Calming the cytokine storm in children and adults

**REFERENCES:**


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**Know your methods! Interactive discussion**

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**Calming the cytokine storm in 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 hyper-inflammatory immune response leading to a fatal cytokine storm(1). Diagnostic criteria according to The HLH Study Group of the Histioctye Society include fever, splenomegaly, bicytopenia, hypertylceridemia and/or hypofibrinogenaemia, hyperferritineamia, low/or 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)(7). In adults MAS-HLH comprises 12.5% of all HLH causing triggers(4, 5). 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 adult 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(6). In general, adult patients do not tolerate doses of 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 adults 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 MAS-HLH and SLE steroids, cyclophosphamide or etoposide are given(10). Cyclosporine can be added in patients with insufficient immediate response(9). The cytokine blocking agent anakinra (anti-IL-1β) given in high doses is emerging as an alternative or additional treatment of adult MAS-HLH(9, 11, 12). 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).

**Conclusion:** Awareness of the clinical emergency MAS-HLH in patients with autoinflammatory/autoimmune mediated disorders is essential for timely recognition and potential life-saving treatment. The management of MASH-LH in adults requires a team of dedicated specialists with experience in the treatment of critically ill patients with immunological disorders and anticipation on its rapidly changing and deteriorating nature.