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Research Article

HAIRY CELL LEUKEMIA: ABOUT THREE CASES

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A B S T R A C T

Hairy cell leukemia is a rare lymphoid neoplasia. The diagnosis remains difficult given the infrequency of the pathology and the similarity with other disease, it liesmainly on the observation of hairy cells in peripheral blood and bone marrow in addition toimmunophenotyping via flow cytometry that highlights the co-expression of numerous markers.

Despite advances in diagnosis and treatment, it's still an area that needs great development. In this case report, we describe the clinicopathologic, biologic and immunophenotypic aspects of threepatients diagnosed with hairy cell leukemiawithin a three years period (2015-2017) at CHU Hassan II, Fès, Morocco.

INTRODUCTION

Hairy cell leukemia (HCL) is a rare slow progressingand chronic B-cell disorder diagnosed in middle age male Caucasians. It constitutes less than 2% of all leukemia's. It is characterized by the presence of non-typical lymphocytes with circumferential villous projections called hairy cells in peripheral blood and boon marrow.It must be differentiated from other HCL-like disorders, including hairy cell leukemia variant HCL-V and splenic diffuse red pulp lymphoma.Although it remained for a long time a fatal disease, great advances in understandingbiology and pathogenic mechanisms transformed it to a chronic disease with sub-normal life expectancy.Therefore the use of newly developed therapy such as purine nucleoside analogs or targeted therapies withBRAF inhibitors opened new horizons, widened the therapeutic optionsand improved the overall prognosis. In this case report, we describe the clinicopathologic, biologic and immunophenotypic of three patients diagnosed with HCL at CHU Hassan II, Fez, Morocco.

Cases Report

Case 1

A 53-years old mal patient, having a history of diabetes and high blood pressure, referred in 2016 for splenomegaly and hemorrhagic syndrome made of repetitive retinal hemorrhages. Physical examination showed a patient in good shape, pale having a 9cm long splenomegaly, without hepatomegaly or lymphadenopathy.

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A complete blood count showedaregenerative normochromic normocyticanemia with hemoglobin level of10g/dl, neutropenia with white blood cell count of $1,5x10^3$/ul,constant monocytosisat $4x10^3$/ul and thrombocytopenia with platelets count of $8x10^4$/ul.

Blood smear showed the presence of 50% of small to medium-size lymphoid cells with rounded or oval nucleus,uncompact thin chromatin, a clear poorly limited cytoplasm sometimes having irregular projections giving it a hairy appearance.

Abdominal ultrasound examination showed an enlarged homogeneous spleen measuring 14,5/9 cm .The sternal puncture was realized but come back inconclusive.

The immunophenotyping showed: a surface immunoglobulin: kappa light chain,lymphoid markers: CD19 +=53%, CD79b +=90%, CD25 +=95%, CD103 +=70%, CD11c +=95%, FMC7 +=92%, CD5-and CD23-.

Based on clinical features and laboratory findings, he was diagnosed with hairy cell leukemia and received one cure of cladribine; after which he became asymptomatic with a correction of the thrombocytopenia, he was followed up with control ofblood count every 3 months and is currently in a 2 years remission.

Case 2

A 61years old mal patient with history of fatigue, weight loss and fever, followed up since 2015 for splenomegaly with general weakness and persistent pancytopenia.Clinically he presented increase in abdominal circumference due to massive splenomegaly. Blood count found out aregenerative normochromic normocytic anemia with hemoglobin level of6,5g/dl, thrombocytopenia with platelets count of

$10x10^4$/ul,and neutropenia with white blood cell count of $1,1x10^3$/ul without monocytosis.
Blood smear showed the presence of 30% of hairy cells in peripheral blood.Bone marrow aspiration was dry, and difficult due to fibrosis.

The immunophenotyping showed: a surface immunoglobulin: lambda light chain, lymphoid markers: CD19 +=42%, CD25 +=92%, CD103 +=45%, CD11c +=92%, FMC7 +=98%, CD5- and CD23-.

Based on clinical features and laboratory findings, he was diagnosed with hairy cell leukemia and received 3cures of cladribine.He was followed up with control of blood count every 3 months but was lost of sight after one year follow up.

Case 3

A 41 years old mal patient with history of recurring hematomas in upper and lower limbs without any trauma and extreme weight loss.Referred in 2017 forenlarged spleen and alteration of general shape. Examination revealed enlarged, firm, splenomegaly 10 cm. Hematological examination found out aregenerative normochromic normocytic anemia with hemoglobin level of 5g/dl, thrombocytopenia with platelets count of $5x10^4$/ul, andneutropenia with white blood cell count of$0,9x10^3$/ul.

Blood smear showed 45% atypical lymphoid cells with round to oval nuclei, moderate cytoplasm and hair like projections. The sternal puncture wasn't performeddue to thrombopenia.
The immunophenotypingshowed: non typical lymphoid markers: low clone of CD19=9.7%, CD25 +=96%, CD103 +=80,4%, CD11c +=94%, FMC7 +=80%, CD5=+54%and CD23-.

He was diagnosed with hairy cell leukemia, based on clinical and cytological criteria although phenotyping wasn't typical with a low clone of CD19. Hedidn't undergo any treatment and died of complications shortly after diagnosis.

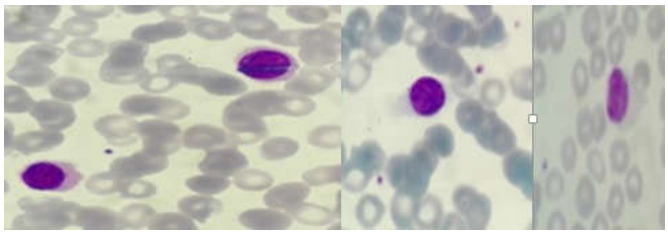
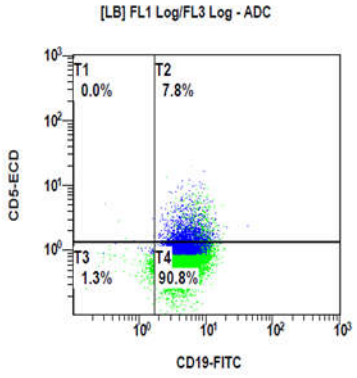


Figure 1 Peripheral blood smears showing our patients hairy cells (Hematology laboratory- CHU Hassan II-Fez)



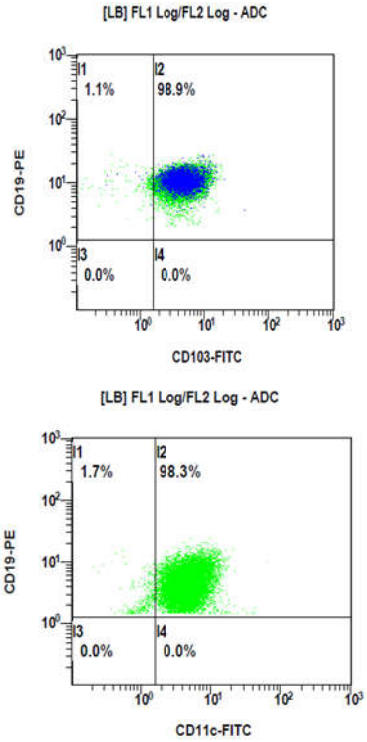


Figure 2 Immunophenotypic profiles of our patients in flow cytometry (Hematology laboratory- CHU Hassan II-Fez)

DISCUSSION

HCL represents 2% of all leukemia's, the overall incidence rate in the USA is less than 1 case per 100.000 persons/year [1]. In France it was estimated at 0,29 per 100.000 persons [2]. InMorocco, the incidence remains difficult to appreciate given the rarity of this diagnosis.On a study carried out in Marrakech on 118 cases of pancytopenia only 1.7% of the patients were diagnosed HCL [3].The ages and sex of our patients joined the ages and sex ratio found inliterature where men were 5 times more diagnosed with HCL than women, and the age range was between 50 to 60 years with a median age of 52 years [4].

Our patients didn't present any risk factors however the description of family cases suggests a genetic predisposition. The role of some environmental factors remains to be clarified: a risk attached to exposure to insecticides, pesticides or herbicides has been identified, as well as a protective effect of tobacco [4].

Clinical features of our patients were similar to those found in literature; it's an indolent disease, manifestations areusually made of general weakness, splenomegaly in 96% of cases, hepatomegaly in 58% of cases and lymphadenopathies in 35% of cases [5]. Ashwell ascharacteristic laboratory findings, that demonstrates that 80% of patients presented with mildpancytopenia associated to false monocytosis, due to the fact that hairy cells are wrongly identified by the automated hematology analyzers as monocytes. Blood smear shows in up to 85% of patients the presence of cells with poorly limited, basophilic cytoplasm showingthin cytoplasmic extensions, theirnucleo-cytoplasmic ratio is low, their oval, round or reiniform nucleus is often eccentric, and theirchromatin is homogeneous and less clumped than the normal mature lymphocyte(Figure 1)[5,6].

In different studies, bone marrowaspirationwas often difficult and non-fruitful it showed in 54% of the patients dry,

hypoplastic to aplastic marrow, as is the case with the sternal puncture performed for 2 our patients because of diffuse reticulin fibrosis, the hemostasis tests of the third one didn't allow realization of the bone marrow [5,6].

The diagnosis of HCL relies essentially on immunophenotypic criteria using flow cytometry. Thepheno type of our patient leukemia cells joined the typical phenotype found in different studies. Besides the usual pan B-cell markers: CD19, CD20, CD22, FMC7,they all insisted on positivity of fourmain and specific anti-bodies:CD11c, CD25, CD103 and CD123(Figure2) [6,7]. Matutes E. and al proposed a scoring system with one point given to each of the last four markers when they are expressed and no point when they are not expressed [8]. A score of 3 or 4 is observed in 98% of HCL cases as is the case for our patients where two had a score of 4(66,66%) and one had a score of 3(33,33%), whereas in other HCL-like disorders, the score is usually low:0 or 1.

Gotic and al described flow cytometry of 46 patients with HCL: it showed CD19, CD22, CD11c in 100% of patients, CD24 in 93%, CD25 in 88%, kappa light chains in 38% and lambda light chains in 35% of patients. The antibody combination CD19 + CD11c was co-expressed in 100% of patients, CD19 + CD25 in 78% of patients [8].

Immunophenotype aberrancies have been well described in HCL, such as negativity for CD103 or CD25; and positivity for CD10 or CD23. In the case of our third patient, it showed a low clone in CD19 expression. This is a feature rarely reported in literature but should be kept in mind while interpreting results of flow cytometry. An alternate marker CD20 should be considered for gating leukemic cells in HCL patients [9,10].

Recent advances in treatment replaced splenectomy and alpha-interferon with purine analogs as used for our patients. It has proven its efficiency and remains nowadays the first line treatment. In a study by Piro and al including 144 patients treated with cladribine, an overall response rate was observed in over 90 to 100 %, acomplete response in up to 85% of patients [10,11].

Furthermore the discovery made in 2011 by Tiacci and al of BRAFV600E mutant,a specific and recurrent clonal mutation identified in up to 80–90%of typical HCL has provided us with new diagnosis tolls through Polymerase Chain Reaction (PCR) that can detect BRAFV600E mutant even if samples contained as few as 0,1% leukemic cells [11,12].It allowed also new therapeutic options by using BRAF inhibitors. Early clinical trials showed that inhibitors of this pathway produce clinical responses in patients who have failed to respond or have relapsed following standard therapy. It can also be the base ground for future therapies by targeting this mutation in hematopoietic stem cells rather than progenitors [13].

HCL is a disease with hope, unlike any other leukemia, quantity and quality of life remains significant with great life expectancy.In different studies; the median free survival rate was of 10 years in 85% to 100% of cases [14].

CONCLUSION

Despite the advances made in HCL management it has not yet been cured, although patient may live a near normal life with the disease, relapses are frequent. For this reason further research is necessary to enhance development of targeted therapy.

Conflict of interest: The authorsdeclarethatthey have no conflict of interest.

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