Histiocyte Society - Office of the Secretariat
332 North Broadway, Pitman, New Jersey 08071 USA
Phone: +1 856-589-6606 Fax: +1 856-589-6614
www.histiocytesociety.org

Recommendations and Considerations from the Histiocyte Society During the Evaluation of Hospitalized COVID-19 Patients for Hyperinflammation

The COVID-19 pandemic has presented an overwhelming problem to humankind and placed a significant burden on the health care community providing care for affected patients. Members of the Histiocyte Society have been approached by members of the medical and patient communities for advice regarding the evaluation of hospitalized patients with COVID-19 disease and suspected hyperinflammatory states such as cytokine storm, hemophagocytic lymphohistiocytosis (HLH), macrophage activation syndrome (MAS), and more limited or localized pulmonary hyperinflammation. At this time, there are sparse data upon which to make evaluation or treatment recommendations for patients suspected to have systemic and/or pulmonary hyperinflammation during severe COVID-19 disease. Based on the Lancet publication by Zhou et al (PMID: 32171076), it appears that many individuals who do not survive COVID-19 have elevated ferritin levels and other laboratory values that could possibly represent a hyperinflammatory state, when compared to those who survive.[1] Ruan et al (PMID: 32125452) also observed differences in C reactive protein and interleukin-6 levels between survivors and non-survivors,[2] and Wang et al observed differences in procalcitonin, lactate dehydrogenase, and aspartate aminotransferase in patients who required intensive care.[3] Nevertheless, most patients do not appear to exhibit the full constellation of clinical symptoms and typical laboratory biomarkers that are typical for HLH/MAS.[4,5] The Histiocyte Society suggests that patients with severe COVID-19 be screened using a combination of general HLH/MAS screening tests as well as those identified to be associated with increased severity and mortality, namely: ferritin, triglycerides, troponin, lactate dehydrogenase, fibrinogen, prothrombin time, d-dimer, interleukin-6, C reactive protein, procalcitonin, and soluble interleukin-2 receptor-alpha (sCD25), along with general laboratory evaluations including complete blood count and comprehensive metabolic panel. Laboratory evidence suggesting a hyperinflammatory state should prompt consultation with physicians experienced in the treatment of such conditions including cytokine storm, HLH, and MAS, and additional laboratory evaluations can then be considered, as appropriate. It may be beneficial to monitor laboratory values at least twice weekly, when possible, during the course of severe COVID-19 to identify or monitor hyperinflammation. Current data are insufficient to allow specific treatment recommendations, though multiple anti-inflammatory strategies are being tested in clinical trials and we urge participation when possible. Physicians should consult with local or regional experts in hyperinflammatory disorders, as well as local infectious disease, ICU, and pulmonary experts regarding recommendations for treatment of COVID-19. When feasible, we encourage the health care community to capture patient data in local databases, larger registries, or formal studies. Tremendous and inspiring efforts are being made to improve the care for patients with severe COVID-19. Members of the Histiocyte Society will continue to support and participate in these endeavors.

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