

Outcome of Patients With Systemic Onset Juvenile Idiopathic Arthritis With Macrophage Activation Syndrome at Onset

Macrophage activation syndrome (MAS) is a well-known complication of rheumatic diseases such as systemic onset juvenile idiopathic arthritis (SJIA), Kawasaki disease and systemic lupus erythematosus (SLE) [1]. However, MAS may be a difficult diagnosis to make when it happens at the onset of the disease.

We reviewed hospital records of 149 pediatric SJIA patients (age range 0.6 years -15 years) seen by us between 2011-2016. MAS at onset was seen in six patients, defined as per 2016 Classification criteria for MAS in SJIA [2]. The data of these 6 patients was analyzed with respect to initial clinical presentation, course, treatment and outcome.

Fever in all six and lymphadenopathy in 5 children were the most common clinical findings. The median duration of fever was 30 (range 7-45) days before the onset of MAS. Arthritis, which was transient in nature was noted in 2 patients (knee, 1; wrist, 1). All the 6 patients developed frank arthritis weeks to months after MAS resolved along with characteristic quotidian fever pattern, and other features of SJIA. Evanescent rashes were noted in 3 patients. Transaminitis (range 116-837 U/L) in five patients was the most common abnormal laboratory parameter, followed by thrombocytopenia (range $15-181 \times 10^9/L$) in four patients. Three children each had cardiac manifestations (2, clinical shock; 1, pericardial effusion), nervous system manifestations (2, seizures; 1, encephalopathy), and hepatosplenomegaly. Leukopenia was seen in four children (range $2.2-6.7 \times 10^9/L$).

Three patients needed intensive care unit care. None of the patients showed any evidence of an underlying infection and had negative blood cultures. All six patients had markedly elevated serum ferritin levels [median (IQR) 8587.5 (1053-22000) ng/mL]. All patients underwent bone marrow aspiration of which four showed hemophagocytosis.

All patients were treated with intravenous steroids followed by oral steroids. Cyclosporine was used in 2 patients and tacrolimus was introduced in one patient, when response to steroids was suboptimal in the form of persistent fever and presence of cytopenia. The clinical response in the form of defervescence was seen within a few days after initiation of the treatment and cytopenias recovered within a week of initiation of treatment. Cyclosporine was continued for 6 months in the first patient and for one year in the second patient, and tacrolimus was continued for two years in the one patient in

whom it was used. These drugs were continued in view of uncontrolled systemic JIA features.

Mean duration of follow-up of patients was 4.1 years (range 1-10 years). Three children had a monocyclic course and went into remission with a standard treatment protocol of steroids and methotrexate. Of the remaining 3 with polycyclic course of SJIA, only one patient is in remission without drugs while the other two patients continue to be on drugs to control their disease.

Minoia, et al. [3] described that of the 362 patients with SJIA with MAS, 22% of MAS episodes were seen at the onset of SJIA [3]. Other authors reported MAS at onset to be more common in SJIA patients than SLE patients [4]. All patients in this series evolved to develop arthritis and classic picture of SJIA in due course. The treatment protocol followed by the authors was similar to previous reports.

The limitation of the study is the small size of patient cohort. MAS at onset of SJIA can be a diagnostic dilemma and it should be a differential diagnosis in any sick child with febrile illness with multiorgan dysfunction, progressive cytopenias and transaminitis in the absence of any evidence of infectious cause. Absence of arthritis at onset of illness should not be a deterrent for diagnosis of SJIA as it may appear later.

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