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The Clinical and Laboratory Scoring for Pediatric Macrophage Activation Syndrom (MAS) In Relation to the Choice of the Medication

Manal Mohamed Helmy Nabe[1]* and Rehab Hamoud Alshammari[2]

[1]Department of paediatric cardiology, El Madina El Monawara, Maternity and Children Hospital, Hail, Saudi Arabia.

[2]Department of Paediatric Cardiology, Royal Commission Hospital, Jubail, Saudi Arabia.

***Correspondence:**
Manal Mohamed Helmy Nabo, Department of Pediatric Cardiology, El Madina El Monawara, Hail Maternity and Children Hospital, Saudi Arabia.

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Keywords

Pediatric Macrophage Activation Syndrome (MAS), Clinical Scoring System, Laboratory Scoring, MAS Diagnosis, Medication Choice in MAS.

The macrophage activation syndrome (MAS) is considered a challenge for diagnosis. The importance of diagnosis is life saving for the patients. Most cases have bad prognosis and about 40% of cases died at the first week of illness. The art of saving the patient life is early diagnosis and proper treatment. The application of scoring for MAS is important to diagnose and choose the best and effective treatment. There are different protocols for treatment but according to the scoring the proper treatment is started and best result is obtained.

There are four items according to which the scoring system is calculated (Table 1). The four items include the followings: clinical, laboratory, genetic and association with other systemic onset disease as systemic lupus erythrymatosis (SLE) and rheumatoid arthritis. The scoring for MAS is calculated according the value of each parameter. The level of ferritin is the most important and clue for the diagnosis of MAS. The level of ferritin takes score started by five up to ten if level is 500 up to 10.000 respectively. The decision at this point is to start pulse therapy using steroid. If the case not improved and the scoring starts to be more than ten and one more parameter is added from the guided list. At that time intravenous immunoglobulin and cyclosporine A is planned to start. The most important and added parameter is deterioration of more than one laboratory test due to wide spread inflammation of the body organs. The decision to start immunosuppressant and biological treatment is taken when genetic is confirmed and the defect in performing- mediated catalytic pathway is diagnoses. This point the score will be doubled reach to twenty due to detection of S CD 25 and natural killer cells (s IL-2R). This is used due to inability of cytolytic lymphocytes to lyse the infected antigen presenting cell (APC), which subsequently results in a prolonged cell-to-cell interaction. The end result is cytokine storm and clinical squeal of MAS [1,2]. In cases that diagnosed as systemic juvenile idiopathic arthritis (sJIA) the cytokine-specific therapy (e.g., anakinra) is used. Anakinra is a recombinant IL-1 receptor antagonist targeting both IL-1α and IL-1β cytokines used [3-5]. Likewise, canakinumab is a monoclonal antibody that specifically targets only the IL-1β cytokine and is a common treatment target in patients with sJIA [3,6].

The parameters for diagnosis MAS (Table 1):

A. Clinical diagnosis
Fever more than 38 C
Organomegally: liver and spleen

B. Laboratory
Complete blood count
Liver function test
Lactate dehydrogenase
Fibrinogen
Triglyceride

C. Genetics
Confirmed by CD 163, CD 25 and natural killer cells (s IL-2R)

D. Association with other systemic inflammatory disease as rheumatoid arthritis or SLE

Discussion

The scoring system of the MAS can facilitate the choice of the best medication for the patients.

First Line of Treatment

For only hyperfirretenemia the use of intravenous methyl prednisolone [IVMP] 30mg/kg/day for 3 to 5 days are most

commonly used as first-line treatment [3,7]. Cyclosporine A (CSA) is a useful agent for initial combination therapy with IVMP or as adjunctive therapy for MAS resistant to IVMP [4]. The scoring system at this point from 10 -20 points.

Second Line of Treatment

In cases with refractory to treatment by the first line due to multiorgan affection in the form of hepatomegaly or splenomegaly. That is confirmed by the high enzyme level and lactate dehydrogenase in addition to the indicator for the first line of treatment in the form of high ferritin level. The scoring system at this point is duplication of twenty. The side effects of IVIG are monitored as headache and if the patient complains from that the adjustment for the dose of IVIG is adjusted and follows up the symptom and signs. The addition of IVIG is used as the inflammation of multiorgan at this point has dramatic response for IVIG [8,9]. In a pediatric MAS study in India [10], 39% of patients received IVMP and CSA, 36% received IVMP alone, 19% received IVMP and IVIG, and 10% received IVMP, CSA, and IVIG. Follow up the laboratory investigation as blood cells and the liver function test decide the duration and the prognosis of the disease [11,12].

Third Line of Treatment

At this point the scoring system is duplicated more and the final result for the score is fourty points. At this point the genetic or other systemic disorder is diagnosed and the need for Anakinra is high. Earlier initiation of anakinra within 5 days of hospitalization was associated a statistically significant reduction in mortality among patients with non-malignancy associated MAS [13]. Treatment with recombinant IL-18 binding protein (IL-18bp) in com-bination with anakinra successfully improved life-threatening hyperinflammation in a patient with sJIA and refractory MAS. IL-18 may also stimulate the inflammatory cascade leading to MAS in patients with sJIA [14].

Special Situations

Likewise, canakinumab is a monoclonal antibody that specifically targets only the IL-1β cytokine and is a common treatment target in patients with sJIA [3,6]. The need to use Tocilizumab is a monoclonal antibody that targets the IL-6 receptor. These cases need to have normal level of ferritin but high liver enzyme level. These patients tend to be afebrile and had lower cell counts and ferritin levels with higher liver enzymes [6,15]. Tocilizumab is confirmed to be used in cass of polyarticular JIA, and sJIA [16].

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