SEVERE APLASTIC ANEMIA: MANAGEMENT CHALLENGES AT THE UNIVERSITY TEACHING HOSPITAL OF BRAZZAVILLE

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ABSTRACT

Introduction: Aplastic anemia is a quantitative deficiency of hematopoiesis responsible of pancytopenia with poor bone marrow. This deficiency is often acquired, infectious or iatrogenic. It can also be constitutional and sometimes idiopathic. If the treatment is well codified in developed countries with an improved long-term prognosis for several years, this disease remains highly fatal in developing countries.

Objectives: to highlight the difficulties in the management of severe aplastic anemia at the University Teaching Hospital of Brazzaville.

Methods: It was a historical cohort, carried out on the basis of the records of patients hospitalized for severe aplastic anemia, between January 2000 and December 2014 (15 years). Included patients had at least two Camitta's criteria.

Results: 30 files were enrolled. In a little over 90% of cases, they were idiopathic aplastic anemia. In 100% of cases the treatment was only symptomatic (red cells and standard plates transfusion, antibiotic therapy), in addition to intravenous Methylprednisolone. The mortality rate was 100% after a median follow-up of 8.3 weeks.

Conclusion: Severe Aplastic anemia remains a dreaded disease at the University Teaching Hospital of Brazzaville. Low socioeconomic status and lack of specific treatment are the two main worsening prognostic factors.

Keywords: Severe aplastic anemia, Bone marrow transplant, Cyclosporin

INTRODUCTION

Aplastic anemia is linked to a quantitative disorder of hematopoiesis. This disorder can be constitutional but more often it is acquired. In this case several factors are involved: drug toxicity, radiation, viral infections and other rarer causes such as immunological diseases. Sometimes no cause is found, it is the idiopathic form. In this latter form the pathophysiological mechanism invoked is that of a dysregulation of the immune system [1-3].
Camitta's prognostic score, the most used, distinguishes moderate and severe aplastic anemia [4]. Moderate forms requires little or no treatment. Severe forms are true medical emergencies. In these cases the symptomatic treatment has an important place. However the hematopoietic stem cells and immunosuppressive drugs have the best long term results. They are raising the hope of a 5-year survival in about 80% when the best conditions are met [3,5].
In Africa mortality from severe aplastic anemia remains globally important [6-11]. In the hope of improving the care of patient, this study was aimed to identify the difficulties in the management of severe aplastic anemia (SAA) at the University Teaching Hospital of Brazzaville (UTHB).

METHODS

It was a historical cohort based on the records of patients hospitalized in the Hematology department of UTHB between January 2000 and December 2014 (15 years).

The records of patients hospitalized for severe aplastic anemia were included. Camitta's criteria were used:

- Granulocytes less than or equal to 0.5 Giga / l
- Platelets less than or equal to 20 Giga / l,
- Reticulocytes less than or equal to 20 Giga / l with a poor marrow bone (myelogram).

The parameters analyzed were:

- Etiologies
- Haematological constants: Hemoglobin (Hb), White blood cells (WBC), Platelets
- Treatment,
- Causes of death.

Information were collected using an Excel sheet.

Thirty cases were included.

The average age was 22.9 years [3 years - 60 years]. The sex ratio Male / Female was 0.57.

SAA was idiopathic in 93.33% of cases (28 patients/30), and toxic due to Chloramphenicol in 6.67% of cases (2 patients/30). Pancytopenia was present in all patients. The average rate of Hb was 4.5 g /dl [2.8 g /dl – 7 g /dl].

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The average rate of Platelet count was 18.3 Giga / l [8 Giga / l – 86 Giga / l]. The average rate of WBC was 200 Giga / l [100 Giga / l – 900 Giga / l]. Table I illustrates the care of patients. Blood transfusions included only the ABO Rh-compatibility. Digestive decontamination associated mouthwash with antiseptic solution and oral administration of ciprofloxacin and amphotericin B.

Table 1: Different treatments used in patients followed for severe aplastic anemia in the Hematology department of the University Teaching Hospital of Brazzaville between January 2000 and December 2014.

Treatment	Effective	Frequency %
Erythrocyte concentrate	30	100.00
Standard platelet concentrate	25	83.33
Digestive decontamination	27	90.00
Antibiotherapy	30	100.00
Ciclosporine+Prednisone	3	10.00
Methylprednisolone +	27	90.00

In case of fever, a broad spectrum antibiotic therapy was instituted. The combination of an aminoglycoside and a ßlactamine represented the systematic therapeutic option for first-line.

After the 7th day and in case of persistent fever, intra venous Fluconazole was added to the previous association. The association Ciclosporin - Prednisone had been used in 10%.

The intravenous Methylprednisolone 10 days with the oral relay of Prednisone were used as background treatment in 90% of cases. Table II shows the different causes of death.

Table 2: Causes of death of patients treated for severe aplastic anemia in the Hematology department of the University Teaching Hospital of Brazzaville between January 2000 and December 2014

Causes of death	Effective	Frequency %
Haemorrhages	16	53.33
Infections	11	36.67
Anemias	3	10.00

Haemorrhages were represented by: melena, rectal bleeding, epistaxis, gingival bleeding, cerebral hemorrhage (suspected), breakthrough bleeding, hematuria, subcutaneous bleeding. Most often these hemorrhages were associated. Infections were dominated by gastro enteritis followed by a lesser-measuring odontogenic and genital infections.

Mortality related to anemia was due either to the lack of financial means or because of the unavailability of blood products. The mortality rate was 100% after a mean follow up of 8.3 weeks.

DISCUSSION

The general measures and the symptomatic treatment are essential for the success of the specific treatment [3, 12, 13].

In rich countries numerous means are implemented to secure all the patient's environment. They reduce the risk of infection [14,15]. Patients are isolated under sterile units composed of individual rooms. These units are equipped with laminar flow to maintain a positive pressure. Preventing the risk of infection is also based on strict hygiene measures applied to the patient and his (her) entourage. The entrance of the nursing staff and visitors in those hospital rooms is conditioned by strict aseptic rules [14]. In poor countries, particularly in black Africa, the lack of resources does not allow the implementation of all the above general measures described [8, 9, 11]. The hematology department of UTHB has no sterile isolation unit. Preventing infection risk is also based on gastrointestinal decontamination. Patients are encouraged to follow strict rules of personal and food hygiene. In Brazzaville Patients' parents are required to provide food, exposing a high risk of exogenous contamination. This situation increase the risk of infection, sometime severe. Infections were the cause of death in about 35% of cases, which is in agreement with many African studies [6, 8, 10, 11].

The bleeding was the first cause of death. The correction of thrombocytopenia and anemia are necessary as symptomatic treatment in the management of SAA. In Brazzaville the availability of blood products is a big challenge. The situation is similar in Nigeria [11]. This is justified by the insufficient number of donors. Bleeding by thrombocytopenia were responsible for almost 55% of deaths. This figure is similar to that found in some African studies, especially in Nigeria [6, 11].

Moreover the absence of phenotyped blood products exposes patients to the risk of immunization and therefore ineffective transfusion.

Corticosteroid therapy was the often used. Some authors doubt the effectiveness of this treatment, thinking it may even be the cause of some major complications [12,16]. The specific treatment of SAA is based at present on two options that make consensus, allograft bone marrow and immunosuppressive drugs other than steroids [5, 12].

The results in terms of long-term survival of these two therapeutic being substantially equivalent. The génoidentique transplantation has an advantage to be a curative treatment [17]. No patient in our series received a specific treatment. The country has no marrow transplantation department. This treatment cost in rich countries is estimated at more than 500 times the average salary of the Congolese. The immunosuppressive therapy is represented by the association between anti lymphocyte serum and cyclosporin [5, 12,18,19].

Those two molecules are also not available in Congo. These concerns are shared by several African authors [8, 9, 11]. Cyclosporin can be payed via private pharmacies. But its cost limits its accessibility: a monthly treatment for a subject of 50 kg costs about 5 times the minimum Congolese wage. This explains its limited use in our series, and its premature abandonment for financial reasons in patients who received it. The health system in the Congo has no social security for public employees or the unemployed. The purchase of all medications, including blood products and medical treatment is entirely the responsibility of patients. Thus, the financial burden linked to this serious and chronic disease rapidly is important for the poorest.

The mortality rate was 100% with a mean follow up of 8.3 weeks. This result is comparable in Nigeria [11]. While in Europe and North America, the survival rate at 5 years as high as 90% depending on series [5, 20 -22].

CONCLUSION

Severe aplastic anemia has a dreaded prognosis at UTHB. Among the causes, there are poverty and lack of specific treatments. The regional cooperation (Central Africa) in order to have a bone marrow transplant unit, and the creation of social security for all could reverse this trend.

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