MACROPHAGE ACTIVATION SYNDROME COMPLICATING PEDIATRIC RHEUMATIC DISEASES IN A TERTIARY REFERRAL CENTER

Alicia de Oliveira Rosas¹, Adriana Rodrigues Fonseca^{1,*}, Flavio Roberto Sztajnbok¹, Rozana Gasparello de Almeida¹, Sheila Knupp Feitosa de Oliveira¹, Marta Cristine Felix Rodrigues¹

1.Universidade Federal do Rio de Janeiro, Rio de Janeiro (RJ), Brazil.

*Corresponding author: adrirfonseca@gmail.com

BACKGROUND

Hemophagocytic lymphohistiocytosis (HLH) is a severe, potentially fatal overwhelming inflammatory reaction. Objectives were to evaluate the clinical and laboratory features, and treatment of pediatric patients who had the diagnosis of macrophage activation syndrome (MAS).

METHODS

Cross-sectional study, undertaken in a tertiary referral center of pediatric rheumatology. Data were retrospectively collected from medical charts of patients admitted between 2010–2019, including clinical, laboratory and treatment variables. The data were collected after ethical approval (number CAAE 02427218.8.0000.5264).

RESULTS

A total of 14 patients were included, 4 of them had two or more MAS episodes totalizing 20 MAS episodes, with female predominance, and median age at diagnosis of 8 years and 10 months. All twenty MAS episodes were triggered by active rheumatic illness and half of them also by infection. Fifteen of them were in patients with systemic juvenile idiopathic arthritis (sJIA), two in juvenile systemic lupus erythematosus (JSLE), two in Kawasaki disease (KD) and one in mixed connective tissue disease (MCTD). Macrophage activation syndrome episodes occurred together with presentation of the underlying rheumatologic disease in 8/14 (57%) patients. Sixteen episodes presented with persistent fever, the main clinical feature, only absent in four episodes of subclinical MAS in patients with sJIA. Other clinical features observed were: hepatomegaly (13/20), lymphadenopathy (8/20), and splenomegaly (7/20). Median ferritin levels were 1,863 ng/mL (464–30,000) and 18 episodes had hyperferritinemia over 500 ng/mL. Most cases (14/20) showed an increase in the ferritin/ESR ratio. Regarding treatment, 19/20 events (95%) received steroids, 8/20 (40%) cyclosporine A, 8/20 (40%) intravenous immunoglobulin, 3/20 (15%) canakinumab, 3/20 (15%) tocilizumab, and one single event etoposide. None patient died. Three events required ICU care (1 patient with sJIA, 1 MCTD and 1 KD), all developed neurological involvement and 1 hemorrhagic manifestation. The median length of hospital stay was 30 days.

CONCLUSION

Despite the fact that hitherto there are no validated diagnostic criteria, most cases studied presented persistent fever which can be an important clinical feature in MAS; however, the diagnosis of MAS still poses a challenge and its recognition is often delayed. Some of the HLH markers are common features of an active systemic rheumatic disease and do not distinguish MAS from active disease. The data studied did not allow an identification of any clinical or laboratory parameter for definitive diagnosis. Future studies are needed to develop a set of criteria for an earlier identification and definitive treatment options aiming at improved outcomes and survival.

KEYWORDS

Inflammation, Rheumatic diseases, Macrophage activation syndrome, Hyperferritinemia.