Macrophage Activation Syndrome in a Child with Systemic Juvenile Rheumatoid Arthritis

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Abstract:

Macrophage activation syndrome (MAS) is a rare and potentially fatal complication of rheumatic disorders in children; we describe a 14-month old boy in whom MAS developed as first presentation of systemic juvenile rheumatoid arthritis (S-JRA). He suffered from fever, bleeding tendency from mouth, gastro-intestinal tract, ecchymosis & site of injections followed by bilateral wrist swellings. Physical examination revealed cervical lymphadenopathy & hepatosplenomegaly. Laboratory findings were abnormal liver enzymes, coagulopathies resembling disseminated intravascular coagulation, anemia, thrombocytopenia and abnormal C.S.F. findings.

Up to the best of my knowledge this could be the **first MAS associated with S-JRA in Iraq.**
Key words: Macrophage Activation Syndrome, Arthritis, Juvenile Rheumatoid

Introduction

Macrophage activation syndrome (MAS) is a clinical entity characterized by serious liver diseases, hematologic abnormalities, coagulopathy resembling disseminated intravascular coagulation, and neurologic involvement. MAS is known to be a severe and potentially life –threatening complication of rheumatic disorder, especially systemic juvenile rheumatoid arthritis (S-JRA) [1].

MAS is a rarely –occurring disorder, and only sporadic case reports or several studies with relatively small number of patients are available in the literatures [2-4]

Here we describe a 14 – month old boy, in whom MAS developed as a complication of S-JRA.

Case Report

A 14 month old boy presented with history of fever, drowsiness, and two attacks of generalized seizures, few hours apart.

Two days later the baby developed severe pallor, irritability, ecchymosis and bleeding from mouth, gastro internal tract and injection sites. On examination: temperature was 40^0C , heart rate 145 per minute,
respiratory rate65 per minute.

The patient looks pale, drowsy and irritable, no jaundice or cyanosis .

There are multiple ecchymotic spots on the upper arms and abdomen with cervical, axillary and inguinal lymph nodes enlargement.
Chest examination reveals good air –entery with no added sounds, heart normal 1st and 2nd heart sounds with no murmur or pericardial rub.
Abdominal examination reveals large spleen, 4 cm below costal margin, hepatomegaly, 6cm below costal margin, with no clinical evidence of ascitis. Fundoscopy was normal.

On Admission CBP showed Hb 4gm /dl, WBC- 3000 /cmm with neutrophils predominance (91%).
Platelets 75000/cmm.ESR 25mm/hr.
Dipstick test for kalaazar was negative ,widal and rose bengal tests were negative, Blood urea

60 mg /dl ,serum creatinine 0.8 mg /dl , **SGPT 275 I.U./L**, alkaline phosphatase 35 unit /ml , **total serum bilirubin 2mg /dl**
Prothrombin time -21 (sec), aPTT -40 (sec), bleeding time more than 10 min. C.S.F. showed sugar 52 mg/ dl, **protein 132 mg /dl** with no cells and negative culture.
Blood cultures twice were negative.
Blood sugar 70 mg /dl, serology for hepatitis negative
Bone marrow (B.M) examination, which was performed as a further work up of hematologic abnormalities showed normocelluler marrow with a cellularity of 95 % .Granulocytic and megakaryocytic lineages were normal in maturation, but erythroid lineage, was hypoplastic with abundant benign looking macrophages.
Echocardiography was normal
Ultra sound reveals slight ascitis fluid**, hepatosplenomegaly** with slight right pleural effusion.

He was diagnosed as DIC secondary to overwhelming sepsis, treated with ceftriaxone 100mg/kg /day, chloramphenicol 100 mg/kg /day. Two blood transfusions with daily fresh frozen plasma for 4 days and 2 doses of vitamin k were given. Bleeding stopped after two days from admission with slight improvement of general condition but the fever persist (which was intermittent high pattern) for 14 days.

At this time we revise most of the investigations regarding bleeding time , PT , aPTT , liver function tests , renal function tests , U/S , all returned to normal except CBP which showed **Hb 9 gm/dl** ,**WBC 14000/cmm with shift to the left , platelets count normal & ESR 135 mm/hr.**

We changed the antibiotics to vancomycin & piperacillen.On day 6 of the new treatment, the baby developed **salmon pink-colored rash** on the abdomen with spike of fever which disappeared when fever subsided, next morning the baby developed **bilateral wrist swellings with synovial thickening** (figure 1), so we changed our diagnosis to **S-JRA with MAS**.

We stopped the antibiotics & started with prednisolone & brufen, the fever subsided within 3 days with marked improvement of general condition

Discussion

In 1985, Hadchouel et al. described seven patients who showed unique clinical features with hematologic, neurologic and hepatic abnormalities in association with S-JRA [5, 6]. Since they suggested the term MAS in 1993, MAS has been commonly used to identify the hemophagocytic syndrome that may develop in children with chronic rheumatic diseases, particularly S-JRA.

MAS is a potentially fulminant disorder, and occur during the clinical course of underlying S-JRA characterized by repetitive disease flares. It is thus very important to differentiate the onset of MAS from a flare of the disease, as they have different treatments and prognoses. Clinically, the patterns of fever and skin rash are somewhat different, although both of the diseases share lymphadenopathy and hepatospelenomegaly [1]. From the aspect of laboratory findings, decreases of blood cells, erythrocyte sedimentation rate, and fibrinogen present striking contrasts to S-JRA. Hypertriglyceridaemia, elevated liver enzymes, and abnormal coagulation profile are consistently found.

The pathognomonic feature of MAS is numerous well differentiated macrophages actively phagocytosing hematopoietic elements in BM. Hemophagocytic macrophage can also be found in spleen or lymph nodes.

The patient described here showed typical clinical and laboratory feature of MAS, however, BM examination revealed false negative result due to a sampling error or the timing of aspiration during disease course [4]. Accordingly, morphologic confirmation is not a prerequisite for the diagnosis of MAS.

Triggering episodes like infection or medication may precede the onset of MAS, and they have been reported in at least 58% to 88% of patients [1,2].

In summary, we report a case of **MAS** triggered by severe infection in 14-months old boy that was

found to have **S-JRA** three weeks later, which could be the **1st case described in Iraq.**

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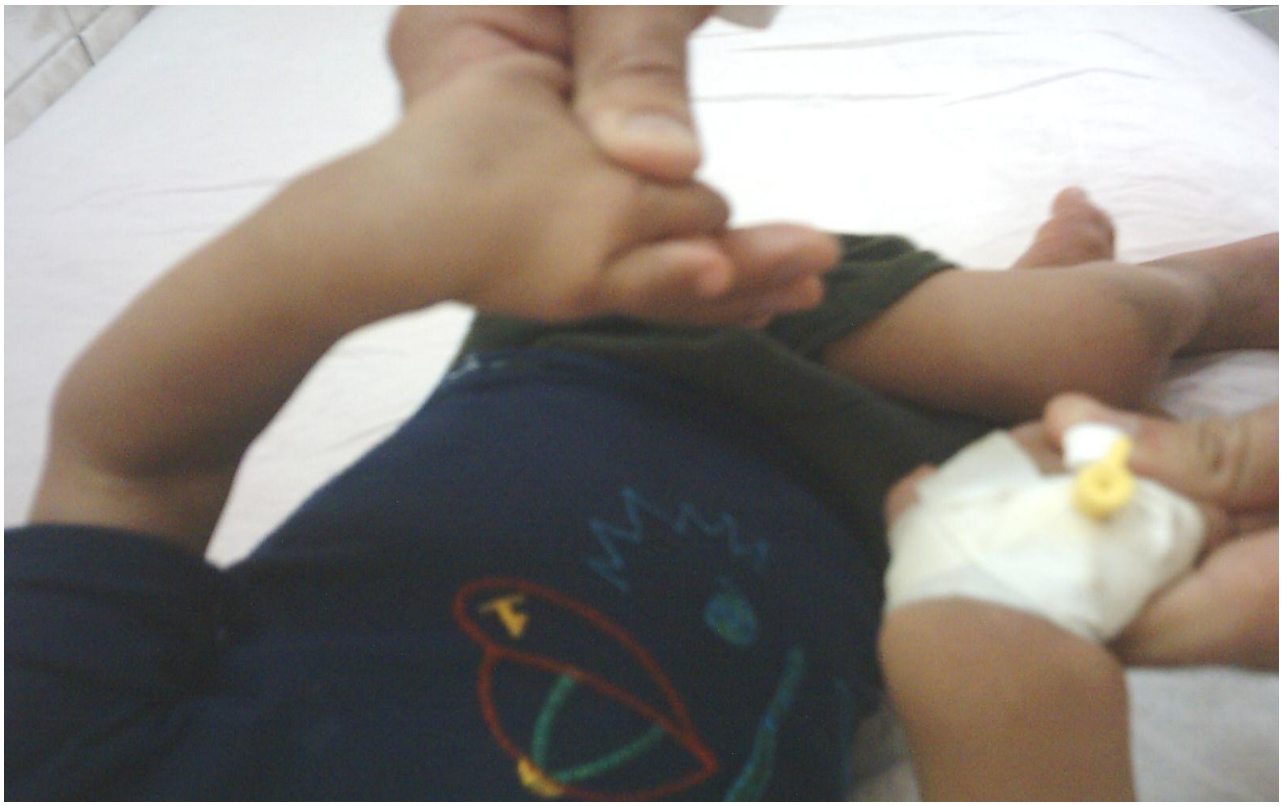

Figure 1 swelling of both wrists