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Autoimmune hepatitis complicated by bone marrow aplasia: A case report

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Abstract

Post-Hepatitis Bone Marrow Aplasia (BMA) is a rare disease characterized by secondary damage to the primary bone marrow cell compartment. Severe bone marrow aplasia associated with autoimmune hepatitis is a well-described form of AM, occurring within 6 months of an increase in Alanine Aminotransferase (ALAT) of at least five times the upper limit of reference values, and is generally negative for known hepatic viruses (A,B,C). We report the case of a 07-year-old patient with no particular pathological history, presenting with autoimmune hepatitis revealed by cholestatic icterus evolving for 1 month with hepatomegaly and hepatic cytolysis and confirmed by positive anti LC1 ACs; the evolution was marked by the appearance of diffuse petechial lesions with gingival hemorrhage revealing pancytopenia on the haemogram linked to severe bone marrow aplasia.

Keywords: Autoimmune hepatitis; Bone marrow aplasia; Immunosuppressant; Marrow transplantation.

Introduction

Autoimmune seronegative hepatitis represents a heterogeneous group of diseases of unknown cause, characterized by necrotic-inflammatory hepatocytic lesions with the presence of specific antibodies and high corticosensitivity. These are rare pathologies that can affect both sexes at any age, and are rarely complicated by severe bone marrow aplasia; the main pathogenic mechanism responsible for bone marrow aplasia in autoimmune hepatitis is immunological dysregulation, due to the presence of immunological abnormalities (a decreased ratio of CD4/CD8 cells in the peripheral blood), the presence of activated cytotoxic T cells secreting interferon-gamma which inhibits hematopoiesis) in HAI, and the good response observed after immunosuppressive treatment [1,2], bone marrow aplasia can develop in up to 1 in 3 cases of clinically identifiable seronegative hepatitis. Severe bone marrow aplasia associated with autoimmune hepatitis has a poor prognosis, often leading to death. Treatment is based on supportive care aimed at managing episodes of febrile neutropenia with appropriate antibiotic therapy, and correcting anemia and thrombocytopenia with transfusions of packed red blood cells and platelets, as well as specific hematopoietic stem cell transplantation and immunosuppressive therapy.

Clinical observation

The child is 07 years old, with no pathological history who had been admitted to our training center for the etiological assessment of cholestatic icterus that had been evolving for 1 month, aggravated by the onset of neurological disorders consisting of agitation, confusion, and alteration of the nychthemeral cycle, with no other associated signs, in particular no hemorrhagic signs or hypoglycemia, and in whom the clinical examination objectified a soft, painless hepatomegaly, all evolving in a background of altered general condition.

The biological workup revealed a collapsed PT, with a Koller negative, with major cytolysis at 25 times normal, with positive

anti LC1 ACs testifying to autoimmune hepatitis at the stage of hepatocellular insufficiency with a picture of hepatic encephalopathy. The patient received three boluses of solumedrol, then was put on corticosteroid therapy 1 mg/kg/D. The evolution was marked by the appearance of lesions diffuse petechiae with gingival hemorrhage revealing pancytopenia on blood count.

A BOM was performed, confirming bone marrow aplasia.

The patient was put on immunosuppressive therapy (immure 2 mg/kg/d) with transfusion of cytapheretic platelets and phenotype Leuk reduced blood if required, with good clinical and biological improvement.

Discussion

Acquired Medullary Aplasia (AM) is a rare disease resulting from secondary damage to the primitive cells of the bone marrow. The destruction of hematopoietic stem cells appears to be due to several factors, including an autoimmune component and genetic abnormalities. AM is considered severe if two of the following criteria are met: neutrophils less than $0.5x10^9$/L, platelets less than $20x10^9$/L, and reticulocytes less than $20x10^9$/L, accompanied by marrow paucity according to examination (marrow cellularity less than 25% or between 25 and 50% with less than 30% residual hematopoietic cells) [3,4]. Severe bone marrow aplasia due to autoimmune hepatitis is a well-documented form, occurring in the months following a rise in Alanine Aminotransferase (ALT) levels of at least five times the upper limit of normal values. It is generally negative for known hepatic viruses (A,B,C) [5]. In our patient's case, autoimmune hepatitis manifested itself with transaminase levels (ALAT, ASAT) above 25 times normal, while presenting normal liver serologies, bone marrow aplasia developed four months later. Seronegative autoimmune Hepatitis (HAI) is a rare disease that can lead to bone marrow failure in 25% of cases. When AM is associated with HAI, the latter manifests as episodes of jaundice and hepatic cytolysis. The course is usually acute, but can sometimes be prolonged or recurrent. HAI-specific antibodies (such as anti-smooth membrane antibodies, antinuclear antibodies and antihepatic cytosol antibodies) are usually negative [6]. Our patient had a prolonged hepatitis evolving for 5 months, which was not resolved until after administration of azathioprine, his immunological work-up was negative and the diagnosis of HAI was retained by positive anti LC1 ACs. Several studies indicate that the main pathogenic mechanism behind bone marrow aplasia in the context of autoimmune hepatitis is immunological dysregulation. This condition is characterized by immunological abnormalities, including a decreased ratio of CD4/CD8 cells in the peripheral blood, as well as the presence of activated cytotoxic T cells that secrete interferon-gamma, thereby inhibiting hematopoiesis. Moreover, a favorable response is generally observed after immunosuppressive therapy [7]. The prognosis of severe bone marrow aplasia associated with autoimmune hepatitis is generally unfavorable, with an oftenfatal course in the absence of treatment. Management relies mainly on supportive care, aimed at treating episodes of febrile neutropenia with appropriate antibiotic therapy, as well as correcting anemia and thrombocytopenia with packed red blood cell transfusions in cases of severe or poorly tolerated anemia, and platelet transfusions in cases of hemorrhagic syndrome or very profound thrombocytopenia, as was the case with our patient. In addition, specific treatment may include hematopoietic stem cell transplantation in young patients with a geno-identical donor (25% sibling match), offering survival in excess of 80% [8]. Our patient was put on immunosuppressive therapy and symptomatic treatment with a good clinical and biological evolution.

Conclusion

Autoimmune hepatitis-related bone marrow aplasia is an extremely rare and serious condition, requiring rapid diagnosis and immediate, appropriate management. Bone marrow transplantation remains the treatment of choice.

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