Macrophage Activation Syndrome Presenting with Pericardial Effusion, Hyponatremia and Renal Involvement

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Background: Macrophage activation syndrome is a rare and life threatening complication of childhood rheumatic disorders. **Case characteristics**: 6-year-old male child with macrophage activation syndrome complicating systemic onset juvenile idiopathic arthritis. **Observation:** He developed pericardial effusion, hyponatremia and deranged renal function. **Outcome**: Improvement on intravenous cortico steroids. **Message**: High index of suspicion can lead to earlier diagnosis of macrophage activation syndrome.

Keywords: *Juvenile idiopathic arthritis, Pancytopenia, Pericarditis, Hemophagocytosis.*

Macrophage activation syndrome (MAS) occurs in heterogeneous group of conditions, including infections, neoplasms, drug-induced and rheumatic disorders. It is described most commonly with systemic onset juvenile idiopathic arthritis (soJIA) [1-3]. We report a rare presentation of severe MAS complicating soJIA presenting with pericardial effusion with hyponatremia and renal involvement.

CASE REPORT

A 6-year-old boy, previously diagnosed as soJIA, presented with a 10-day history of high grade continuous fever, cough, pain abdomen, loose motion, breathlessness, and swelling over the feet for past 6 days. He was symptomatic for last six months and was diagnosed elsewhere as soJIA six month previously. He was being treated with naproxen 250 mg twice-a-day with only partial relief of symptoms. On admission, his weight and height were 15 kg and 107 cm, respectively. His vitals were: temperature 103°F, pulse 154 minute, respiratory rate 54/minute, and blood pressure 102/60 mmHg.

On examination, patient had respiratory distress, severe pallor, clubbing and pedal edema. Bilateral ankle joints were swollen and tender without any joint deformity. Chest examination revealed bilateral crepitations, muffled heart sounds and systolic murmur (grade 3). Liver was 6 cm below costal margin in mid-clavicular line and spleen was 5 cm below costal margin.

Investigations showed pancytopenia (hemoglobin 5.5 gm/dL, total leucocyte count 2800/mm^3 and platelet count 1.1 $10^6/mm^3$), hyponatremia (serum sodium 126 mEq/L), deranged renal function (serum urea 90 mg/dL serum creatinine 1.5 mg/dL) and elevated liver enzymes (alanine aminotransferase 62 U/L, aspartate aminotransferase 52 IU/L, alkaline phosphatase 191 IU/L). C-reactive protein, serum potassium and serum calcium were in normal range. Antinuclear antibody and rheumatoid factor were positive. Bacterial infection was suspected initially; blood for culture and sensitivity was sent, and antibiotics were administered. All bacterial cultures were negative. Urine examination showed albuminuria (1+), peripheral smear for malarial parasite, widal test, HIV and brucella antibody tests were negative. IgA antibodies against tissue glutaminase (TTG) were also negative. Erythrocyte sedimentation rate (ESR) was markedly raised (125 mm/hour). Chest radiograph showed massive cardiomegaly with cardiothoracic ratio of 70%. Moderate pericardial effusion was documented by transthoracic echocardiography. Ultrasonography of the abdomen showed hepatosplenomegaly with altered echotexture of liver, and bilateral increased renal cortical echogenecity with maintained corticomedullary differentiation.

Over the next 2 days, patient's condition worsened with increasing respiratory distress. He was shifted to intensive care unit and started on oxygen; antibiotic therapy was stepped up. On further evaluation, serum ferritin was 1587.4 ng/mL serum LDH was 755.3 mg/dL and serum triglycerides were 325.5 mg/dL. Mantoux test and sputum for acid-fast-bacilli were negative. This failure to improve, in combination with his past history of soJIA, hepatosplenomegaly and a very high ferritin level led to a preliminary diagnosis of macrophage activation syndrome (MAS). Bone marrow aspiration revealed macrophages phagocytosing hematopoeitic elements which confirmed the diagnosis of MAS. Immunosuppressive treatment in the form of high-dose methylprednisolone (30 mg/kg daily) was commenced. Fever and respiratory distress improved after giving high dose steroids for three days, cardiac size decreased on

chest radiograph and repeat transthoracic echocardiogram showed minimal pericardial effusion and trivial tricuspid and mitral regurgitation.

DISCUSSION

MAS is a severe, potentially life-threatening complication of soJIA characterised by the excessive activation of well-differentiated macrophages. In less than 10% of the patients with soJIA a pericarditis will develop, often asymptomatic, and only rarely inducing a tamponade [4]. The diagnostic criteria for MAS complicating soJIA include reduced white blood cells, reduced platelet count, elevated aspartate aminotransferase, hypofibrino-genemia, central nervous system impairment, hemorrhages, hepatomegaly and histologic evidence of macrophage hemo-phagocytosis in bone marrow aspirates [5]. Other less common findings include hypertriglyceridemia, hypoalbuminemia and hyponatremia [2]. Hyponatremia is one of the strongest laboratory discriminators for MAS [5].

MAS is well described in the pediatric population with soJIA, and has a median age of 5 years at presentation [6]. Multisystem involvement and deranged renal function may be a poor prognostic sign [1]. Natural killer cell activity is decreased in patients with MAS associated with soJIA [7]. Treatment is based on immunosuppression; cyclosporin (with or without corticosteroids) has been used as the first-line treatment [2,8,9].

This patient was initially given only naproxen for soJIA at peripheral health centre by treating physician. He presented to us with fever and prominent respiratory failure, with pericardial effusion and deranged renal function. Non-response to antibiotics and negative cultures should raise suspicion of MAS and prompt us to undertake investigations for its diagnosis.

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