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Adult Macrophagic Activation Syndrome: About a Case

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Abstract

Macrophagic activation syndrome or lymphohistiocytic hemophagocytosis is characterized by an uncontrolled and uncontrolled stimulation of the immune system which results in the infiltration and destruction of multiple organs by cytotoxic cells and macrophages with hemophagocytosis, and systemic hyper inflammation.

Clinically, it results in fever, organomegaly, weight loss, and biologically in bi/pancytopenia, cytolysis/cholestasis, hyperferritinemia, and hemostasis disorders. The histological demonstration of the macrophage with hemophagocytosis remains the gold standard, whereas it is often absent at the very beginning, which can complicate the diagnosis. In adults, the clinical course is lymphohistiocytic hemophagocytosis mild, resolving with treatment of the etiology in question, with rapidly fatal multiorgan failure.

The aetiological diagnosis remains an essential step in the management since this syndrome is mainly secondary in adults.

Keywords: macrophage activation, diagnosis, infection, myelogram

Introduction:

Macrophagic activation syndrome (MAS), or hemophagocytic lymphohistiocytosis, is a rare dysfunction of the reticuloendothelial system responsible for an inappropriate and accentuated immune response against the host.

It is characterized by a nonspecific activation of the monocyte-macrophage system, the translation of which is proliferation and tissue infiltration of activated histiocytes-macrophages, with phagocytosis of the figured elements of the blood leading to peripheral cytopenias [1].

A distinction is made between primary macrophage activation syndromes, associated with genetic abnormalities, and secondary macrophagic activation syndromes, which can be induced by several aetiologies which have in common a significant stimulation of the immune system, in particular viral, bacterial and parasitic infections, neoplasms, with malignant hemopathies in the first place [2].

We report the observation of a patient hospitalized in the internal medicine department of the Avicenne military hospital in Marrakech for a macrophagic activation syndrome complicating a Klebsiella pneumoniae bacteremia

Vol. 5, No. 01; 2021

ISSN: 2581-3366

Observation:

This is a 30-year-old patient who was hospitalized in the internal medicine department for the management of a prolonged fever dating back 8 months, associated with intermittent watery diarrhea, weight loss of 14 kg and pain. inflammatory appearance of large and small joints. Clinical examination revealed a fever of 39 ° C with a deterioration in general condition. Examination of the lymph node areas revealed painful centimetric left sub angulo maxillary lymphadenopathy, centimetric bilateral axillary and infra centimetric inguinal lymphadenopathy on mucous skin examination, purpuric spots were found on the 2 feet and maculo-papules on the left forearm and slightly on the abdomen with oral thrush. The rest of the somatic examination did not show any other abnormality, including no hepatomegaly or splenomegaly Abdominopelvic ultrasound revealed homogeneous splenomegaly The complete blood count showed anemia at 7g / dl, normochromic normocytic a regenerative, thrombocytopenia at 80,000 / l, the white blood cell count was normal with 5000 blank / mm3. The hemostasis assessment was without abnormality. The biochemical assessment revealed an inflammatory syndrome with a CRP at 75 mg / l, an elevated LDH at 504 U / L, a level of ferritinemia raised at 1380ng / ml, a hypertriglyceridemia at 2.44 g / l, and a hypoalbuminemia at 21.5 g / l, hepatic tests and renal function were correct. The HBV, HCV, syphilis, CMV, rubella, toxoplasmosis and leishmaniasis serologies were negative.

The medullogram revealed a rich marrow with the presence of quite a number of macrophages with some images of macrophagic magmas (figure 2) and images of hemophagocytosis consistent with the diagnosis of MAS (figure 1).

The blood culture was positive for Klebsiella pneumoniae, which allowed us to retain the infectious etiology of MAS in our case.

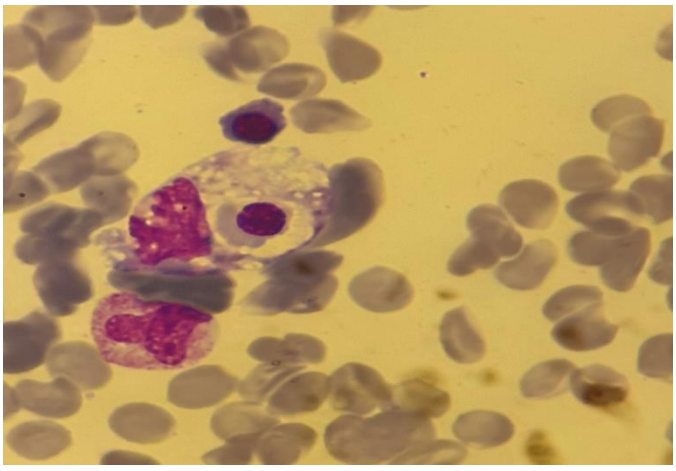

Figure 1: microscopic image of a MGG stained myelogram (× 1000) showing an image of hemophagocytosis (arrow): acidophilic erythroblast phagocytosed by a macrophage with a clear halo.

Vol. 5, No. 01; 2021

ISSN: 2581-3366

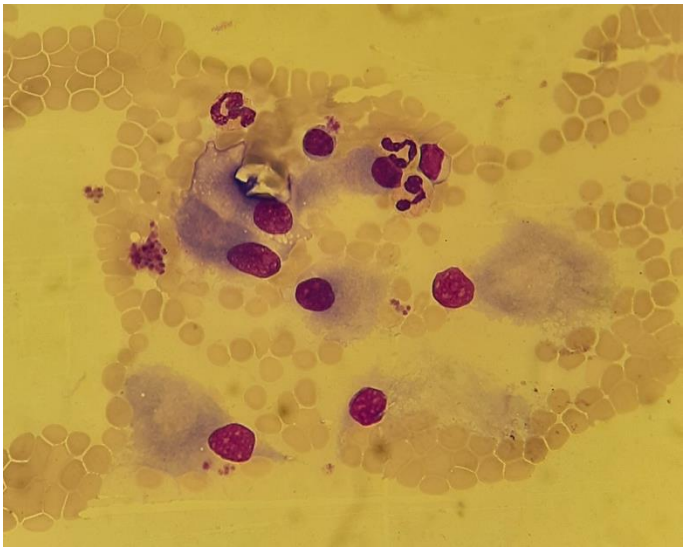

Figure 2: microscopic image of MGG stained myelogram (× 1000) showing multiple activated macrophages.

Discussion:

Hemophagocytic syndrome (HS) is divided into two entities. Primary hemophagocytic syndrome (PHS), with autosomal recessive inheritance, is found in the pediatric population, rarely with late expression in adulthood [3,4,5] and reactive hemophagocytic syndrome (RHS), non-genetic, occurring in all ages. This article is devoted to SHR which generally affects adults. The term "macrophagic activation syndrome", synonymous with SHR in the French-speaking literature, corresponds in Anglo-Saxons to SHR of rheumatological origin. [1] However, the distinction between an SHP and an SHR does not necessarily reflect reality.

SHP often follows a trigger and a heterozygous genetic mutation is sometimes found in SHR. [4,7] Finally, their clinical expression is similar.

The annual incidence of HS in the general population is estimated to be 1 in 800,000 people [2]. A review of the literature that included 775 cases of HS found a male / female sex ratio of 1.7 and a median age at diagnosis of 50 years [3], as in our case it is an adult subject.

HS is characterized by a prolonged febrile state, hepatosplenomegaly associated or not with lymphadenopathy, cytopenia affecting the three lineages in a variable manner, as well as multi-visceral involvement. In the series by Ramos-Casals et al. [4], the fever is universal (96%), frequently above 39 ° C. Hypertrophy of the hematopoietic organs is noted in two thirds of cases. Lung involvement is frequent, focal deficit, acute confusional state, convulsions, and even coma are described. Renal involvement is terminal in 50% of cases when it is present. [8]

We find a rich marrow with an infiltration by histiocytes and macrophages of benign cytological appearance, the number of which is discreetly increased. Macrophages are morphologically benign (small nucleus, fine chromatin, sometimes nucleolus, with a low nucleocytoplasmic ratio) and contain numerous intracytoplasmic vacuoles containing blood elements (erythrocytes, erythroblasts, granulocytes, platelets, lymphocytes) or their hematopoietic precursors intact or

Vol. 5, No. 01; 2021

ISSN: 2581-3366

partially digested. A single cell can phagocytize several cell types at the same time. [3]
However, it should be remembered that hemophagocytosis is a physiological phenomenon and for some authors, the percentage of macrophages in hemophagocytosis is an important diagnostic criterion (> 2% for Wong et al [9], and> 3% for Tsuda et al. al [10]). No study has found a relationship between the number of medullary histiocytes and the severity of the disease [11]. Imakushu [12] and Henter [14] require an image of hemophagocytosis without any notion of percentage.
Other laboratory abnormalities are often associated; aregenerative anemia with hemolysis stigmata [14], abnormalities in hemostasis due to hypofibrinogenemia or thrombocytopenia progressing to disseminated intravascular coagulation [15,16], increased LDH, hepatic cytolysis and hyponatremia.
The MAS is based on the presence of both clinical, biological, and cytological or histological criteria. The French group of NHL (JANKA 2012; GFLHH 2007) has defined diagnostic criteria, it consists in having at least five criteria out of the eight to make the diagnosis of MAS (table 1). Our patient met six out of eight criteria [4, 8].

Diagnostic criteria: At least five of the eight criteria
Fever
Splenomegaly
Cytopenias affecting at least two lineages Hemoglobin <9 g / dL yes 7 Platelets <100,000 / mm3 80,000 Polynuclear neutrophils <1000 / mm3
Ferritin > 500 µg/L oui 1380ng/ml
hypertriglyceridemia> 3 mmol / L and / or **hypofibrinogenemia** (<1.5 g / L)
Soluble IL2 receptor (sCD25) > 2400 U/mL
Decreased or absent NK activity
Hemophagocytosis (marrow, spleen, lymph nodes)

Table I: diagnostic criteria of macrophagic activation syndrome according to the French group of HLH and presented by the patient

In our study, the diagnosis of MAS was based on the following criteria:

- Fever yes 39
- Cytopenias affecting at least two lines: Hemoglobin <9 g / dL (Hg = 7 g / dL) and
- Platelets <100,000 / mm3 80,000
- hyperFerritinemia 1380ng / ml
- hypertriglyceridemia at 2.44 g / l and hypoalbuminemia at 21.5 g / l
- Hemophagocytosis by spinal cord smear

The etiological diagnosis of MAS in adults remains a very important step in view of its numerous and sometimes underestimated aetiologies. The current pathophysiological model

Vol. 5, No. 01; 2021

ISSN: 2581-3366

includes a predisposing factor and a triggering factor. The predisposing factor is a cause of acquired or not acquired immunosuppression, responsible for the dysfunction of cytotoxic cells, such as malignant hemopathy, infection by the human immunodeficiency virus (HIV), immunosuppressive treatments, transplantation of hematopoietic stem cells, etc. In this predisposing terrain, infection, sometimes the introduction of treatment for the known disease, or its natural course, triggers SHR. [3]

Ramos-Casals et al. three types of pathologies, alone or associated, can be found at the origin of SHR in 2197 patients: infections (50%), cancers (47%) and autoimmune diseases (13%) (Table 2). , three series report similar results with a preponderance of neoplasms (48-60%) compared to infections (23-34%). [17.18]

as in our case, infectious origin is the most common cause. Viruses are the main infectious agents, in particular Epstein Barr virus (EBV), with 66-69% of infections. [19] Koch's bacillus is the main bacterium.10 Certain parasitoses such as leishmaniasis or toxoplasmosis are sometimes involved. [8] Among neoplasms, 94-100% are hematologic diseases, mainly non-Hodgkin T lymphomas. Systemic diseases such as systemic lupus erythematosus (SLE) are responsible for 3-13% of SHR. [8] Transplants, transplant rejection or immunosuppressive treatments are recognized aetiologies. [20] Some SHRs occur after surgery, vaccination, or with diabetes, kidney failure, cirrhosis, or pregnancy. [8,21] Sometimes no predisposing / triggering factor is found, the syndrome is said to be idiopathic.

Table 2: Pathologies associated with SHR [8]

50% infections
· 69% viral: EBV >> HIV> HSV> CMV> viral hepatitis> influenza, parvovirusB19 · 19% bacteria: mainly tuberculosis · 5% parasites: histoplasmosis, leishmaniasis, malaria, toxoplasmosis · 3% mushrooms · 4% non-specific
47 % neoplasms
· 94% hematologic neoplasia: 67% non-Hodgkin lymphoma · 3% solid tumor · 3% not specified
13% autoimmune diseases
· 48% systemic lupus erythematosus · 20% Still's disease · 7% rheumatoid arthritis · 4% vasculitis · 4% chronic inflammatory bowel disease · 17% other
4 % idiopathic / unknown
EBV: virus d' Epstein Barr; VIH: virus de l'immunodéficience humaine; HSV: virus herpès simplex; CMV: cytomégalovirus.

Vol. 5, No. 01; 2021

ISSN: 2581-3366

The prognosis of MAS is often pejorative, with significant mortality, especially since it is underestimated by clinicians [22], hence the importance of vigilance during clinical exploration, as well as good clinical-biological collaboration.

Conclusion:

MAS is a rare situation in everyday practice, which unfortunately makes it underestimated and the cause of significant mortality. The diagnosis should be made in the event of febrile pancytopenia, and the aetiological assessment is guided by questioning and clinical examination. Infectious etiologies are dominated by viruses.

Bibliography :

1 Claire Larroche Le syndrome d'activation macrophagique acquis de l'adulte : comment le reconnaître et le traiter ? Revue du rhumatisme 79 (2012) 194–200

2 S. Valade · E. Canet · E. Mariotte Syndrome d'activation macrophagique d'origine infectieuse : le point de vue du réanimateur Méd. Intensive Réa (2018) 27:239-248

3 Drs FIONA NOVOTNY a, FEDERICO SIMONETTA b, KAVEH SAMII b, Prs YVES CHALANDON b et JACQUES SERRATRICE Syndrome hemophagocytaire reactionnel Rev Med Suisse 2017 ; 13 : 1797-803

4 Zhang K, Jordan MB, Marsh RA, et al. Hypomorphic mutations in PRF1, MUNC13-4, and STXBP2 are associated with adult-onset familial HLH. Blood 2011;118:5794-8.

5 Ueda I, Kurokawa Y, Koike K, et al. Late-onset cases of familial hemophagocytic lymphohistiocytosis with missense perforin gene mutations. Am J Hematol 2007;82:427-32.

6 Emile JF, Abla O, Fraitag S, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood 2016;127:2672-81.

7 Zhang K, Chandrakasan S, Chapman H, et al. Synergistic defects of different molecules in the cytotoxic pathway lead to clinical familial hemophagocytic lymphohistiocytosis. Blood 2014;124:1331-4.

8 Ramos-Casals M, Brito-Zerón P, López-Guillermo A, et al. Adult haemophagocytic syndrome. Lancet 2014;383:1503-16.

9 Wong K. F., Chan J. K. Reactive hemophagocytic syndrome, a clinico-patliologic study of 40 patients in Oriental population. Ain J Med. 1992; 93:177-80.

10 Tsuda H., Shirono K. Serum lipids in adult patients with hemophagocytic syndroine. Am J Hematol. 1996;53:285

11 Tiab M., Mechinaud F., Hamidou M., Gaillard F., Raffi F., Harousseau J. L. Syndromes hémophagocytaires: une série de 23 observations. Ann Med Interiie (Paris). 1996; 147:138-44.

12 Imashuku S. Differential diagnosis of hemophagocytic syndrome: underlying disorders and selection of the most effective treatment. Int J Hematol. 1997;66:135-5

13 Henter J. l., Elinder G., Soder O., Ost A. Incidence in Sweden and clinical features of familial hemophagocytic lymphohistiocytosis. Acta Paediatr Scand. 1991;80:428-35.

14 Michot M , Hiéc M, Galicier L , Lambotte O, Michel M, Bloch-Queyratf C , Herminef O, Le syndrome d'activation lymphohistiocytaire de l'adulte La Revue de médecine interne 34 (2013)

15 Wong KF, Chan JK. Reactive hemophagocytic syndrome – a clinicopathologic study of 40 patients in an Oriental population. Am J Med 1992;93:177–80.

16 Kaito K, Kobayashi M, Katayama T, Otsubo H, Ogasawara Y, Sekita T, et al. Prognostic factors of hemophagocytic syndrome in adults: analysis of 34 cases. Eur J Haematol 1997;59:247–53.

17 Rivière S, Galicier L, Coppo P, et al. Reactive hemophagocytic syndrome in adults: A retrospective analysis of 162

18 Parikh SA, Kapoor P, Letendre L, et al. Prognostic factors and outcomes of adults with hemophagocytic lymphohistiocytosis. Mayo Clin Proc 2014; 89:484-92.

19 Li J, Wang Q, Zheng W, et al. Hemophagocytic lymphohistiocytosis: Clinical analysis of 103 adult patients. Medicine (Baltimore) 2014 ;93:100-5.

20 Abdelkefi A, Ben Jamil W, Torjman L, et al. Hemophagocytic syndrome after hematopoietic stem cell transplantation: A prospective observational study. Int J Hematol 2009;89:368-73.

21 Tumian NR, Wong CL. Pregnancy-related hemophagocytic lymphohistiocytosis associated with cytomegalovirus infection: A diagnostic and therapeutic challenge. Taiwan J Obstet Gynecol 2014;54:432-7.

22 R.RekikaF.MorazinaA.LumbrosoaJ.StirnemannbP.MontraversaR.Gauzita Reactive haemophagocytic syndrome and multiple organ failure in intensive care unit patients Annales Françaises d'Anesthésie et de Réanimation Volume 23, Issue 12, December 2004, Pages 1189-1191