Case study

Macrophagic activation syndrome revealing Hodgkin lymphoma: Case report

ABSTRACT

Macrophage activation syndrome (MAS), or hemophagocytosis syndrome, is a clinical-biological entity characterized by proliferation and non-specific activation of macrophages of the reticulo-histiocytic system, with phagocytosis of formed blood elements. It is a rare pathology associating clinical signs: fever, hepato-splenomegaly, lymphadenopathy and biological abnormalities (bi- or tricytopenia, hepatic cytolysis, elevation of LDH, coagulopathy) with an image of hemophagocytosis on a cytological or histological sample. None of these signs are specific. However, the association with hypertriglyceridemia and hyperferritinemia is very strongly suggestive of SAM. This syndrome can be primary in children or secondary to various conditions at any age. Viral infections by herpes viruses (especially Epstein-Barr and cytomegalovirus), by intracellular germs (tuberculosis), but also by the pyogenic bacteria are, together with neoplasias (lymphomas mainly) and some autoimmune diseases (lupus and Still), the main causes of SAM to look for. If T or NK lymphomas are the classic causes of reactive SAM, its association with Hodgkin's lymphoma is exceptional. It is a diagnostic and therapeutic emergency given the risk of progression to fatal multi-visceral failure in the absence of rapid treatment.We report here a case of SAM that revealed Hodgkin's lymphoma in a 5-year-old child.

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INTRODUCTION

Macrophage activation syndrome (MAS) is a rare disease [1], characterized by a very exaggerated and uncontrolled immune response.It is potentially fatal if not quickly treated [2].

If lymphomas are classic causes of MAS, the association with Hodgkin's lymphoma (HL) is exceptional [3].

CASE REPORT

The patient is a boy aged 5 and a half, who presented 36 days before admission with a prolonged fever. On clinical examination, the child is febrile at 39.5 C, splenomegaly and cervical lymphadenopathy. The biological assessment showed hypochromic microcytic anemia with hemoglobin level at 7.6 g/l. Mean corpuscular volume is 70 fl and mean corpuscular hemoglobin content is 23pg, hyperferritinemia 1366 ng/ml, thrombocytopenia 98 g/l, hypertriglyceridemia 3.16 g/l, sedimentation rate 100mm in the first hour, fibrinogen 7.5 g/l, c-reactive protein 328 mg/l. Hepatic cytolysis (Aspartateaminotransferase 251 ui/l, alanineaminotransferase 182 ui/l, LDH 1054 ui/l), and hemophagocytosis in the bone marrow. Thus, in the presence of Henter et al'sfive criteria, the diagnosis of macrophage activation syndrome was made.The etiological assessment revealed a reactivation of the Epstein-Barr virus (EBV), raising the suspicion of lymphoma. On the cervico-thoraco-abdominal CT scan: appearance in favor of homogeneous hepatosplenomegaly (Figure 1) with above and below diaphragmatic lymphadenopathy (Figure 2). Cervical lymph node biopsy: in favor of scleronodular type Hodgkin lymphoma. The patient was transferred to the pediatric oncology department.

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DISCUSSION

The standard definition of SAM is based on the criteria of Henter et al., 2004 [3]. Diagnosis is possible when at least five of the following signs are present: fever, splenomegaly, cytopenia (at least two of: hemoglobin less than 9 g/dl, platelets less than 100 G/l, neutrophils

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less than 1 G/l), hypertriglyceridemia (greater than 3 mmol/l) or hypofibrinogenemia (lower than 1.5 g/l), hyperferritinemia (greater than 500 µg/l), increase in CD25 (greater than 2400 IU/ml), decrease in NK lymphocyte activity and the presence of hemophagocytosis in the bone marrow, spleen or lymph nodes. Hypertriglyceridemia and hyperferritinemia are the most suggestive abnormalities of SAM when associated with cytopenias [4] as is the case of our patient. The liver balance sheet is always disturbed during SAM. Usually the LDH level is high. When the diagnosis of SAM is made, the search for the triggering element is imperative for the prognosis. In the case of our patient, infection with the Epstein-Barr virus was the triggering factor.

The study by Takahashi et al. had clearly demonstrated the difference in prognosis between lymphoma-related SAM versus other SAM etiologies. In these SAMs, the median survival was short (83 days), like overall survival (8%), which differed from other SAMs linked for two thirds to viral infections and associated with 83% overall survival [5]. Among MAS secondary to lymphomas, the discovery of HL is an exceptional situation, the most common being T or NK lymphomas [6]. The LH associated with a SAM seems a particular entity. In all cases, HL precedes or is contemporary with the discovery of SAM. Another particularity is the very strong association with EBV, which again contrasts with the classic forms of LH (20–40%) [7]. The presence of EBV raises the hypothesis of an immune deficiency with respect to EBV, thus patients with a history of infectious mononucleosis presenting a high risk of developing LH [8]. Finally, the evolution is rarely favorable.

CONCLUSION

The diagnosis of SAM should be considered in the presence of persistent fever associated with characteristic biological signs. When the diagnosis of SAM is retained, all means must

be implemented to identify the triggering cause. the possibility of an exceptional LH should not be ruled out.

Figure 1

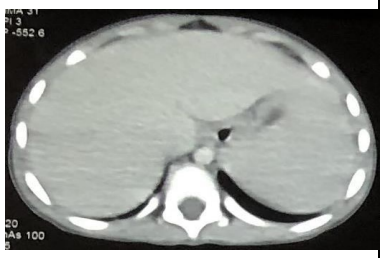

Figure 2

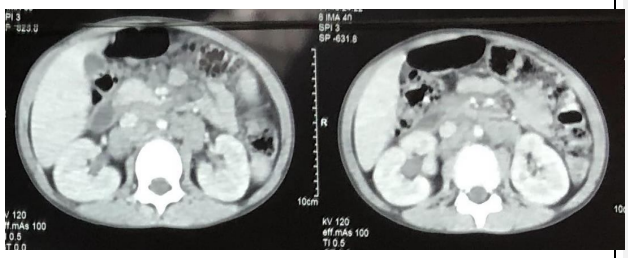

Fig 1and 2: The cervico-thoraco-abdominal CT scan

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