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Coagulation Disorders After Reperfusion of Pancreatic Allografts

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THE use of pancreaticoduodenal grafts instead of segmental pancreatic grafts has markedly reduced the incidence of early postoperative graft thrombosis. Nevertheless there is still a significant number of pancreatic grafts that are lost in the early postoperative period due to graft thrombosis.[1] Graft thrombosis seems to be a specific problem of pancreas grafts; it is nearly unknown in kidney transplantation.

The reasons for this problem are certainly multifactorial. Besides technical problems and low blood flow within the graft itself, the typical ischemia/reperfusion injury[2] resulting in tissue edema and severe damage of the endothelial cells within the graft must be taken into account. Up to now, however, it has not been completely clear whether local or generalized disorders of the coagulation system might be crucial in this respect. To clarify this question, a prospective study was conducted.

MATERIALS AND METHODS

A consecutive series of 10 patients with bladder-drained pancreaticoduodenal and renal allografts[3] was studied. The grafts were perfused with 2000 to 3000 mL of University of Wisconsin solution. The portal vein and the celiac axis were reconstructed with vascular grafts from the donor. Cold ischemia time ranged between 8 and 16 hours. Quadruple immunosuppressive therapy was used in all patients. Anticoagulation therapy was started with low-dose heparin and low molecular weight dextran only 10 hours after reperfusion of the graft. Antithrombin III (AT III) was substituted starting 4 to 6 hours after reperfusion in order to achieve plasma levels of >80%.

Starting 30 minutes before reperfusion until the 10th postoperative day, the following parameters were analysed: prothrombin, AT III, thrombin–antithrombin III complexes (TAT), coagulation Factor XIII, and fibrin D dimers.

RESULTS AND DISCUSSION

Immediately after reperfusion of the pancreatic grafts, a dramatic consumption of prothrombin could be found. Six hours after reperfusion, prothrombin activity was reduced to 55% in the average graft, indicating an immediate and strong activation of the coagulation cascade in these patients. Normalization of the prothrombin activity was not seen before the 2nd postoperative day.

The high amounts of thrombin, which result from the strong activation of prothrombin as shown before, were bound in part to AT III, the most important physiological thrombin inhibitor. Thus, AT III levels in plasma dramatically decreased immediately after reperfusion of the pancreatic graft. AT III levels <40% could be found in single cases despite early AT III substitution, indicating a significantly increased risk of spontaneous thrombosis in these patients.[4] As one would expect, plasma TAT levels increased up to 20-fold above normal at the same time. Again, normalization was not seen before the first 24 hours after reperfusion.

Coinciding with the strong hypercoagulability seen in these patients, fibrinolysis also was activated. Thus, fibrin-D-dimers started to increase 2 hours after reperfusion and reached their maximal value 10 hours later. Contrary to the activation of the coagulation cascade, activated fibrinolysis could be demonstrated only in one fourth of the patients.

Coagulation Factor XIII, which is necessary for stabilization of fibrin, dropped dramatically immediately after reperfusion as the parameters mentioned before. However, recovery of Factor XIII plasma levels took more than 10 days, suggesting that ongoing nonspecific destruction of the Factor f.e. by PMN-elastase might occur in these patients.

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Taken together, these results demonstrate that pancreatic transplantation induces a state of hypercoagulability in the early postoperative period in nearly all patients. This is followed by reactive hyperfibrinolysis in some patients. It is tempting to assume that lesions within the graft that are induced by ischemia/reperfusion injury and resemble the picture of genuine pancreatitis are responsible for this phenomenon.[5,6] This hypercoagulability might well be one of the key factors in development of early postoperative graft thrombosis. Thus, at least in our opinion, anticoagulation with low-dose heparin and aggressive substitution of AT III seems to be advisable in pancreatic transplantation. By using this therapeutic regimen in a consecutive series of 65 patients, we did not see any graft thrombosis at all, resulting in a 1-year graft function rate of 90%.

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