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Serum Levels of Interleukin-6, Tumor Necrosis Factor- α , and Interleukin-2 in Rejecting Human Small Bowel Allografts

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CYTOKINES play critical roles in the immune response, particularly in the self-defense system. Activated human monocyte/macrophage is a major source of interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α).¹ Interleukin-2 (IL-2) is released primarily by activated T lymphocytes following antigen presentation.² We conducted a study to monitor various cytokines (IL-6, TNF- α , and IL-2) after small bowel transplantation and evaluated whether or not the serum cytokine level could reflect the rejection of human small bowel allograft.

MATERIALS AND METHODS

Three patients (two adults, one child) undergoing small bowel transplantation with FK 506 at the University Hospital of Pittsburgh, were the subjects of this study. One of them received small bowel allograft alone and the others received liver and small bowel allografts simultaneously. Their serum levels of IL-6, TNF- α , and IL-2 were monitored daily (from preoperation day to 29 to 42 days) by a two-step sandwich enzyme immunoassay method using an enzyme-linked immunosorbent (ELISA) kit (R&D System Inc. Minneapolis, Minn). Sixteen serial biopsies of allografts were performed during this cytokine-monitoring period.

RESULTS

There were clinically and pathologically six episodes of acute cellular rejection (ACR) in three patients during the monitoring periods. As shown in Fig 1, there were three episodes of ACR in a patient during the cytokine-monitoring period and coincidental elevation of IL-6 was noted in all three instances. Although there was an elevation of IL-2 or TNF- α during the monitoring period, it did not necessarily reflect the rejection episodes. The other two cases demonstrated a similar monitoring pattern (data not shown). Serum levels of IL-6, TNF- α , and IL-2 fell rapidly following antirejection therapy, a bolus of solumedrol.

DISCUSSION AND CONCLUSION

IL-6 and TNF- α (pleiotropic cytokines) regulate immune responses and acute phase reactions.¹ This study indicates

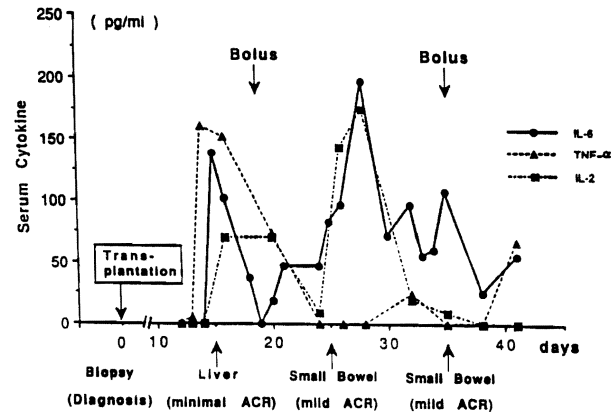


Fig 1. Serum levels of IL-6, TNF- α , and IL-2 in an adult patient with small bowel and liver transplantation. There was no evidence of bacterial or viral infection in this period.

that elevation of IL-6 and other cytokines during the ACR of small bowel or liver allograft probably reflects a part of acute phase reaction that occurred in a transplanted recipient. In conclusion, these results suggest that the daily monitoring of serum levels of TNF- α , IL-2, and particularly IL-6 is useful in the diagnosis of graft rejection, and is also helpful in evaluation of the therapeutic effect of antirejection therapy.

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