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Letter to Editor

Transfusion Strategy in Crimean-Congo Hemorrhagic Fever Treatment

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Crimean-Congo hemorrhagic fever (CCHF) is an acute tick-borne viral hemorrhagic zoonotic disease with increasing human health impact [1]. It is a fatal emerging infectious disease characterized by fever and hemorrhagic manifestations. CCHF virus is a single-stranded RNA Nairovirus from the Arbovirus group. This virus is endemic in Iran [1].

CCHF has four steps in the clinical presentation including; incubation period, pre-hemorrhagic stage, hemorrhagic state, and convalescence. The incubation period following a tick bite is usually between 3-7 days and 14 days after blood transfusion. The onset of the illness is sudden, with fever, myalgia, dizziness, headache, neck stiffness, and vomiting, followed by development to the hemorrhagic state. Actually, the CCHF clinical manifestation is variable from asymptomatic to the mild or severe form. The hemorrhagic state develops from the 3rd to the 5th day and presents with petechial rash and purpura on the skin. Hemorrhagic phenomena may include melena, hematuria, epistaxis, and bleeding from mucosal surfaces or needle punctured sites [1-2].

Although Thrombocytopenia and Leukopenia are the main laboratory findings in CCHF disease and Lymphocyte count varies according to the host's immune response, patients with progressive fatal clinical manifestations have a relative increase in neutrophil and a decrease in lymphocyte and monocyte counts. The relative increase in neutrophil counts leads to excessive cytokine release. This excessive secretion of cytokines has toxic effects on the activation of endothelial cells and vascular permeability, which cause vascular dysfunction, disseminated intravascular coagulation, hemorrhage, hypotension, and shock. The decrease in lymphocyte counts results in humoral antibody response depletion [3].

During CCHF progression, some patients present a clinicopathologic condition characterized by higher fever, hepatosplenomegaly, hyperferritinemia, and increased hemophagocytic macrophage proliferation, and activation in the reticuloendothelial system. This condition could be considered as secondary Hemophagocytic lymphohistiocytosis (HLH) [3-4]. Secondary HLH is a fatal hyper-inflammatory condition involving a cytokine cascade, with elevations of

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cytokines secreted by T-lymphocytes and macrophages (IL2, IL6, TNFα, IFNγ), which lead to the over-activation of antigen-presenting cells and CD8+ T cells, and hematopoietic cells devoured by activated macrophages. Uncontrolled T-lymphocytes (CD4+) activation and overproduction of proinflammatory cytokines with macrophagic-based hemophagocytosis are well established in secondary HLH [4-6].

CCHF is not a recurrent or relapsing disease, and it does not impose any long-term sequelae, with the only relevant outcome being survival. There are four major important aspects in the treatment of CCHF; close monitoring, supportive treatment, early antiviral agents, and the treatment of complications like the hemorrhagic state [1-2].

Some studies did not support Ribavirin (a synthetic purine nucleoside analog) as an effective antiviral agent in the CCHF treatment, however, a majority of researchers consider the significant role of Ribavirin [1,2,5]. We prescribe Ribavirin to our patients in the early stage, and consider steroids in the hemorrhagic period before disseminated intravascular coagulopathy (DIC) development. Platelet count, fibrinogen, and D-dimer levels are important for the early detection of DIC, which also allows the early correction of coagulation parameters [2-3].

Platelet (Plt) transfusion is reserved for patients with Plt count lower than 20000 or a hemorrhagic state with Plt count lower than 100000. We prescribe Intravenous immunoglobulin and Methylprednisolone for the severe form of CCHF with refractory thrombocytopenia. Even though immunosuppression is known to exacerbate viremia, however, the use of immunosuppressive agents along with intravenous immunoglobulin and Methylprednisolone might be considered in the treatment of the patients with CCHF, who have uncontrolled hemophagocytosis and severe bleeding symptoms.

Fresh Frozen Plasma (FFP) transfusion is indicated for the correction of coagulopathy. We transfuse FFP when PTT, PT and the international normalized ratio (INR) are at least 3 times greater than the upper limit of the normal range and are accompanied by a hypocoagulopathy state. We prescribe 15 ml/kg FFP and evaluate the patient’s condition after 4 hours. FFP could be repeated every 8-12 hours, if necessary. The prothrombin complex concentrates (PCC), which contains the human coagulation factors including II, VII, IX and X together with the endogenous inhibitor proteins S and C, must be considered when faced with severe coagulopathy in a patient having limited cardiovascular reserve (low cardiac output condition) or when we have an observed target.

Packed red blood cell transfusion is necessary only if the hemoglobin concentration becomes lower than 8 mg/dL, or if there is significant documentation indicating tissue oxygen delivery disturbance, like a rise in the arterial blood lactate.

It is presumed that the electrolyte balance, fluid substitution, hemodynamic support, appropriate blood product transfusion, and augmentation of the patient's hemostasis profile all have a significant effect on the patient's outcome, and careful attention should be accorded to these aspects.

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