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Factors Responsible for Hepatic Artery Thrombosis After Pediatric Liver Transplantation

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THROMBOSIS OF the hepatic artery (HAT) continues to be a serious complication following orthotopic liver transplantation (OLTx). Several studies have failed to identify possible risk factors that may be related to thrombosis of the hepatic artery. Nonetheless, a clear definition of the responsible factors is necessary to formulate guidelines and protocols for the prevention and management of this dreaded complication.

In the present study two homogeneous and comparable populations of pediatric patients consisting of children who developed thrombosis of the hepatic artery after OLTx (HAT group) and those who did not (control group) have been identified. An accurate statistical comparison between these two groups has been carried out in an attempt to identify the responsible factors leading to thrombosis and to develop a management protocol for this complication.

MATERIALS AND METHODS

Patient Population

During the calendar year 1986, 66 consecutive children under the age of 10 years underwent an initial liver transplant at the Children's Hospital of Pittsburgh. The methods of patient selection, techniques for OLTx, protocols for immunosuppressive management and postoperative care have been described in detail previously.¹ A running continuous suture with a "growth factor" was used for the arterial anastomoses. Some small-diameter vessels were anastomosed using interrupted sutures.

The clinical management of all transplant recipients was comparable. Only hepatic artery thrombosis (HAT) that occurred within 15 days of transplantation has been considered in the HAT-group of patients. In these cases the diagnosis was clinically suspected in the presence of fulminant hepatic necrosis, biliary leak, or recurrent bacteremia and was always confirmed either by sonogram or angiography.

Cases in which a major complication occurred in the postoperative period were excluded from the study. Thus, only patients with a relatively uneventful postoperative course during the first month were included as a control group. The records of all these patients were reviewed. Twenty-eight different perioperative variables from both the donor and the recipient were recorded.

The anticoagulation therapy consisted of dextran 40, heparin, aspirin, or persantine and was administered in a random fashion.

Statistical Analysis

The variable listed in Tables 1 and 2 were investigated to determine whether there was any statistically significant difference ($p < 0.05$) between "cases" (HAT group) and "controls" (uneventful 15 days postoperative course).

Statistical analysis was performed at the Epidemiology Data Center of the University of Pittsburgh, utilizing the BMDP statistical software package.

Table 1. "Surgical Factors" Analyzed for Possible Relationship with the Occurrence of Thrombosis of the Hepatic Artery

Variable	Hepatic Artery Thrombosis	Controls	p Value
Size of the hepatic artery (diameter) <3 mm	55.6%	24.1%	<0.05
Level of the anastomosis	Not significant		
Anomalies in arterial anatomy	Not significant		
Kind of arterial reconstruction			
End-to-end	72.2%	93.1%	<0.05
Others	27.8%	6.8%	
How many times the anastomosis was intraoperatively done			
One	66.7%	96.6%	<0.02
Two or more	33.3%	3.4%	
Suture material	Not significant		

RESULTS

HAT occurred within 15 days after the transplant (mean = 5.3 ± 1.2 days) in 18 patients (26% of the cases) and they were considered in this study as the hepatic artery thrombosis group. Nineteen of the remaining 48 patients developed other major complications in the immediate postoperative period (primary nonfunction, bleeding, sepsis, bowel perforation, biliary leak) and thus were excluded. The control group consisted of 29 out of 48 patients (42%) in whom the postoperative course was relatively uneventful. The two groups were comparable in terms of age, sex, body weight, blood type predominance, and indication for OLTx.

Three surgically related factors were identified as being significantly associated with HAT (Table 1), including (a) the diameter of the artery, determined intraoperatively, (b) the type of arterial reconstruction, and (c) the number of times the anastomosis was redone to achieve a satisfactory result.

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Table 2. Medical Factors (Intraoperative Transfusion and Anticoagulant Prophylactic Treatments)*

	Yes		<i>p</i> Value	No	
	Thrombosed	Control		Thrombosed	Controls
Type of Transfusions					
Whole					
Blood	23.5%	13.5%	NS	76.5%	86.2%
FFP	94.1%	69.0%	<0.05	5.9%	31.0%
Platelets	64.7%	41.4%	NS	35.3%	58.6%
Perioperative anticoagulant therapy					
	50%	10.9%	<0.01	50%	89.7%

*ABO compatibility, preoperative and intraoperative coagulation patterns, and blood loss were not significantly different between HAT and controls.

The incidence of HAT was significantly higher ($p < 0.05$) in children who received an intraoperative transfusion of fresh frozen plasma (FFP), compared to children who did not receive FFP at all (Table 2). Other preoperative and intraoperative variables did not show any significant differences between groups. The postoperative anticoagulant treatment was another medical-related factor that was correlated significantly ($p < 0.01$) with the occurrence of HAT; it was administered in almost 90% of the controls, which only 50% of the patients who eventually developed thrombosis received it. A multivariate analysis of the variables that were found to have a significant influence on the occurrence of HAT revealed that the anticoagulation treatment was the only independent variable.

DISCUSSION

Hepatic artery thrombosis after transplantation, a devastating postoperative event associated with significant morbidity and mortality, occurs in about 7 to 8% of the whole liver transplant population.²⁻⁶ In the present study, 26% of children under 10 years of age who underwent an initial liver transplant, developed thrombosis of the hepatic artery within

15 days. This HAT group was compared to 29 patients (42% of the total series) who had a relatively uneventful postoperative course.

Three "surgical" factors, consisting of the diameter of the hepatic artery (less than 3 mm), the type of arterial anastomosis (end-to-end hepatic anastomosis versus other reconstructions, such as use of iliac allograft or aortic conduit), and the number of times the arterial anastomosis had to be redone to achieve a satisfactory intraoperative result, were all found to be statistically different ($p < 0.05$), in comparing the HAT and the control groups. Similarly, two "medical" factors, consisting of the intraoperative administration of FFP and postoperative anticoagulant treatment with either heparin or dextran 40, were also found to be statistically different ($p < 0.5$) between groups.

This is the first report in which perioperative anticoagulant therapy has been identified as such an important and statistically independent factor in the prevention of hepatic artery thrombosis after liver transplantation. The risk (odds ratio) of developing HAT in patients who did not receive anticoagulant therapy was almost eight and five times greater than in patients who received heparin and dextran, respectively.

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