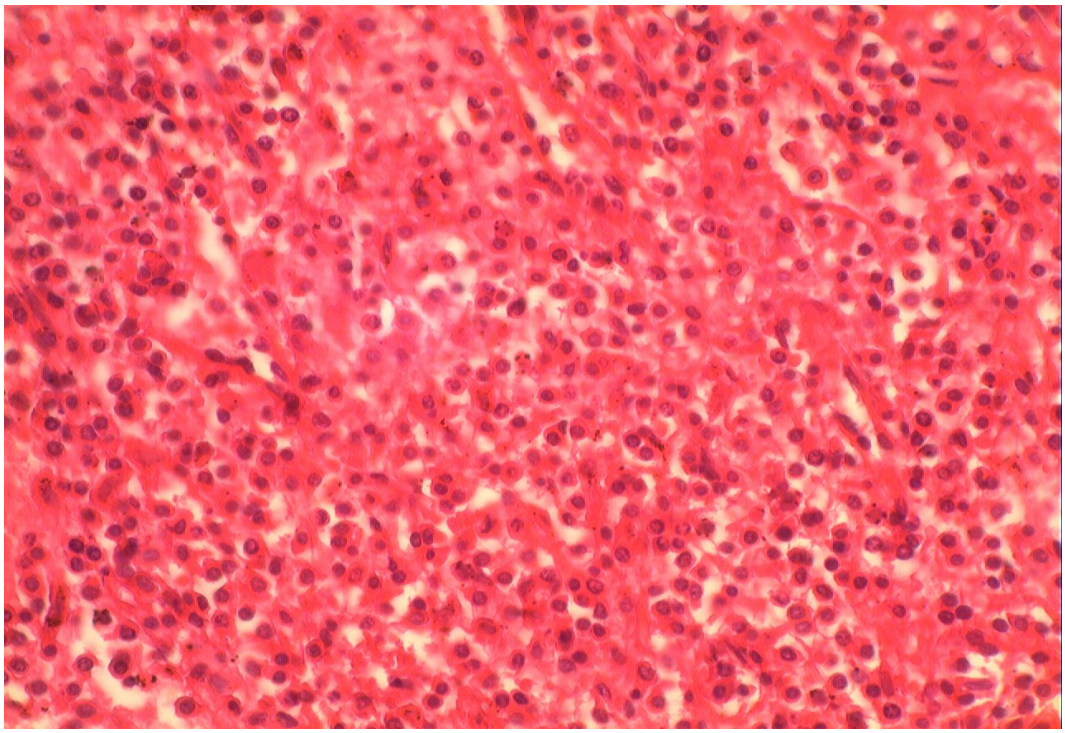

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Figure 4::microphotography at medium magnification showing a proliferation of diffuse architecture tumor made from fairly zoomorphic lymphoid cells to cytoplasm sometimes clarified heating eosin x G 25 staining

(Pathology Anatomy Laboratory: MHA)

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