Calming the cytokine storm in children and adults for the Treatment of Adult MAS–HLH in RHEUMATIC DISORDERS

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a rare and often overlooked clinical manifestation of an aberrant hyperinflammatory immune response leading to a fatal cytokine storm(1). Diagnostic criteria according to The HLH Study Group of the Histiocyte Society include fever, splenomegaly, bicytopenia, hypertylceridemia and/or hypofibrinogenemia, hypoferritinemia, low/absent NK activity, increased soluble CD-25 levels and hemophagocytosis(2). Prompt recognition and differentiation from severe sepsis is essential to improve the outcome. HLH reflects a disbalanced immune system in response to infectious, malignancy, or autoinflammatory/autoimmune mediated triggers(1). The latter group of patients are regarded as having Macrophage Activation Syndrome (MAS–HLH)(3). In adults MAS–HLH comprises 12.5% of all HLH causing triggers(4). The most frequent immunological disorders associated with adult HLH–MAS are systemic lupus erythematosus and adult onset Still’s disease, but every other immunological disorder can be involved(4,5).

Treatment: Treatment of adults HLH patients requires swift recognition and an experienced team of specialists that are acquainted with the critical factors influencing the balance between co-morbidity, cytokine storm induced septic-like symptoms and toxicity of chemo-immunotherapy(4). In general, adult patients do not tolerate high dose etoposide that are given in HLH–94 based chemo-immunotherapy schedules that have been shown effective in children(7,8). Dose and frequency modifications of etoposide may avoid prolonged neutropenia, infectious complications or hepatic toxicity. The same precautions account for adult patients with MAS–HLH in which treatment differs from the HLH schedules. A step up approach depending on clinical features and severity is warranted(9, 10). High doses of corticosteroids are recognized as first-line treatment(9, 10). In patients with insufficient immediate response, Cyclosporine can be added in patients with insufficient immediate response(9). The cytokine blocking agent anakinra (anti-IL-1) given in high doses is emerging as an alternative or additional treatment of adult MAS–HLH(11, 12, 13). Another promising cytokine blocker is anti-IL-6 (tocilizumab). Etoposide at a reduced dose can be initiated in patients with severe non-responsive and active disease or CNS-involvement(10).


REFERENCES: