

Inflammatory Responses in Liver Transplantation

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Abstract

Successful liver transplantation requires proper mitigation of stress responses. Systemic effects caused by liver cirrhosis, invasive surgery, ischemia-reperfusion injury, rejection, and infection, all of which are relevant to liver transplantation, are mediated by inflammatory factors. Recently, the detailed mechanisms of inflammation have been elucidated. Damage-associated molecular patterns (DAMPs) released from cells damaged by ischemia or injury, or pathogen-associated molecular patterns (PAMPs) released by pathogens, are recognized by internal cell receptors or cell surface receptors, leading to the synthesis of inflammatory proteins including proinflammatory/anti-inflammatory cytokines, which are then secreted by the cells. These cytokines stimulate the production of additional cytokines, causing a vicious circle of inflammatory responses, such as innate immune responses by macrophages. In addition, lymphocytes activated by these cytokines stimulate adaptive immunity. During liver transplantation, the general preoperative condition of the patient and surgical invasiveness are associated with organ failure and ischemia-reperfusion injury, which can lead to transplant rejection. It has been suggested that progressive immunodeficiency and organ failure as a result of pre-transplant cirrhosis are associated with postoperative multiple organ failure and death, and that elevated intraoperative DAMPs correlate with organ failure. Furthermore, DAMP receptors and inflammatory cytokines are increased by ischemia-reperfusion injury, indicating its role in promoting innate and adaptive immunity. In addition, inflammatory signals induced by postoperative infections are similar to those induced by ischemia-reperfusion injury and rejection, indicating that pathogen-derived inflammation can also lead to rejection. In summary, most complications in liver transplantation can be explained in a unified manner by abnormal inflammatory responses; therefore, controlling inflammation might be of benefit for the struggle of safe and effective liver transplantation.

Key words: inflammation, invasion, liver transplantation