Auxiliary Liver Transplantation in Fulminant Failure

ABSTRACT. Fulminant hepatic failure (FHF) is defined as a syndrome of acute liver failure with the development of hepatic encephalopathy and severe hypoprothrombinemia occurring within 2 months of the onset of symptoms or jaundice in a person without preexisting liver disease. Total orthotopic liver transplantation (OLTX) is a lifesaving therapeutic option for patients with FHF, but currently requires lifelong immunosuppression to maintain the graft. Auxiliary partial orthotopic liver transplantation (A-OLTX) is a procedure whereby only a portion of the native liver is removed, and the remainder of the native liver is left in situ. A-OLTX provides temporary support until the native liver recovers and immunosuppression can be withdrawn.

We describe the successful application of emergency A-OLTX in a young girl who accidentally ingested Amanita phalloides mushrooms and developed FHF. PEDIATRICS 1997;100(2). URL: http://www.pediatrics.org/cgi/content/full/100/2/e10; auxiliary liver transplant, fulminant hepatic failure, emergency, Amanita phalloides.

ABBREVIATIONS. FHF, fulminant hepatic failure; OLTX, orthotopic liver transplantation; A-OLTX, auxiliary partial orthotopic liver transplantation.

CASE REPORT

A 13-year-old girl went wild mushroom picking with her family in a local reservoir and inadvertently harvested several Amanita phalloides mushrooms (death cap). Upon their return home, her family prepared a meal consisting of the olive green-brown capped mushrooms with white gills and a white stem in a sauce with spaghetti. Within 12 hours, the family sought medical attention because of symptoms of abdominal cramping, nausea, vomiting, and watery diarrhea. The patient and her family were seen in a local emergency facility and sent home with prochlorperazine and advised to maintain good fluid intake. However, because of persistent symptoms, the patient returned for evaluation. Initial laboratory studies 2 days after ingestion revealed serum aspartate aminotransferase (AST) 281 IU/L (normal: 10–45), alanine aminotransferase (ALT) 392 IU/L (9–50), and alkaline phosphatase 222 IU/L (150–420). She was treated with intravenous fluids, prochlorperazine, and intravenous penicillin G (250 mg/kg/day). Her physical exam was notable for asterixis and hepatomegaly. Within 72 hours of ingestion, her AST increased to 1290 IU/L, ALT 2094 IU/L, and prothrombin time 37 seconds (control 10.3–14.1 seconds). She was transferred to the University of California, San Francisco Medical Center for management of FHF and listed for liver transplantation. Laboratory studies performed thereafter revealed serum AST >4500 IU/L, ALT >6000 IU/L, total bilirubin 3.4 mg/dL ([58.1 μmol/L] normal: 0.1–1.2 mg/dL), prothrombin time 56 seconds, and ammonia 80 μmol/L (11–35). She became progressively lethargic and encephalopathic. On day 4 after ingestion, a donor organ became available. The donor liver was split using standard techniques such that an adult received the right lobe, and the girl received a left A-OLTX. She was begun on immunosuppression with cyclosporine, mycophenolate mofetil, and prednisone. Her explanted liver section demonstrated extensive diffuse centrilobular necrosis consistent with Amanitin poisoning (Fig 1). Her coagulopathy and serum transaminases rapidly corrected after A-OLTX. A nuclear hepatobiliary scan at 5 days after A-OLTX revealed equal functioning of the native liver and grafted liver with visualization of the biliary tree and gallbladder by 20 minutes (Fig 2A). By 8 days after A-OLTX, hepatobiliary scan showed the native liver had improved function with excretion of tracer into the intestine by 10 minutes but the grafted liver had less function (Fig 2B). The A-OLTX was surgically removed and all immunosuppression was stopped. Repeat histology of the native liver revealed only 10% to 20% of the parenchyma necrotic (Fig 3). She recovered rapidly and was discharged home in 16 days. Follow-up at 4 months revealed a normally functioning regenerated native liver with normal biochemical parameters that continues 9 months after ingestion.

DISCUSSION

Liver transplantation for FHF has been well-accepted in recent years, accounting for 5% to 10% of indications for OLTX. Survival rates have varied substantially between centers ranging from 50% to over 90%. This variation has been due in large part to the difficulty in finding donors within the short time span before irreversible brain injury, and the use of marginal donors with poor initial graft function in this context. Progress in recent years has included the development of improved prognostic scores for the selection of patients for OLTX and the use of intracranial pressure monitoring for selection of viable candidates and perioperative monitoring.

Despite improvements in transplantation therapy, recovery of the native liver obviating the need for lifetime immunosuppression is the optimum outcome for patients with acute liver failure. To achieve this end, artificial liver support and the use of auxiliary liver grafts with preservation of the native liver have been introduced. Although artificial liver devices have had limited success to date, up to 40% of patients supported with auxiliary liver transplants may have recovery of their own liver with subsequent withdrawal of immunosuppression.

FHF caused by acute toxic ingestions offer an ideal setting in which to perform A-OLTX. The insult is discrete, structural damage may be minimal, and no infectious agent is involved.

Emergency A-OLTX for FHF has the distinct advantages of permanently stopping immunosuppressive therapy with withdrawal of the auxiliary graft and allowing recovery of full native liver function as demonstrated in the present case. Obviously, A-OLTX is not appropriate therapy for all patients. Criteria for prediction of those patients who are expected to have complete native liver regeneration and who could benefit from A-OLTX...
For FHF, young age, viral hepatitis or acetaminophen overdose as etiologies of FHF, and a delay between the onset of jaundice and encephalopathy less than 7 days are recognized predictors of a favorable outcome for patients with FHF.\textsuperscript{1,5} Amanita phalloides ingestion is a rare enough condition such that prognostic criteria are not well recognized. The extent of hepatic injury might be expected to influence outcome because liver regeneration is required for ultimate recovery. Our patient had extensive diffuse centrilobular necrosis in her native liver at the time of emergency A-OLTX, and her native liver recovered completely. This finding is in agreement with other reports indicating that the extent of hepatocyte necrosis on liver biopsy is of no value in predicting outcome.

Fig 1. Sample from the liver at time of auxiliary transplant shows extensive necrosis in zone 2 and 3 (mid-zonal and central, center of photo to right lower) with focal involvement of zone 1 (periportal, upper left). This view shows some viable periportal hepatocytes. Congestion of the necrotic zones is also present (center) (hematoxylin and eosin, 50X).

Fig 2. A, Nuclear hepatobiliary scan obtained 5 days after A-OLTX reveals equal functioning of the native liver (on the left) and grafted liver (on the right) with visualization of the biliary tree and gallbladder by 20 minutes. B, Nuclear hepatobiliary scan obtained 8 days after A-OLTX reveals the native liver has improved function with excretion of tracer into the intestine by 10 minutes but the grafted liver has negligible function.
predicting the survival of patients with FHF. Surviving hepatocytes, even if few in number but if relatively damage-free, have the potential for extensive regeneration with time and the potential for ultimate complete recovery of the native liver. Situations where there is injury from a limited single hepatotoxin exposure, as in the current case, may theoretically be the most appropriate candidates for emergency A-OLTX. Based on our successful case, application of emergency A-OLTX should be considered a therapeutic option for children with FHF from *Amanita phalloides* ingestion or other hepatotoxins when the native liver has the potential to regenerate and recover.

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