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Case Report

Association of Bone Marrow Necrosis and Macrophage Activation Syndrome. Diagnoses Difficulty And Complexity Of Treatment : About à Case In The Hematology Département of Treichville University Hospital.

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Abstract

Summary Context: Macrophage activation syndrome and bone marrow necrosis are all extremely rare phenomena that can each be secondary to pathologies including neoplastic, infectious or even congenital. These conditions are most often discovered late and in conditions where the patient›s vital prognosis is at stake, making their management difficult. The association of these two conditions is an extremely rare phenomenon and little described by the authors. We describe a simultaneous discovery of bone marrow necrosis and macrophage activation syndrome in a patient received for treatment of febrile pancytopenia.

Presentation of Cases: 37-year-old patient hospitalized for exploration and management of subacute febrile pancytopenia in whom the diagnosis of bone marrow necrosis was made on the basis of bone marrow cytology and activation syndrome macrophage according to the HLH 2004 and H-score criteria. The etiological investigations carried out in this direction made it possible to find immunosuppression (HIV1+) complicated by opportunistic infection (Mycobacterium Tuberculosis).

Conclusion: From this work, we show the complexity linked to the management of such a diagnostic association (marrow necrosis and macrophage activation syndrome) occurring in conditions of immunosuppression with opportunistic co-infection.

Keywords: Bone marrow necrosis, Macrophage Activation Syndrome, Immunosuppression and Urinary tuberculosis.

1.Introduction

Bone marrow necrosis and macrophage activation syndrome (MAS) are rare and serious conditions associated in the majority of cases with neoplastic, infectious and especially hematological pathologies. Bone marrow necrosis with an estimated prevalence of 0.3% is defined by the appearance of marrow juice containing unidentifiable cellular elements on a heterogeneous pink background unlike SAM which is defined by clinical, biological and cyto-histological, reflecting non-specific activation of monocytes/macrophages, a lack of cytotoxic activity of Natural Killer (NK) lymphocytes and T-CD8+ lymphocytes with tissue infiltration of activated macrophages associated with high mortality varying from 22-59% according to studies . The first case of post-viral SAM was described in 1979 by Risdale et al . Knowledge of the conditions can quickly guide the etiological investigation and treatment. Most of the time, high mortality related to these conditions seems to be linked to a delay in diagnosis and treatment. This work shows the complexity of managing these conditions and is a first observation of such an association. Thus, we describe the case of a 37-year-old patient who was diagnosed with bone marrow necrosis and macrophage activation syndrome (MAS) in the context of exploring febrile pancytopenia secondary to HIV-related immunosuppression. 1 with opportunistic infection (Urinary tuberculosis) [1-3].

Observation

Ms. KF is a 37-year-old patient, housewife, residing in Abidjan and with no known medical-surgical history. She was hospitalized on September 18, 2023 for the investigation of febrile pancytopenia with deterioration in general condi-

tion. The patient had been symptomatic for approximately 3 months before admission. The signs were marked by a dry cough, neurosensory signs and anemic decompensation (headache, dizziness, exertional dyspnea and palpitations) for which she would have been transfused (1000 ml of packed red blood cells) without any notion of hyper sweating or weight loss. The clinical examination found a patient with.

- An altered general condition WHO 3,
- An anemic syndrome: mucocutaneous pallor, tachycardia;
- Hemolytic signs: jaundice and Coca-Cola urine;
- A tumor syndrome: Hackett type II splenomegaly with painful hepatomegaly with a blunt lower border;
- Without hemorrhagic syndrome.

In Front of This Table, the Examinations Carried Out Made It Possible to Find:

- on myelogram: on aspiration, the marrow juice had a citrine yellow appearance with numerous cellular debris including giant cells with numerous lipid vacuoles. Presence of neutrophils, almost all necrotic. Conclusion: cytological appearance suggests bone marrow necrosis (Figure 1).

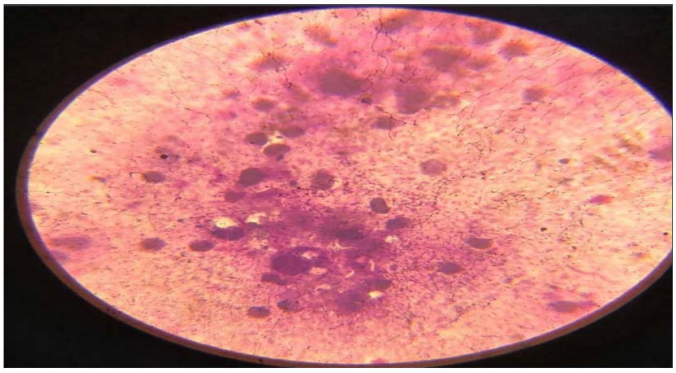

Figure 1: Image of Necrotic Cells with Some Debris

- Macrophage activation syndrome was retained (see table I): The probability is 99% with H-Score > 250 points. According to the HLH -Score 2004, 5 criteria are necessary to evoke a SAM.

Table I: The Elements of The Sam According to H Score and Hlh-Score 2004 In Our Patient.

The elements of the H-score criterion	Points	Elements of the HLH-2004 score	yes	No
Terrain immunodépression	18	Fièvre à 40°c	+	
Température 40°c	49	Splénomégalie	+	
Hépatosplénomégalie	38	Pancytopénie(Hb=4,7g/dl ; PLT= 82G/L et PNN= 1,2G/L)	+	
Pancytopénie	34	Triglycéride élevé	+	
Ferritine 3239 ng/L	35	Ferritine élevée	+	
Triglycéride 3.2 mmol/L	44	Image d'hémophagocytose au myélogramme		+
Fibrinogène 1.8 g/L	30	CD 25 soluble non réalisé		+
ASAT 69 UI/L	19	Activité NK non réalisé		+
Image d'hémophagocytose	0	Fibrinogène ≤ 1,5		+
Total	267	Total	5 critères	

Among the assessments carried out for diagnostic purposes, HIV-1 serology and urine testing for Mycobacterium by PCR came back positive. The sputum Baar performed as well as the hepatitis B and C serologies were negative in our patient. A biochemical assessment for prognosis was carried out (see table 2).

Table 2: Represents the Biochemical Parameters of Our Patient.

Biochemical parameters	Values
Gamma GT	203 UI/L
ALAT	24UI/L
Alkaline phosphatase (ALP)	442 UI/L
Bilirubin Total	30 UI/L
Conjugated bilirubin	26UI/L
LDH	667 UI/L
Urea	0,18 g/dl
Creatinine	12 mg/l
D-Dimers	3290
CRP	92 mg/l

From a therapeutic point of view, the management of macrophage activation syndrome requires the use of immunosuppressants (Etoposide), corticosteroids, immunoglobulins but above all treatment of the causal condition. Therefore, it was necessary to evaluate the risk/benefit ratio, due to the risk of immunosuppression linked to the use of corticosteroids or immunosuppressants, with the possibility of worsening of one or both (2) infections. existing. The provision of anti-tuberculosis drugs in a context of hepatic cholestasis was also difficult to initiate immediately in our patient because of the metabolism and elimination of the drugs. The emergency was therefore hematological resuscitation but our patient died on the 5th day of her hospitalization.

4. Discussion

Bone marrow necrosis (NM) is characterized by a bone marrow infarction leaving an eosinophilic background, poorly defined necrotic cells and preservation of cortical bone. Its incidence is estimated by some authors varying from 0.5 to 33% with a high frequency in patients after serious infections. Most of the time, bone marrow necrosis occurs in 90% of cases in patients with neoplastic pathology (malignant hematological diseases and metastatic solid cancers) and 10% can be associated with infections or even sepsis during sickle cell crises. Macrophage activation syndrome (MAS) is a nosologically entity comprising hereditary and acquired causes related to uncontrolled activation of lymphocytes and macrophages leading to phagocytosis of blood elements and release of pro-inflammatory cytokines (IL2, TNF-alpha, IL1, IL6, IL10 and INF-gamma). The majority of these cytokines measured during SAM are elevated justifying the term.

Hyper-inflammatory syndrome or "cytokine storm". To our knowledge, no publication has been the subject of such an association. Most patients diagnosed with SAM or spinal cord necrosis describe a similar clinical picture dominated by a deterioration in general condition, fever, signs of hemolysis (jaundice, hepatosplenomegaly and pallor) but also certain biological characteristics including cytopenia's (bi or pancytopenia), hepatic cytolysis with cholestatic syndrome, an increase in hemolysis stigmata (lactate dehydrogenase and free bilirubin) and a biological inflammatory syndrome. The vital prognosis of each of its conditions is related to the precocity of treatment but especially of the causal condition. The analysis of a few large series of studies on SAM has, however, made it possible to identify certain factors of poor prognosis, independently of the etiology, in particular age. over 30 years, the presence of a DIC, serum ferritin greater than 500 ng/l, hyperbilirubinemia greater than 34 mole/l, anemia with a hemoglobin level less than 10g/dl. thrombocytopenia less than 100 G/l, neutropenia below 0.5 G/l and increased alkaline phosphatase Most of these factors were found in our patient. The involvement of HIV in SAM has been described in the context of opportunistic infections. Bacterial infections concern 9% of etiologies in adults. Among the bacterial agents, mycobacteria predominate. Most tuberculosis diagnosed during SAM is extra-pulmonary with high mortality, especially in the absence of treatment [4-7].

It was difficult to say whether SAM and bone marrow necrosis were secondary to immunosuppression caused by HIV or to tuberculosis. Biological liver damage is found in 40% of SAM cases. This involves cytolysis, which may be accompanied by hepatocellular insufficiency. Cholestasis tends to occur late and is linked to a poor prognosis in SAM, an element found in our patient. Chronic developments of SAM are possible, particularly during AIDS. Untreated, the progression of SAM is fatal. Our patient died in a picture of multi-organ failure with severe sepsis. Such an observation was made by certain authors. Treatment in our patient would have consisted primarily of correction of cytopenias but also of management of the opportunistic infection and HIV immunosuppression. This treatment could be associated with immunosuppressants such as Etoposide = VP 16 and a high dose of corticosteroid therapy [8-10].

5. Conclusion

This observation draws the attention of practitioners to pancytopenia occurring in the context of immunosuppression. We should consider the possible existence of these conditions (SAM and/or bone marrow necrosis). This work also shows the complexity and importance of rapid and adequate management of these conditions if the clinical and biological conditions finally allow it to improve the vital prognosis of patients.

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Conflict of Interest

None

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