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Chronic Myeloid Leukemia Update: The experience of the Military Hospital of Marrakech

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Abstract **Original Research Article**

Background: Chronic myeloid leukemia (CML) is a clonal BCR–ABL1-positive myelo-proliferative disorder resulting from an acquired genetic mutation, characterized by the presence of the Philadelphia chromosome. CML is associated with significantly high granulocyte numbers in the bone marrow and peripheral blood. ***Methods and Material:*** This retrospective study conducted at the Hematology Laboratory of the Military hospital Avicenna in Marrakech aimed to assess the epidemiological, clinical and cytological profile of the CML. We have evaluated the demographic, clinical, and hematological data of 42 patients from January 2013 to May 2019. ***Results:*** A total of 42 cases of CML were included. The average age was 42 years. The male gender was predominant with a sex-ratio (M/F) at 3. The most frequent reason for consultation was splenomegaly (90%) either isolated or associated with a deterioration of the general condition and / or a hemorrhagic syndrome and / or thrombosis. All patients were diagnosed in the chronic phase. The complete blood count (CBC) had showed hyperleukocytosis exceeding 20G / l in all our patients. A normochromic normocytic anemia was showed in 96% of cases. Thrombocytosis in 14% of cases. All patients had smear myelemia blood. All patients underwent a myelogram, which revealed hyperplasia of the granular line with the presence of numerous dystrophic megakaryocytes. A cytogenetic study was performed in 20 patients (47,6% of cases) and which revealed the Philadelphia chromosome, thus confirming the diagnosis of CML in these patients. ***Conclusion:*** A patient with an increased WBC count, abdominal pain, left side distension, and hepato-splenomegaly should clearly be evaluated for CML. Exploration of CML in diverse populations can provide a deeper understanding of its molecular characteristics and thereby help in finding better treatment opportunities.

Keywords: Leukemia, myelogenous, chronic, BCR-ABL positive, myelo-proliferative disorder.

INTRODUCTION

Chronic myeloid leukemia (CML) is classified as a myeloproliferative neoplasm predominantly composed of proliferating granulocytes. On a cytogenetic and molecular level, most patients with CML demonstrate BCR-ABL fusion genes in hematopoietic progenitor cells, which result from a reciprocal translocation t(9;22) (q34;q11.2); this translocation leads to a shortened chromosome 22, called the Philadelphia chromosome [1]. The BCR–ABL1 fusion gene codes for BCR–ABL1 transcripts and fusion proteins with high tyrosine kinase activity. The molecular pathogenesis of CML is well understood, but the mechanism that leads to the gene translocation is unknown [2]. The CML accounts for approximately 20% of adult leukemias. Forty percent of patients with CML are asymptomatic, in whom the disease is detected solely based on laboratory abnormalities. It has a worldwide annual incidence rate of 0.87 people per 100,000, increasing with age up to 1.52 in patients older than 70 years [3, 4]. It is characterized by a biphasic or triphasic clinical course in which a benign chronic phase is followed by transformation into an accelerated and blastic phase. Progression from chronic phase to accelerated phase usually involves the accumulation of additional cytogenetic aberrations and the arising of resistance to therapy [3]. The aim of this study was to assess the epidemiological, clinical and cytological profile of the CML at the Laboratory of Hematology at the Military Hospital Avicenna (HMA) in Marrakech.

MATERIALS AND METHODS

Patients and data collection: we retrospectively collected the demographic, clinical, and hematological data of 42 CML patients who had been referred to different medical units of the Military hospital

Avicenne in Marrakech (Hematology, Medecine A and B, Emergency, External patients) from January 2013 to May 2019. The demographic data included age, gender, clinical symptoms and signs, such as splenomegaly, hepatomegaly, and lymphadenopathy. The hematological data included total leukocyte and platelet counts, and levels of hemoglobin.

Diagnosis: circumstances of discovery were either a suspicious clinical symptomatology, or fortuitous discovery of an anomaly in the complete Blood Count (CBC). Patients were examined for the presence of a palpable liver, spleen, and lymphadenopathy. The findings were then confirmed by ultrasound. The routine blood tests included total and differential CBC, The diagnosis of CML was confirmed either by cytogenetic analysis for Philadelphia chromosome or RT-PCR based BCR-ABL analysis (Applied Biosystems 7500 Real time PCR system).

Statistical methods: the frequency of standard descriptive statistics such as mean and standard deviation were used to summarize patient characteristics.

RESULTS

Patients characteristics

The patients included in this study were between 27 and 57 years old with an average age of 42 years. The male gender was predominant with a sex-ratio (M/F) at 3. While 3 (7,14%) patients were below 30 years of age, 20 (47,6%) were between 31-40 years, 10 (23,8%) were between 41-50 and 9 (21,45%) were more than 51 years of age Table 1.

Table-1: The demographical characteristics of CML patients.

		N	%	Mean
Age	<30	3	7,14	30
	31-40	20	47,61	37
	41-50	10	23,8	45
	>51	9	21,45	56
	All patients	**42**	**100%**	**42**
Sex	Male	33	78,57	-
	Female	9	21,43	-
	Total	**42**	**100%**	**-**

The Clinical features of CML patients

Patients were clinically asymptomatic in 45% of the cases. The most frequent reason for consultation was splenomegaly 'SPM' either isolated (5%) or associated with a deterioration of the general condition 'DGC' (10%) and / or a hemorrhagic syndrome 'HS'and / or thrombosis (40%). All patients were diagnosed in the chronic phase.

As for comorbidities, 5 patients (11,9%) had type 2 diabetes, and 10 (23,8%) had hypertension.

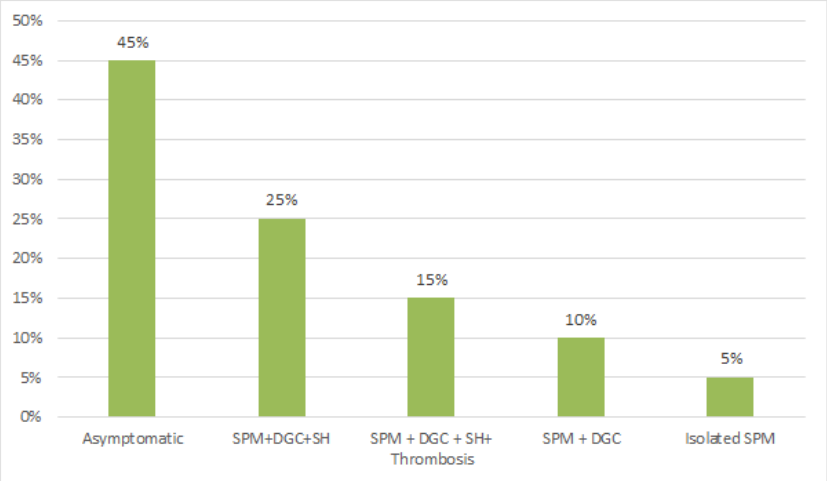

Fig-1: Clinical Features of CML patients

The biological features of CML patients

The hematological data for all the patients have been summarized in Table 2. Complete blood count (CBC) and smear blood: It showed an hyperleukocytosis exceeding 20G / l in all our patients. 47,6% of the patients had a WBC count between 100–400, while some others had a count as high as >400 (4,7%). A normochromic normocytic anemia was showed in 96% of cases. Most of the study patients had hemoglobin levels between 80−120 g/l (88%). Thrombocytosis in 14% of cases. All patients had smear myelemia blood, varying between 57 and 88% with a blast rate of less than 5%.

Table-2: The Hematological features of CML patients.

N=42			
		N	%
WBC count (G/l)	20-99 100-400 >400	12 18 2	28,5 42,8 28,7
Hb (g/dL)	<8 8-12 >12	3 37 2	7 88 5

Myelogramm

All patients underwent a myelogram, which revealed a very rich marrow with an hyperplasia of the granular line (74-90%), with the presence of numerous dystrophic megakaryocytes. Myeloblasts rate was less than 10%.

Karyotype

A cytogenetic study was performed in 20 patients (47,6% of cases) and which revealed the Philadelphia chromosome, thus confirming the diagnosis of CML in these patients.

DISCUSSION

CML is a chronic myeloproliferative disorder that arrays clinically from a dormant to rapidly disastrous disease [5]. It accounts for 20% of leukemias in adults. It has a worldwide annual incidence rate of 0.87 people per 100,000, increasing with age up to 1.52 in patients older than 70 years. There is a slight male predominance. The median age of diagnosis is 56 years old [3,4]. We found in our study a lower median age during diagnosis, and comparable incidence of CML in males and females [6]. The disease presents in one of three phases: chronic phase, accelerated phase, or blast crisis. Progression from chronic phase to accelerated phase usually involves the accumulation of additional cytogenetic aberrations and the arising of resistance to therapy. All of our patients were diagnosed in the chronic phase and had a hyperleukocytosis, 45% of patients were asymtomatic and 55% had splenomegaly either isolated or associated with a deterioration of the general condition and / or a hemorrhagic syndrome and / or thrombosis and that was comparable to other studies [7-9]. Diagnosis of CML is generally straightforward. In most cases, the diagnosis can be made on the basis of a characteristic blood count and differential (excessive granulocytosis with typical left shift of granulopoiesis). Confirmation of diagnosis is obtained by the identification of the Philadelphia chromosome, 22q- or BCR–ABL1 transcripts, or both, in peripheral blood or bone marrow (BM) cells. In 5% of cases the Philadelphia chromosome cannot be detected and confirmation of diagnosis depends on the confirmation of the BCR–ABL1 fusion by either fluorescent in situ hybridisation (FISH) or by reverse transcriptase polymerase chain reaction (RT-PCR) [10]. According to the literature anemia is not frequently found (<50 %) [11]. However, our patients had anemia in 96% and this can be explained by the diagnostic delay. The thrombocytosis was found in 14%, less than in other studies [12]. The results of the blood smear and myelogram were similar to those reported in the literature [13]. The karyotype was performed in 47,6% of our patients and revealed the Philadelphia chromosome. Molecular biology plays an essential role in the identification of the BCR-Abl 1 transcription. The need for skills and technical facilities sophisticated as well as the high cost of these exams cytogenetics and molecules have limited their achievement in all our patients. Multi-center studies with higher sample sizes and continued follow-up periods are therefore required to validate our findings in the Moroccan population. Exploration of CML in diverse populations can provide a deeper understanding of its molecular characteristics and thereby help in finding better treatment opportunities.

CONCLUSION

A patient with an increased WBC count, abdominal pain, left side distension, and hepato-splenomegaly should clearly be evaluated for CML. Exploration of CML in diverse populations can provide a deeper understanding of its molecular characteristics and thereby help in finding better treatment opportunities.

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