

## Original Research Article

## Medullary Aplasia in the Child: Epidemiological, Clinical and Biological Aspects in the Hematology Laboratory of CHU Hassan II of Fez

Dr. Amadou Djibrilla<sup>1\*</sup>, Pr. Imane Tlamcani<sup>1</sup>, Dr. Imane Jamai<sup>1</sup>, Dr. Boubacar S. Marou<sup>1</sup>, Dr. Nazik El Hammouni<sup>1</sup>, Pr. Moncef Amrani<sup>1</sup>, Dr. Boubacar Efare<sup>2</sup>, Pr. Hinde El Fatemi<sup>2</sup>

<sup>1</sup>Hematology Department CHU Hassan II of Fez, Morocco

<sup>2</sup>Department of Anatomy Pathology CHU Hassan II of Fez, Morocco

### \*Corresponding Author:

Dr. Amadou Djibrilla

Email: [amdjibrilla@gmail.com](mailto:amdjibrilla@gmail.com)

**Abstract:** Medullary aplasia (MA) is a rare and severe affection. It is much rarer in children. The etiologies are multiple: constitutional, acquired, and idiopathic. In order to evaluate the epidemiological, clinical and biological aspects of bone marrow aplasia in a pediatric population, we carried out a retrospective study of 9 cases collected in the hematology department in collaboration with the department of anatomy pathology of the Hassan II CHU in Fez over a four-year period from January 2013 to December 2016. Age ranged between 1 and 14 years, with a sex ratio of 3.5. The anemic, hemorrhagic and infectious syndrome was noted respectively in: 9, 7, and 6 cases. The hemoglobin varied between 3.3 and 7.3 g/dl with an average of 5 g/dl, anemia is normochrome normocytic regenerative in all our patients. Neutropenia was found in 100% of patients, and all patients had thrombocytopenia with platelet counts ranging from 500 to 105000/mm<sup>3</sup>. The BOM-coupled myelogram was performed in all patients, confirming the diagnosis of AM. For the etiologies, Fanconi Anemia was evoked in 4 cases and idiopathic in 5 patients.

**Keywords:** Medullary aplasia in the child, epidemiology, biology, laboratory CHU Hassan II Fez.

### INTRODUCTION

Medullary aplasia (MA) is a quantitative medullary insufficiency, secondary to the complete or partial disappearance of the haematopoietic tissue, without abnormal cell proliferation. It can be a constitutional MA (genetic intrinsic cause), acquired MA (extrinsic or environmental cause) or idiopathic when the cause is not known. It is more common in adults than in children. It is a rare disease whose clinical severity as well as overall mortality, although markedly decreased, remains important during the first few months of the disease [1, 2]. Death usually occurs as a result of severe hemorrhage or severe septic shock. In view of its clinical severity and its poor prognosis, we propose to study the epidemiological, clinical and biological characteristics of MA in children in the hematology laboratory in collaboration with the anatomical pathology laboratory of the CHU Hassan II of Fez.

### MATERIALS AND METHODS

#### Study Framework

The myelograms carried out in the Hematology laboratory of the CHU Hassan II of Fez, showing a medullary hypoplasia whose diagnosis of MA has been confirmed in the anatomo-pathology department of the same CHU.

#### Type of study and sample

This is a retrospective study carried out in the laboratory of hematology of CHU Hassan II of Fez over 4 years from 01/01/2013 to 31/12/2016. Myelogram results were used as a source of data collection. The information collected was socio-demographic data (age, sex and provenance), history, clinical, para-clinical, and etiology information.

#### Technical

The blades were received and then stained by the technicians or residents of the service at May Grunwald Giemsa (MGG) (at least 4 blades), the remaining slides are retained for further examination if necessary. Two peripheral smears are made then colored at the same time as the myelogram. The readings were made by the hematologist or his collaborators, under the optical microscope Bitetes DM 2500 MEDICAL CLAES at low (x 10) and strong (x 100 at immersion) magnifications.

### RESULTS

#### Frequency

Two thousand one hundred and sixty-four (2164) medullary punctures were received in 4 years, of which only 9 were in favor of medullary hypoplasia or 0.4%. All of this bone marrow hypoplasia have

benefited from a BOM that has confirmed medullary aplasia.

**Age and sex**

All ages were affected with an average age of 9.1 years (extreme: 1 and 14 years). There is a male predominance of 7 cases, that is to say 77.7% against 2 women or 22.3%. Sex-ratio 3.5.

**Geographical distribution:**

Among our 9 patients, 5 cases are from Fez, which represents 55.5% of the cases.

**Patient History:** (Table 1)

In the patients' history we noted that 5 cases (55.6%) were without significant pathological ATCD, two cases (22.2%) had a first-degree inbreeding of parents, two cases (22.2%) a delay staturo-weight.

**Table 1: Patient distribution by background**

Antecedents	Number (s)
Without antecedent	5
Delay in weight	2
Consanguinity	2

**Clinical and para-clinical aspects**

*Clinical aspects*

**1. Admission times**

The interrogation finds in all cases a symptomatology that precedes the hospitalization from two weeks to three years. Half of our patients had an admission period of less than one month.

**2. Clinical signs:** (Table 2)

Medullary aplasia is clinically manifested by at least one syndrome constituting the syndrome of medullary insufficiency namely:

- ✓ Anemic Syndrome:  
It has been found in all our patients, dominated by a mucocutaneous pallor of varying intensity.
- ✓ Hemorrhagic syndrome:  
It was found in 7 of our patients, 77.7%. This hemorrhage is sometimes cutaneous (purpura, ecchymosis, petechiae), sometimes it concerns the mucous membranes (gingivorrhagies, epistaxis).
- ✓ Infectious Syndrome:  
It was found in 6 of our patients, 66.6% of the cases, secondary to infections occurring in a field of spinal cord insufficiency.
- ✓ The 3 signs of spinal cord insufficiency:  
They were found in 6 of our patients, in 66.6% of cases.

**Table 2: Distribution of patients according to clinical signs**

Clinical signs	Number
Anemic syndrome	9
Infectious Syndrome	6
Hemorrhagic Syndrome	7

**3. Para-clinical signs:** (Table 3)

**3.1. Blood count: NFS**

**1. Hemoglobin:**

Hemoglobin levels varied between 3.3 and 7.3 g / dL with a median of 5 g/dl. Five (5) patients had Hb <5g / dl (55.5%), three (3) patients had Hb levels between 5 and 7 g/dl (33.3%) and one (1) patient had Hb > 7 g/dl, (11.1%).

**Table 3: Distribution according to the result of the hemogram**

Hemogram	Number(s)
Neutropenia	
< 200/mm <sup>3</sup>	5
200 and 500/mm <sup>3</sup>	4
>500/mm <sup>3</sup>	0
Anemia	
Normochrome Normocytic	8
Normochrome Normocytic	1
Microcytic hypochrome	0
Regenerative	0
Aregenerative	9
Thrombocytopenia	9

**2. VGM, CCMH, reticulocyte level:**

The VGM values varied between 82 and 117 µ. Eight (8) or 88.8% of our patients had normocytic normocytic anemia. Macrocytic anemia was found in one of our patients, or 11.1% of the cases. The MHCC ranged from 34% to 36% and the level of reticulocytes was between 4000 and 21000/mm<sup>3</sup>. All our patients had argenerative anemia.

**3. White blood cell count (GB);**

All patients had leucopenia and neutropenia (100%). The neutrophil rate varied between 50/mm<sup>3</sup> and 270/mm<sup>3</sup>. Two patients had neutrophil <200/mm<sup>3</sup> (22.3%), 7 patients had a neutrophil level of between 200 and 500/mm<sup>3</sup> (77.7%). All our patients were in agranulocytosis.

**4. Rate of platelets:**

All patients had thrombocytopenia (100%). The platelet count varied between 500 and 105.000/mm<sup>3</sup>.

**3.2. Myelogram:**

The myelogram was performed in all our patients (100%). It was desert in two of our patients, 22.3% of the cases and poor in 7 patients, 77.7% of the cases.

**3.3. Osteomedullary biopsy (BOM):**

The BOM confirms the existence of MA in all our patients in 100%.

### 3.3. The karyotype:

Karyotype was performed in all our patients, of whom 4 had chromosomal fragility in favor of AF. Five (5) had a normal karyotype.

### 3.4. Other exams

A review of the etiology as well as aiming of the ground was carried out in our patients, thus the C Reactive Protein (CRP): was high in all of our patients or 100%, between 98 and 105 mg/L. The rate of sedimentation (SV) was accelerated in our 9 patients between 90 and 120mm at the first hour. On the other hand, blood ionography, liver function tests, viral hepatitis A, B, C serology, Cytomegalovirus (CMV), HIV, EBV and toxoplasmosis serology were normal in our patients.

### Etiologies

The etiological investigation was in favor of Fanconi anemia suspected in 4 patients in 44.4%. No etiology was found in 5 patients in 55.5%.

## DISCUSSION

### Epidemiology:

#### Frequency;

Medullary aplasia is a rare disease, with an incidence of 10 cases per year, which is twenty times less than multiple myeloma and ten times less than acute leukemia [2]. According to the studies, the estimation of the incidence of bone marrow aplasia is difficult to define, and probably varies according to the criteria used to confirm the diagnosis.

#### Age and Sex:

The incidence of MA is much more frequent in young subjects before the age of 20 years, but even more frequent in older subjects over 50 years [3]. In our series the age varies between 1 and 14 years, and this is identical to the results reported by Najean.Y *et al* in France [4]. In our series there is a high frequency of male sex, or a sex ratio of 3.5, which is identical to that of Tolo-Diebkilé A *et al* [5] in a study carried out at Yopogon University Hospital in Abidjan, reported a predominance male, whose sex ratio was 1.13. These results are similar to those reported by Koffi *et al.* [6] who also found a male predominance. On the other hand, the study of Yao T *et al* [7] carried out at the CHU of Treichville, found a female predominance with a sex ratio to 0.7.

### Health Clinics

In our series the anemic syndrome predominates in 100% of the cases, followed by the haemorrhagic syndrome present in 77.7% of the cases, and finally the infectious syndrome found in 66.6% of the cases. These results are similar to those reported by Yao T [7]. On the contrary, in the study conducted at the CHU Rennes [8] pediatric department, haemorrhagic syndrome was present in 85.7% of cases, with an equal predominance of anemic and infectious

syndrome (42.8%), where as the syndrome followed by anemic syndrome and haemorrhagic syndrome in the study conducted at Yopougon University Hospital [5].

### Para-clinical:

#### NFS:

In our study all our patients have a pancytopenia on their NFS either in 100%, even observed in the series of the CHU of Rennes [4]. According to the Yopougon CHU study, the hemogram showed pancytopenia in 85.3%, bicytopenia in 11.8% and anemia isolated in 2.9%. In our patients, the hemoglobin varied between 3.3 and 7.3 g/dL with an average of 5 g/dl, and 90% had hemoglobin <7 g / dl, Is similar with the Yopougon series [5], whose hemoglobin varied between 1.5 and 9.9 g/dl, with an average of 5.15 g/dl, while 62% Hb <6 g/dl. On the other hand, in the series of the CHU of Rennes [8], the hemoglobin varied between 7 and 11.5 g/dl, with an average of 9.8 g/dl. All our patients had neutropenia, the neutrophilic ratio of which varied between 50 and 830/mm<sup>3</sup>, where as in the study at Rennes [8], only 50% had neutropenia.

In our series the platelet count varied between 500 and 105.000/mm<sup>3</sup>, for the study of Yopougon [5], the platelet rate varied between 3000 and 260000, with an average of 64797/mm<sup>3</sup>.

### The myelogram:

In our study, the myelogram was desert in 22.2%, and poor in 77.7% of the cases, while for the study made at Yopougon University Hospital, it was desert in 55.9% and poor.

### BOM

In our study, the BOM made it possible to make the diagnosis in all the patients, in 100%.

### Etiologies

In our study, the etiological investigation strongly suspected an anemia of Fanconi (AF) in 4 of our patients in 44.4%. AF This is the most frequent MA Constitutional. It is autosomal recessive and the most frequent of heterozygous subjects. The classic table combines small size, facial dysmorphism, cutaneous and thumb anomalies, and secondary appearance pancytopenia worsening with age; malformations Associated are inconstant and highly variable. Delayed staturo-weight: it is practically constant and present at birth, secondary to intrauterine growth retardation and facial dysmorphism. The myelogram initially shows a poor marrow, or frankly hypoplastic, there is no specific appearance on the cytological plane. In this clinical and biological presentation, the diagnosis of AF was suspected in 4 of our patients, so all the etiological balances were without particularities for the 5 other patients from which we had concluded an idiopathic MA.

## CONCLUSION

MA refers to quantitative medullary insufficiency, which is the cause of cytopenia affecting the three bloodlines. It is of severe clinical manifestation and includes several para-clinical data necessary for etiological research.

## ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and / or National Research Committee and the 1964 Helsinki Declaration and its subsequent amendments or comparable ethical standards.

## REFERENCES

1. Medullary aplasia. (2009). National protocol of diagnosis and care for a rare disease. High Authority for Health (HAS).
2. Medullary aplasia. (2016). Hematology biology, CHU 49000 Angers France.
3. Socié, G., Ferry, C., Robin, M., & Mary, Y. (2015). *Aplastic anemia EMC-hematology*, 113-131.
4. Najean. Y. (1992). Aplastic anemia. In: Breton-Gurios J, Reyes F, Rochant H, Vernant JP: *the hematology of Bernard Dreyfus*. Paris: Flammarion, 17: 755.
5. Tolo-Diebkile, A., Koffi, K. G., Nanho, D. C., Sékongo, Y. M., Kouakou, B., Me, N., Ayemou, R., & Sanogo, I. (2009). *Medullary aplasia: a clinical, clinical, etiological and evolutionary profile*. Mali Medical.
6. Koffi, K., Attia, A. K., Danho, N. C., Sango, I., & Sangaré, A. (2003). Seroprevalence of hepatitis B in spinal aplasia: experience of the clinical haematology department of Yopougon-Abidjan University Hospital. *Med Afr Noire*, 50 (11), 496-8
7. Yao, T., Abisse, A., Danho, B., Moumouni, K., & Téa, D. (1990). Study of medullary aplasia: about 12 cases diagnosed at the Treichville. *African Medical Publications*, 110.
8. Medullary aplasia in IIIe-et-Vilaine Institute of Health Surveillance, September 2006.