

potential risk of neurological damage generally mandates prompt discontinuation of OKT3.

The mechanism of OKT3-induced encephalopathy is unclear. OKT3 may crossreact with surface antigens shared by both lymphocytes and cells of the central nervous system (5). Alternatively, the cytokines released by OKT3 may disrupt neuroendocrine functions (6). In addition, our recent practice of administering indomethacin concomitantly with OKT3 to prevent first-dose reactions to OKT3 may have played a contributory role. Since October 1989, four episodes of encephalopathy (patients 3-6) have been observed in 55 renal transplant patients who have received indomethacin 50 mg orally or rectally q. 6-8 hr for 48-72 hr after initiation of OKT3 treatment. This corresponds to a prevalence of 7.3%. In comparison, only 2 episodes of encephalopathy (patients 1 and 2) had been observed among 173 patients who received OKT3 without indomethacin between January 1987 and December 1989 (incidence 1.2%, $P < 0.05$). In earlier studies, indomethacin has been associated with various central nervous system side-effects such as somnolence, feelings of dissociation, paranoia, and even psychosis (7-10). Concurrent administration of indomethacin may further enhance the propensity to develop encephalopathic complications in patients receiving OKT3, perhaps especially in the presence of ongoing acute allograft rejection (1). Further postmarketing studies are required to clarify the pharmacoepidemiology of this drug-induced syndrome. A high index of suspicion of this adverse reaction should be maintained when encephalopathic or psychotic episodes develop in patients receiving OKT3.

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ESOPHAGEAL COMPLICATIONS IN ORTHOTOPIC LIVER TRANSPLANT PATIENTS¹

Although serious esophageal complications are not uncommon after liver transplantation, these have received little attention in the literature (1). We report here the nature and treatment of major esophageal complications encountered in 7 (0.6%) of 1154 adult liver transplant recipients at the University of Pittsburgh between January 1, 1986 and March 31, 1990. Of 4 perforations of the distal esophagus (Table 1), 3 were thought in retrospect to have been caused by pretransplant sclerotherapy. The complication in 2 recipients was diagnosed one or 2 days posttransplantation, and in a third at the time of liver replacement. The fourth perforation was secondary to multiple hemostatic sutures placed during transplantation near the esophagogastric junction. Two patients had intractable esophageal bleeding from multiple ulcerations caused by cyto-

megalovirus and one patient with an Epstein-Barr virus infection developed an esophageal clonal B cell lymphoma.

The treatment for the 7 patients is summarized in Table 1. Three of the 4 patients with esophageal perforation died from 2 to 198 days after the diagnosis in spite of treatment with thoracic and/or transabdominal drainage, exclusion by temporary ligation of the lower esophagus, or an attempt at esophagectomy and colon interposition. The single survivor closed his perforation spontaneously after cervical esophagostomy and prolonged subdiaphragmatic drainage.

One of the 2 patients with massive bleeding survived after total esophagectomy and colon interposition 5 months later. The other died of multiple bacterial infections and disseminated tuberculosis 2 months after the hemorrhage was controlled with suture ligation of multiple bleeding sites through a longitudinal esophagostomy, cervical esophagostomy, tube gastrostomy, and temporary ligation of the esophagus at the esophagogastric junction. The patient with lymphoma had regression of the lesion when immunosuppression was reduced, but hepatic

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TABLE 1. University of Pittsburgh results^a

	Age	Diagnosis	OLT ^x date	Complication	diagnosis date	Treatment	Hospital stay (days)	Outcome
X.N.	31	CAH-B	6/4/88, 6/9/88	Perf.	6/2/88	ex., ces., gs.	64	D
G.J.	53	CAH-B	2/2/89	Perf.	2/20/89	ee., ces., gs.	19	D
R.A.	38	CAH-B	3/30/89	Perf.	4/6/89	1 ex., ces., js., 2 ci.	198	D
H.R.	33	SBC	3/5/90 (also gas- trectomy)	Perf.	3/12/90	ces.	133	A
S.B.	53	CC	9/26/88	Bleed	11/3/88	1 esl., 2 ex., gs.	99	D
M.A.	64	PBC	3/13/89	Bleed	4/7/89	1 ee., ces., 2 ci.	185	A
B.J.	34	CAH-C	1/10/86, 6/19/88	LPD	3/10/88	ege.	18	A

^a CAH, chronic active hepatitis due to B (-B) or C (-C) virus; PBC, primary biliary cirrhosis; SBC, secondary biliary cirrhosis; CC, cryptogenic cirrhosis; ex., exclusion; ces., cervical esophagostomy; gs., gastrostomy; ee., esophagectomy; js., jejunostomy; ci., colon interposition; esl., esophagectomy with suture ligation; ege., esophagogastrrectomy; Perf., perforation; LPD, lymphoproliferative disorder (B cell lymphoma).

rejection followed, necessitating retransplantation. He then had a recurrence of the lesion that was treated with esophagogastrrectomy. Five months later, the lymphoma recurred above the suture line, but this regressed after cyclosporine was stopped and treatment was started once—and subsequently twice—per week with the new immunosuppressive agent FK506 (2, 3). He now is tumor-free almost 3 years after the first liver transplantation, 18 months after retransplantation and 8 months after the change in immunosuppression.

An obvious conclusion from these observations is that major esophageal complications in the transplant population have a very high morbidity and mortality. Aside from the added burden of immunosuppression, liver transplant patients are particularly vulnerable because of their general disability from liver failure, the frequent involvement of the esophagus secondary to liver disease, and the consequent high rate of endoscopy in the days or weeks preceding transplantation. Furthermore, it is obvious that pretransplantation sclerotherapy for both treatment of bleeding esophageal varices and prophylaxis does carry a certain risk of perforation of the esophagus (4, 5), which may not be diagnosed, as in 2 of our patients, until after transplantation. After sclerotherapy, a high degree of suspicion is necessary in order to rapidly diagnose any possible perforation. When sepsis or bleeding were controlled with effective drainage or esophagectomy, later reconstruction and esophageal replacement was possible in one case. In another patient with esophageal lymphoma, a radical esophagogastrrectomy and primary reconstruction were performed without incident.

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COMBINATION THERAPY WITH GANCICLOVIR AND INTRAVENOUS IgG FOR CYTOMEGALOVIRUS INFECTIONS IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS

Successful liver transplantation and postoperative immunosuppression has produced a group of patients who are susceptible to infections by opportunistic organisms. With the advent of more selective immunosuppressive techniques, we have noted a decrease in serious bacterial and fungal infections after liver transplantation. Viral infections, however, remain a significant cause of morbidity and mortality. Cytomegalovirus is the most common viral pathogen identified in opportunistic infections in transplant patients and has been implicated as the offending

organism in 50% of all posttransplant infections (1). CMV infections can produce a variety of symptoms. Fever is the most common manifestation and may be the only clinical sign. Infection of the gastrointestinal tract is common and may produce vomiting, diarrhea, or GI bleeding. CMV infection of the transplanted liver can produce hepatitis that is difficult to distinguish from rejection. Pulmonary infection is the most dreaded form of the disease and has a mortality rate of up to 85–90% (2). Traditionally, treatment of CMV infections after