Macrophagic activation syndrome

Revealing tuberculosis (case report)

Abstract

We present a case involving an immunocompetent infant diagnosed with miliary tuberculosis complicated by macrophage activation syndrome. Macrophage activation syndrome (MAS), also known as bone marrow hemophagocytosis, presents as a non-specific clinical condition characterized by fever and hepatosplenomegaly. A 22-month-old infant from a non-consanguineous marriage, the only child in the family, was admitted to a regional hospital due to prolonged fever lasting 15 days. The syndrome can manifest as a primary disorder (familial HLH) due to various genetic mutations or as a sporadic secondary disorder triggered

by infections, autoimmune diseases, or malignant conditions. The early initiation of antibacillary treatment in AMS complicating tuberculosis without the use of immunosuppressive drugs provides better management and improves the vital prognosis.

Keywords: hemophagocytosis, antibacillary treatment, immunosuppressive drugs, Macrophage activation syndrome

Introduction: Macrophage activation syndrome (MAS), also known as bone marrow hemophagocytosis, presents as a non-specific clinical condition characterized by fever and hepatosplenomegaly. Common laboratory findings include pancytopenia, hypertriglyceridemia, and hyperferritinemia. Despite its rarity, MAS has been reported in association with tuberculosis. Here, we present a case involving an immunocompetent infant diagnosed with miliary tuberculosis complicated by macrophage activation syndrome

Observations: A 22-month-old infant from a non-consanguineous marriage, the only child in the family, was admitted to a regional hospital due to prolonged fever lasting 15 days. There was no history of tuberculosis contagion, but the infant had a history of consuming unpasteurized milk. The fever was accompanied by anorexia and weight loss.

Initial investigations revealed normal results from cerebrospinal fluid and urine tests, sterile blood cultures, anemia with hemoglobin levels of 8g/l, and a C-reactive protein (CRP) level of 200 mg/l. Treatment with a third-generation cephalosporin was initiated and continued for 7 days without improvement. The fever persisted, and the infant's general condition worsened.

On day 21 of fever, the patient was transferred to a level 3 hospital. Upon admission, the infant appeared conscious but pale, with a skin rash corresponding to the fever peak. The infant was hypotonic, experiencing polypnea and tachycardia, and was irritable. The body temperature was recorded at 38°C, with no presence of purpuric

spots or jaundice. The patient was hemodynamically stable but exhibited hepatomegaly, with a liver span of 12 cm.

The paraclinical work-up revealed hypofibrinogenemia (1.4 g/l), hyperferritinemia (926 ng/ml), hypertriglyceridemia (2.70 g/l, reference range: 0.6-1.50), hypoproteinemia (48 g/l), and anemia (8 g/dl). Both the tuberculin skin test (TST) and gastric tube test for BK were negative, while Quantiferon testing returned positive results.

Chest X-ray findings displayed an interstitial syndrome consistent with a tubercular miliary appearance (see figure 1), while thoraco-abdominal CT scan results exhibited bilateral micronodular infiltration of symmetrical and homogeneous distribution throughout the parenchyma, indicative of an interstitial syndrome. No mediastinal adenopathy was observed, and homogeneous hepatomegaly was noted (see figure 2).

Additionally, the medullogram revealed evidence of haemophagocytosis (see figure 3).

The patient was commenced on anti-bacillary treatment, resulting in a favorable outcome

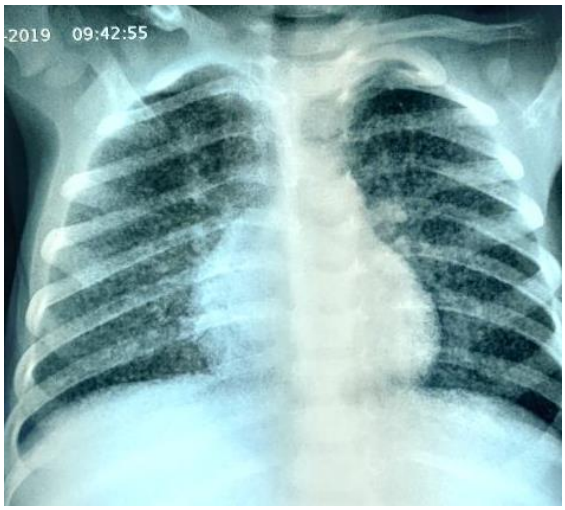
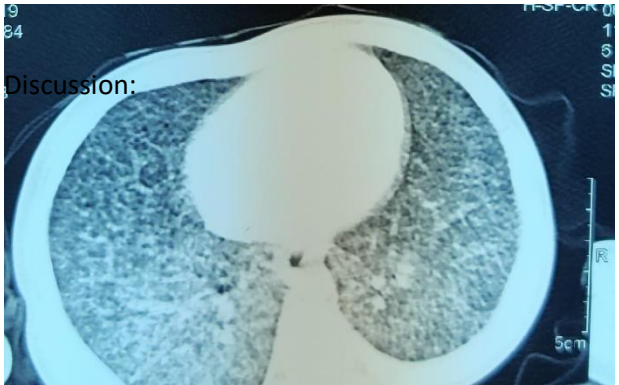
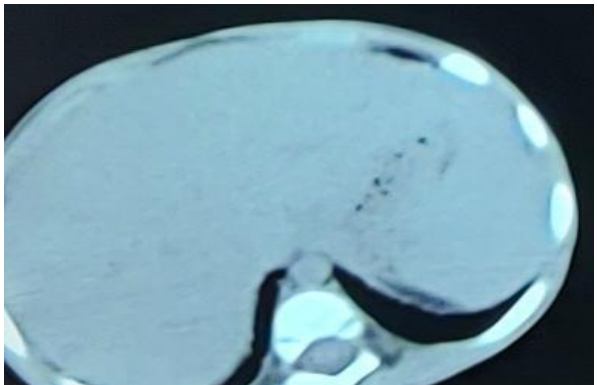


Figure 1: Chest X-ray demonstrating a tubercular miliary pattern





Discussion:

Figure 2: Bilateral micronodular infiltration symmetrically and homogeneously distributed throughout the parenchyma, resulting in an interstitial syndrome. No mediastinal adenopathy is evident (A). Figure 2B: Homogeneous hepatosplenomegaly

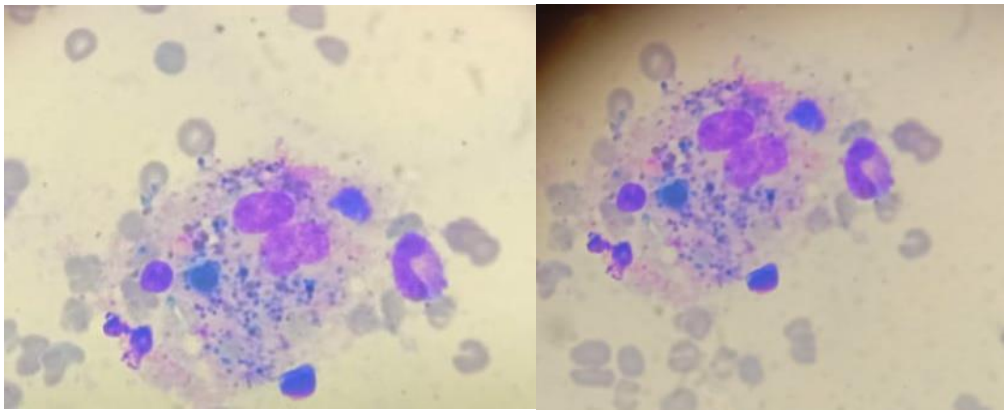


Figure 3: Presence of numerous images showing haemophagocytosis

Macrophage activation syndrome (MAS), also known as hemophagocytic lymphohistiocytosis (HLH), was initially described by Scott and Robb-Smith in 1939. It is characterized by an inadequate immune response, marked by the proliferation and activation of macrophages, leading to excessive phagocytosis of hematological precursors such as erythrocytes, platelets, etc. This syndrome can manifest as a primary disorder (familial HLH) due to various genetic mutations or as a sporadic secondary disorder triggered by infections, autoimmune diseases, or malignant conditions.

According to the histocytes society protocol entitled HLH 2004 (2), the diagnosis of HLH can be established if five of the following eight diagnostic criteria are met (i) fever (27 days), (ii) splenomegaly, (iii) cytopenia (≥ 2 lines) anaemia (haemoglobin <9.0 g/dL), thrombocytopenia (<100,000 cells) and neutropenia (ANC <1,000), (iv) hypertriglyceridaemia (≥265 mg/dL) and/or hypofibrinogenaemia (<1.5 g/L), (v) haemophagocytosis (bone marrow, spleen, lymph node), (vi) low/absent NK cell activity, (vii) hyperferritinaemia (2500 mcg/L) and (viii) increase in soluble CD25 >2400 units/mL. In our case, six out of eight criteria were present.

Joshua Osawicki et al conducted a search of the English-language literature and identified 13 other cases of tuberculosis complicated by HLH in children or adolescents. The age of the patients at presentation ranged from 2 weeks to 17 years. With the inclusion of the current case, there were 8

patients aged 2 months or less. Three patients died, despite immunomodulatory therapy combined with anti-tuberculosis treatment in two. In 1 fatal case, which occurred in a non-endemic setting (USA) and despite a thorough investigation, the diagnosis of tuberculosis remained unknown until an autopsy was performed. Of 11 surviving patients, 3 received treatment only antituberculosis and 8 received both antituberculosis and immunotherapies (4 had corticosteroids, 5 had intravenous immunotherapy, 1 cyclosporine and 1 etoposide). In 10 out of 14 cases, there was evidence of disseminated TB, including in 6 of the patients aged 2 months or less, with pulmonary disease in the remaining 4 cases. All patients had fever, 13 of 14 had organomegaly and 13 of 14 had thrombocytopenia and/or pancytopenia (3).

Often, in the literature, when tuberculosis is associated with macrophagic activation syndrome, the two elements are diagnosed simultaneously. In addition, the diagnosis of tuberculosis may be identified late in the course of the diagnosis of MAS(4).

Thanks to PCR, the diagnosis of tuberculosis was detected in 70% of cases, whereas culture was only able to detect tuberculosis in 3.3% of cases. (5)

Conclusion: Macrophagic activation syndrome is a serious, often unrecognised, life-threatening condition which can complicate various infectious diseases. tuberculosis, the early initiation of antibacillary treatment in AMS complicating tuberculosis without the use of immunosuppressive drugs provides better management and improves the vital prognosis

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