CHRONIC MYELOID LEUKEMIA IN CHILDREN IN MAURITANIA ABOUT 12 CASES EXPERIENCE OF THE PEDIATRIC HEMATOLOGY-ONCOLOGY DEPARTMENT AT THE NATIONAL ONCOLOGY CENTER

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ABSTRACT

Introduction: Chronic myeloid leukemia is a malignant hematological disorder belonging to the group of myeloproliferative syndromes; it is rare in children. The advent of tyrosine kinase inhibitors (TKIs) has revolutionized its management. The objective of our study is to investigate the epidemiological, clinical, biological, therapeutic, and evolutionary profile of patients followed for CML.
Materials and methods: This is a descriptive retrospective study spanning 12 years (2011-2023), involving children followed at the pediatric hematology-oncology department at the National Oncology Center in Nouakchott.
Results: In our study, the medium age of the patients studied was 10.6 years with a sex ratio of 1.
At diagnosis, 58,3% of patients were in chronic phase, % in accelerated phase, and 16,6% in blast crisis. Splenomegaly, fever, and asthenia were the most represented symptoms, and pallor was nearly constant. The medium WBC count was 153,000/mm³, platelet count 524,000/mm³. Anemia was consistently present with a medium level of 7.1 g/dl. The Philadelphia chromosome was found in 3 out of 3 tested children. Hydroxyurea was prescribed for patients in the pre-phase. Blast crisis was treated with acute leukemia protocols. Imatinib was prescribed for 10 patients with adherence difficulties. Among the 12 patients included in our study, 7 patients are alive on treatment, 3 discontinued treatment, and 2 have died.

Keywords: *Chronic Myeloid Leukemia –Childhood–Mauritania*

1. **Introduction**

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm resulting from the t-translocation (9:22) and the resulting BCR-ABL1 fusion. CML is rare in pediatrics, in adolescents and young adults. It accounts for about 2-3% of all pediatric leukemias in children under 15 years of age and about 9% of all leukemias in 15- to 19-year-olds [1,2]. Given its lower incidence, most of the data used to guide management comes from the adult population. However, there is no clear evidence that risk assessment tools and treatment guidelines for adults can be applied to pediatric patients. There is evidence to suggest that CML is often more aggressive in pediatric

patients for many different reasons, such as underlying biology and host factors, requiring integration into optimal treatment of CML in younger individuals [3,4].
Over the past two decades, tyrosine kinase inhibitors (TKIs) have revolutionized the way CML is treated, hematopoietic stem cell transplantation (HSCT) is now generally reserved for patients who cannot tolerate or are resistant to TKIs, or those who have or are progressing to a blast crisis.
The objective of this work was to describe the epidemiological, clinical, hematological and cytogenetic data and, in particular, the therapeutic approaches adopted for cases of chronic myeloid leukemia (CML) diagnosed in the pediatric onco hematology department at the National Oncology Center in Nouakchott.

2. Patients and method:

This was a retrospective study of 12 cases of CML collected at the registry level of the Department of Hematology and Pediatric Oncology at the National Oncology Center in Nouakchott over a period of 12 1/2 years from March 2011 to September 2023. All patients with a confirmed diagnosis of chronic myeloid leukemia were included. Data collection was carried out by studying and analyzing the medical records of the 12 patients followed for chronic myeloid leukemia. The data analysis was carried out using Excel 2016 software.
The evaluation of the response to imatinib was made on the hematologic and molecular response:
1. Complete hematological response at 3 months:
The complete hematological response is defined by:
-a white blood cell count < 10000/mm³
- a platelet rate < 450000/mm³
- a non-palpable spleen
2. Molecular Response at 12 Months:
A major molecular response (12-month MMR) is defined by a BCR-ABL transcript ratio ≤ 0.1%.
An intermediate molecular response (12-month RMI) is defined by a BCR-ABL transcript rate between 0.1 and 1%.
Absence of molecular response at 12 months if the BCR-ABL transcript level is > 1%.

We performed a descriptive analysis of the sociodemographic, clinical, biological, therapeutic and evolutionary characteristics of patients. For quantitative variables, we calculated the means.

Results

At the level of the hospital registry of the National Oncology Center (CNO) in Nouakchott, 143 cases of pediatric leukemia were recorded between 2011 and 2023, including 12 cases of chronic myeloid leukemia, or 8.4% of the total number of leukemias recorded in children and adolescents during this period.

The mean age of patients was 10.6 years with extremes ranging from 5 to 15 years. The most affected age group was between 12 and 14 years old, representing half of the children. Our series was composed of 6 Boys and 6 Girls with a sex ratio of 1.

The 12 children came from 7 different regions. No particular history was noted in all patients. The circumstances of discovery were marked by the heaviness of the left hypochondrium and fever in 12 patients, 9 patients had an alteration in general condition and 3 had bone pain.

Clinically, pallor was present in the 12 patients with a tumor syndrome (splenomegaly, peripheral lymphadenopathy) hepatomegaly in 5 patients.

The laboratory work-up included a blood smear associated with a blood smear revealing hyperleukocytosis in all patients with a mean level of 153000 /mm³ and extremes ranging from 26000 to 578000 /mm³.

Leucocytes	Limites	Nombre	Pourcentage
PNN	<10000/ mm³	1	8,3%
	10000-100000/ mm³	7	58,3%
	100000-200000 / mm³	4	33,3%
Lymphocytes	<10000/ mm³	1	8,3%
	10000-50000/ mm³	10	83,3%
	50000-100000/ mm³	1	8,3%
Monocytes	<10000/ mm³	6	50%
	10000-50000/ mm³	5	41,6%
	>50000/ mm³	1	8,3%
Basophilie	<1%	1	8,3%
	>1%	8	66,6%
Eosinophile	<1%	2	16,6 %
	1-3%	3	25 %
	>3%	5	41,6 %

Table 1: the distribution of leukocytes from our patients

All patients had anemia at diagnosis, the mean hemoglobin level was 7.1 g/dl, with extremes ranging from 2.3 to 10.8 g/dl. Anemia was normocytic in 44% of patients, macrocytic in 1/3 of patients and microcytic in a quarter of our patients.
Thrombocytosis was noted in 50% of our patients and 30% had thrombocytopenia, the mean rate was 524,000/mm³ with extremes ranging from 4000 to 2,050,000/mm³.
The blood smear study showed myelemia in all patients.

The level of blood blasts varied in patients between 0% and 90% Allowing the phase of the disease to be specified: 7 children were in the chronic phase (<10% of blasts), 3 in the accelerated phase (10%-19% of blasts) and 2 in the blast phase (>19% of blasts).

The myelogram was performed in only 5 children and showed a proliferation of the myeloid lineage in all 5 patients.

Molecular biology exploration was possible in the 12 children, PCR was performed by the Expert-BCR-ABL-Gene Xpert kit (Cepheid) with maximum sensitivity of 0.003% (RM^{4-5}) and objectified the presence of the BCR-ABL transcript in 100% of patients. It was used for disease monitoring.
The karyotype was performed in only 3 children allowing the detection of the Philadelphia chromosome.
Therapeutic management required hospitalization and non-specific treatment (hydration, analgesic, antibiotic) in six children, 50% of the patients had a blood transfusion.
Six of our patients (50%) were put on hydroxyurea in the prephase while waiting for confirmation of the diagnosis, at a dose of 50 mg/kg/day for 1 week to 1 month.
Ten children were started on treatment with first-line Tyrosine Kinase Inhibitor (Imatinib) at a dose of 340 mg/m²/day.

2 children in the blast phase were put on chemotherapy and immunosuppressants.
The course was marked by a heterogeneous therapeutic response in the 10 patients
Response to imatinib treatment:
The complete hematological response at 3 months was observed in all 10 children (100%).
Molecular Response (MR) at 12 months was major (MMR) in 3 children (30%), Intermediate (RMI) in 3 children (30%)
Relapse of the molecular response:
Relapse was observed in 2 children, after 2 and 5 years of remission of the successively major and intermediate molecular response. Both relapses were attributed to poor adherence to treatment.
Lack of molecular follow-up after treatment:
4 children (40%) were unable to benefit from molecular monitoring of treatment response, 3 children dropped out of treatment.
Response to treatment in the blast phase:
The 2 children in the blast phase were put on chemotherapy (Purinethol, Doxorubicin and Aracytin), the 2 children died.
Treatment tolerance:
In 2 children put on imatinib, there was a dermatological attack with depigmented lesions on the body (legs, thighs, back, etc.).
Thrombocytopenia at 46000/mm³ in a child resolved after temporary discontinuation of imatinib.

3. Discussion

The demographic profile of our patients was comparable to the literature [5,6,7] however, some similar studies reported a higher average age of 14 to 19 years [9,10,11], suggesting that it is a disease of adolescence rather than childhood.
In our series, 75% of the children came from cities far from Nouakchott, the place of the only reference center for cancer pathology. This refers to one of the reasons for irregularity or even abandonment of follow-up, which is the distance to be covered to come to the consultation.
The clinical data of our patients were also comparable to the literature [6,9,12,13,14], including bone pain which was present in 25% of our patients.
Biologically, leukocytosis was consistent in our work, with varying rates as in different similar studies [6,9,20,21]. Anemia was observed in all children in our series as was the case in African studies [6,9], however
Thrombocytosis was present in 50% of our patients compared to 20% in an African study [9].
Diagnosis by molecular biology was the gold standard by the search for the BCR-ABL transcript which was detected in all the children in our series, however the non-availability of genetic tests in our country limits the accessibility of our patients to the karyotype of which only 25% had a karyotype, with a detection of the Philadelphia chromosome in all these children, elsewhere, accessibility to genetic exploration is better, exceeding 75% [6,9], with detection of the Philadelphia chromosome in 94%.
The weakness of the karyotype performance in our patients was explained by the inadequacy of our technical platform.
The evolution on Imatinib was satisfactory from a hematological point of view in our work with a 3-month hematologic response of 100% as well as in the literature with rates varying between 75 and 100% [7,9,14,22,24]. However, the molecular response at 12 months was moderate in our 30% series, comparable to similar studies with a rate of 35% [14,22].
The tolerability of imatinib was generally satisfactory, and the hypopigmentation reported in our work has been reported in a few studies [7,9].
Treatment dropout was high in our patients, 25%, which was probably attributed to insufficient health education in our population.

4. Conclusion

Chronic myeloid leukemia is rare in children, tyrosine kinase inhibitors (TKIs) have revolutionized its therapeutic management, however, diagnostic and therapeutic inadequacies remain frequent in developing countries, impacting the prognosis of this disease as well as the quality of life of patients.
Despite access to care at the national oncology center and free tyrosine kinase inhibitors for indigent patients, late diagnosis, poor compliance and abandonment of treatment worsen the prognosis of CML in children in Mauritania.

5. **Références**

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