Chapter 20

Liver Transplantation for Primary and Secondary Hepatic Malignancies: Radiologic Considerations

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Hepatic carcinoma has been treated surgically by segmental resection and for 27 years by orthotopic liver transplantation.¹⁻¹¹ At the early period of its development, orthotopic liver transplantation had been considered to be the theoretical choice of treatment for patients with primary or secondary liver cancer. However, it has been found that there are limits to what this procedure can achieve for these diseases. After liver transplantation, there is a high rate of tumor recurrence which is related to the biologic nature, extension, or insufficient removal of the tumor. There also exists contraindications to this operation in patients that have positive lymph nodes, direct invasion of surrounding organs, or peritoneal seeding of the tumor cells. In addition, the malignancy that arises at one of the upper abdominal organs and extends to neighboring structures has been thought to be beyond surgical cure.

More recently, Starzl et al.¹² introduced the organ cluster (hepatic, pancreatic, and duodenal) transplant for

hepatic and other upper abdominal malignancies after removal of all of the upper abdominal viscera. Grossly, the relationships among the upper abdominal organs-the stomach, duodenum, liver, pancreas, and proximal jejunum-are various and complex, but it is possible to consider them as one large anatomic unit. In the embryo, the liver and the pancreas originate from the ventral and dorsal diverticula of the foregut, which rotate and differentiate into the final stages of organ development. Thus, there exists a direct communication among these organs through the ductal or enteric system. The arterial blood flow to most of these organs originates mainly from the celiac axis and drains into the liver via the portal vein. The vasculature has an intimate correlation with their lymphatic and nervous systems. Thus, by radical excision of this foregut compartment, below or above the transverse colon, it may be possible to remove all of the malignancy, not only that which is confined to the liver but also that

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which has been considered as a contraindication to liver transplant or even surgery.

In the early organ cluster operations, the void in the upper abdomen was usually filled with the cadaveric organ cluster graft which consisted of the liver, pancreas, duodenum, and proximal jejunum. However, when using the liver-pancreas allograft, it was often difficult to obtain a suitable donor at an appropriate time. The procedure was also accompanied by an unexpectedly higher incidence of lethal or severe pancreatic complications. These problems necessitated a change in transplant procedure.^{13, 14} Only the liver was transplanted while still removing the entire organs.

PATIENTS AND SURGICAL TECHNIQUES

At the University of Pittsburgh, in the period ending December 31, 1989, more than 2,350 patients have undergone liver transplantation. Of these patients, 134 had liver malignancies with the histologic diagnoses shown in Table 20-1. Nonfibrolamellar hepatocellular carcinoma was present in 61 patients (46%) consisting of 42 males with an age range of 4 to 69 years and a mean age of 48 years. There were 19 females with an age range of 4 to 65 years and a mean age of 35 years. There were 29 patients (22%) with cholangiocarcinoma or bile duct carcinoma, or both. In this group, there were 21 males ranging in age from 25 to 60 years (mean age 45 years). There were 8 females ranging in age from 35 to 63 years (mean age 44 years).

Neoplasms that originate in the biliary tract, duodenum, stomach, or pancreas, or tumors that originate in the liver parenchyma and involve the other adjacent organs, including the transverse mesocolon, have been, in the past, considered nonresectable. The procedure of upper abdominal exenteration was performed on 38 of the 134 patients listed in Table 20–1. The postoperative histologic diagnosis is shown in Table 20–2. All of this subset of 38 patients were subjected to upper abdominal exenteration with replacement of the liver and pancreas in 23 patients or the liver only in 15 patients. All of these patients had a combination of extrahepatic neoplasm with intrahepatic

TABLE 20-1.

Malignant Neoplasms	Treated by	VOrthotopic Liver	Transplantation

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Neoplasm	No.
Hepatocellular carcinoma	61
Cholangiocarcinoma/duct cell carcil	noma 29
Fibrolamellar carcinoma	9
Epithelial hemangioendothelioma	9
Sarcomas	8
Islet cell carcinoma	7
Carcinoid	5
Hepatoblastoma	3
Metastatic adenocarcinoma	3
	134

TABLE 20-2.

Malignant Neoplasms Treated by Upper Abdomina; Exenteration and Liver or Liver and Pancreas Transplantation

Neoplasm	No.	(M:F)
Cholangiocarcinoma	17	(9:8)
Hepatocellular carcinoma	8	(4:4)
Pancreatic neuroendocrine	4	(3:1)
Carcinoid	3	(2:1)
Sarcomas	4	(2:2)
Cancer of pancreas	1	(1:0)
Adenocarcinoma of colon	_1	<u>(0:1)</u>
,	38	(21:17)

metastases, or intrahepatic tumor with extrahepatic lymph node or direct tumor extension involvement.

The recipient operation consists of three parts: (1) the upper abdominal exenteration involving the tumor, (2) transplantation of the liver or liver and pancreas, and (3) intestinal reconstruction. Upper abdominal exenteration includes the removal of the tumor together with the stomach, duodenum, liver, pancreas, spleen, and variable lengths of the proximal jejunum and ascending and transverse colon. Transection of the bowel is at the terminal ileum, the splenic flexure of colon, and the jejunum about 10 to 20 cm distal to the ligament of Treitz. In most cases, the stomach is transected at the esophagogastric junction, or just distal to it, leaving a 3- to 5-cm cuff of stomach. The celiac axis is transected at its origin. When the tumor is thought not to involve the lymph nodes around the celiac axis, for example, in cases of multiple liver metastases from the colon or duodenum of a small original lesion, the proximal stomach with an intact left gastric artery can be saved for the postoperative benefit of food ingestion. The retrohepatic cava is removed with the specimen. The paraaortic lymph nodes are removed and an immediate microscopic examination is performed in all cases.

The operative method of transplanting the liver alone is essentially the same as that used for regular orthotopic liver transplantation. Minor modifications are vascular anastomoses: the graft portal vein is anastomosed to the proximal stump of the recipient's superior mesenteric vein and a Carrel patch of the graft celiac axis is anastomosed to the recipient's celiac axis instead of being joined to the common hepatic artery. When the recipient celiac axis is saved, the arterial reconstruction is made using the iliac arterial graft that is often used in liver transplantation. Reconstruction of the biliary system is by choledochojejunostomy using a Roux-en-Y loop.

Transplantation of the liver and pancreas differs from the above in the following ways:

1. The superior mesenteric vein of the graft is anastomosed to that of the recipient below the pancreas.

2. The arterial reconstruction is by anastomosis of the graft's Carrel patch, containing the celiac axis and the superior mesenteric artery, to the anterior wall of the abdominal aorta at the level of the celiac axis. When the re-

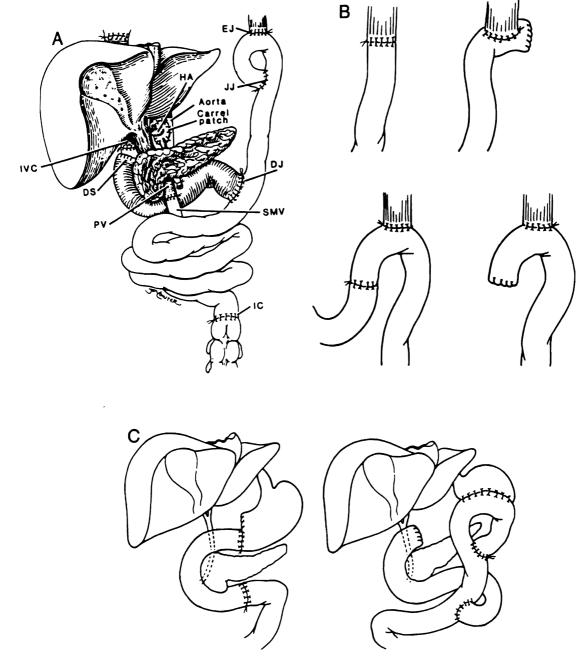


FIG 20-1.

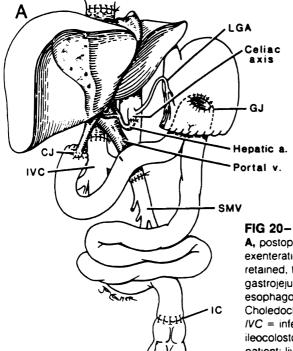
A, postoperative cluster transplant with the donor liver, pancreas, and duodenum after upper abdominal exenteration. Blood supply via hepatic artery (*HA*) from the aortic Carrel patch and the portal vein anastomosed to the superior mesenteric vein (*SMV*). *EJ*

cipient's celiac axis is retained, either the iliac artery or the thoracic aorta of the donor is used for the arterial graft. The graft is anastomosed to the recipient's infrarenal abdominal aorta. Biliary reconstruction is unnecessary.

In most cases, when the liver alone is transplanted, the proximal jejunum is joined to the esophagus or the gastric cuff in an end-to-end or end-to-side fashion with or = esophagojejunostomy; JJ = jejunojejunostomy; DJ = duodenojejunostomy; IC = ileocolostomy; IVC = inferior vena cava; DS = duodenal stump; PV = portal vein. **B**, variations in esophagojejunostomies. **C**, variations in jejunal anastomoses.

without the circular loop, as shown in Figure 20-1, A and B. When the stomach is saved, the proximal intestinal reconstruction is by end-to-side gastrojejunostomy (Fig 20-2, A) As mentioned above, the Roux-en-Y loop is used for biliary reconstruction. The distal intestinal reconstruction is by end-to-end or end-to-side anastomosis between the terminal ileum and the transverse or descending colon.

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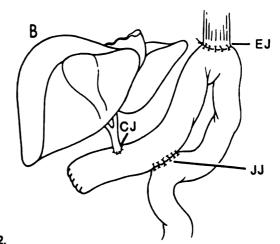


FIG 20-2.

A, postoperative orthotopic liver transplant after upper abdominal exenteration (no pancreas transplanted). If left gastric artery (LGA) is retained, then a portion of the stomach can be retained for a gastrojejunostomy (GJ). If LGA cannot be retained, then esophagojejunostomies are used as in Figure 20-1, A and B. Choledochojejunostomy (CJ), either end to end or end to side (B), is used. IVC = inferior vena cava; SMV = superior mesenteric vein; IC = ileocolostomy. B, variation of anastomosis in the postoperative apancreatic patient: liver transplant only and no gastric remnant. EJ =esophagojejunostomy: JJ = jejunojejunostomy.

When liver-pancreas transplantation is performed, the duodenal stump of the graft is closed and the proximal intestinal reconstruction is the same as done with the liver alone. The distal end of the graft's jejunum is joined to the side of the recipient's jejunum. The distal intestinal reconstruction is the same as described above. When the stomach is saved, a proximal anastomosis is made between the recipient's stomach and the graft's duodenum along with an end-to-end anastomosis between the distal end of the graft's jejunum and the proximal end of the recipient's jejunum. Thus, the continuity of the gastrointestinal tract is kept intact.

In Table 20-2, cholangiocarcinoma and bile duct carcinoma are grouped together because of a unresolved problem in differentiating the two tumors pathologically. There were nine males with an age range of 28 to 57 years and a mean of 40 years, and eight females with an age range of 35 to 51 years and a mean of 41 years. Liver and pancreas transplantation was utilized in nine patients and liver only in eight. Primary hepatocellular carcinoma with extrahepatic extension was seen in eight patients with an equal sex distribution with the males ranging in age from 33 to 57 years (mean age 45 years) and the females ranging in age from 19 to 55 years (mean age 36 years). A liver and pancreas transplant was performed four times in three patients and a liver-only transplant six times in five patients. Primary pancreatic neuroendocrine neoplasms metastatic to the liver were seen in four patients: in three males ranging in age from 37 to 42 years and in one 41-year-old woman. A liver and pancreas transplant was performed in three patients and a liver-only transplant in one. Duodenal carcinoid was seen in three patients; two males 27 and

55 years of age and one 37-year-old woman. Liver and pancreas transplantation was performed three times in two patients and liver-only transplantation in one patient. The group of four sarcomas comprised spindle cell sarcomas of the duodenum with extension into the liver in two patients, a 42-year-old man and a 30-year-old woman, and gastric leiomyosarcomas in two patients, a 49-year-old man and a 32-year-old woman.

IMAGING BEFORE AND AFTER TRANSPLANTATION

The Preoperative Assessment.-The preoperative assessment of these patients is the same as for other liver transplant candidates for benign disease except that the determination of the presence or absence of an intrahepatic malignancy must be carefully reviewed for evidence of extrahepatic tumor and vice versa.

The chest film is routine for all patients, but certainly even more important for those patients in whom one wishes to exclude metastatic disease. As our experience grows, chest computed tomography (CT) may well complement a "negative" chest film as a better imaging modality for detection of pulmonary metastases.

CT, magnetic resonance imaging (MRI), and ultrasound (US) are used to evaluate the size and extent of liver and juxta-liver neoplasms. The extent of intrahepatic involvement is important to determine whether partial hepatectomy would be adequate or whether an orthotopic liver transplant would be the more logical procedure of choice. Extrahepatic spread of intrahepatic lesions or intrahepatic spread of extrahepatic lesions must be carefully assessed which at times can be very difficult. Lymph node involvement is of great importance as to the choice of surgical procedure, but is also directly related to tumor recurrence, as survival in lymph node-positive hepatic neoplasms is considerably worse than in lymph node-negative patients.⁷

The following three cases are representative:

Case 1: A 23-year-old white woman presented with proven nonfibrolamellar hepatocellular carcinoma which measured 11 cm in diameter and was metastatic to five hepatic hilar lymph nodes (Fig 20-3). The perigastric, peripancreatic, and mesenteric lymph nodes were normal histologically. The patient was treated by upper abdominal exenteration and liveronly transplant in mid-1989, and is alive without disease on her most recent follow-up examination at 219 postoperative days. She is receiving additional chemotherapy in her hometown.

Case 2: A 35-year-old woman presented with a 3year history of sclerosing cholangitis. A preoperative endoscopic retrograde cholangiogram revealed a common bile duct stricture with complete obstruction. A percutaneous transhepatic cholangiogram was unsuccessful. The 9.5-cm hepatic hilar neoplasm was felt histologically to be a bile duct carcinoma with extension into the liver. One porta hepatis node was positive for tumor and 12 of 19 extrahepatic nodes showed metastatic neoplasm (Fig 20-4). The patient was treated with a total upper abdominal exenteration and a cluster transplant consisting of the liver, pancreas, and attached duodenum. Pulmonary metastases were noted at 217 days and she died of recurrent neoplasm at 304 days.

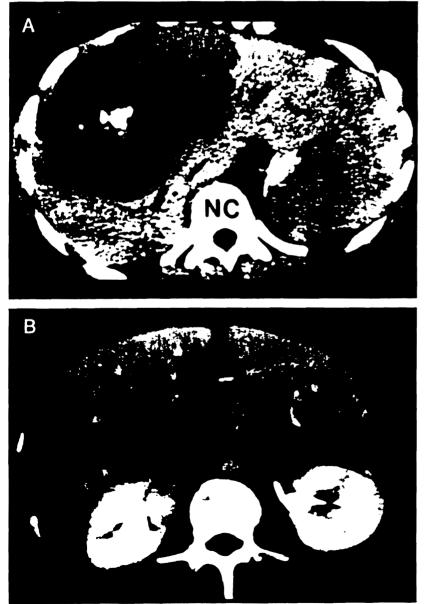


FIG 20-3.

A and **B**, nonfibrolamellar hepatocellular carcinoma metastatic to hilar lymph nodes. *NC* = noncontrast.

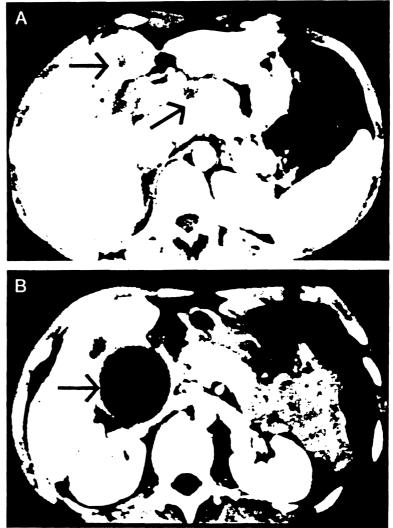


FIG 20-4.

Bile duct carcinoma, liver metastases (**A**, *arrows*) and massive abdominal lymph node metastases **B**, the dilated gallbladder (*arrow*).

Case 3. A 37-year-old white woman presented with a 2-cm malignant carcinoid of the second portion of the duodenum with multiple liver metastases (Fig 20-5). She was treated with an upper abdominal exenteration and a cluster transplant consisting of liver, pancreas, and duodenum. She is alive without detectable recurrence at the latest follow-up, 461 days posttransplantation.

Endoscopic retrograde cholangiography (ERC) or percutaneous transhepatic cholangiography (PTC) is used routinely to assess both intra- and extrahepatic ducts for sclerosing cholangitis, ductal carcinoma, and those patients with large intrahepatic neoplasms that are suspected to be cholangiocarcinogenic with ductal changes. Primary sclerosing cholangitis (PSC) or bile carcinomas are frequently difficult or impossible to distinguish. Approximately 10% of patients with PSC have occult cancer on hepatectomy specimens. Retrograde or antegrade cytology brushings of any suspicious area should be performed.¹⁵ The diagnosis of bile duct carcinoma may well preclude liver removal with liver-only transplantation and require strong consideration for total upper abdominal exenteration.

The Postoperative Assessment.—The evaluation of patients transplanted for hepatic malignancies is the same as for nonmalignant transplants with two major exceptions: the detection of recurrent or residual neoplasm and an understanding of the surgical anatomy in those patients subjected to cluster transplantation.

Figure 20–1,A is an illustration of a cluster transplant (liver, pancreas, and duodenum) following an upper abdominal exenteration consisting of removal of the liver, pancreas, duodenum, all or part of the stomach, a segment of jejunum, the terminal ilium, ascending colon, transverse colon, and a portion of the descending colon. The gastrointestinal tract is reconstituted as a esophagojejunostomy, end-to-side jejunojejunostomy, end-to-side duodenojejunostomy, a blind-ending duodenal stump proximal to the ampulla of Vater, and ileocolonic anasto-

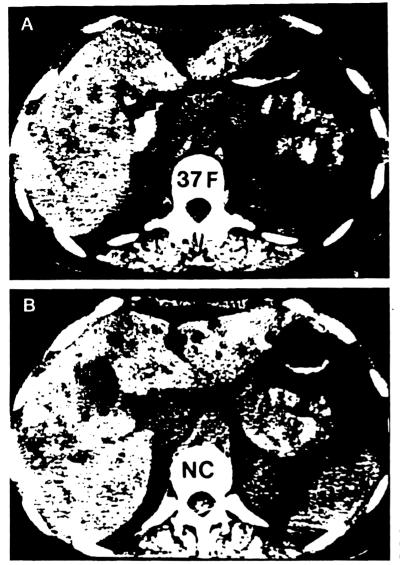


FIG 20–5. A, malignant carcinoid of second portion of duodenum (*arrow*) in a 37-year-old woman with multiple liver metastases. *NC* = noncontrast.

mosis. Modification of the proximal anastomosis is seen in Figure 20-1, B and modifications of the duodenal and gastroduodenal and gastrojejunal anastomoses are shown in Figure 20-1, C. Note should also be made of the Carrel patch in the ventral aspect of the aorta containing the hepatic artery and the tied-off left gastric artery. If the left gastric artery can be preserved, a portion of the stomach is retained, which has the distinct advantage of preventing gastroesophageal reflux.

Surgical variations of the liver-only transplant are shown in Figure 20–2. Figure 20–2, A shows a gastrojejunostomy with preservation of the left gastric artery, a choledochojejunostomy, and the usual ileocolonic anastomosis. Figure 20–2, B shows a esophagojejunostomy, a side-to-side jejunojejunostomy, a choledochojejunostomy, and a blind-ending jejunal afferent loop.

The plain film of the abdomen in the cluster patient needs particular assessment and an understanding of the

surgical anatomy (Fig 20-6). Intestinal staples are used in certain gastrointestinal tract surgical anastomoses and are labeled according to Figure 20-1, A. This is particularly helpful when one subsequently injects intraluminal contrast material in search of extraluminal leakage, or unusual and initially mystifying intestinal routes.

In the absence of the stomach air bubble and in the usual presence of left upper quadrant postoperative fluid, there is no constant relationship of the left upper quadrant jejunal gas to the diaphragm. The nasogastric tubing is usually down the efferent jejunal loop. The radiolucent gas shadow in or near the duodenal stump may simulate extraluminal gas and may be very difficult to assess on plain films.

A Gastrografin (diatrizoate meglumine) or barium upper gastrointestinal (GI) series will readily fill the jejunal loops but will often *not* fill the duodenum through the duodenojejunal anastomosis. Precontrast anteroposterior,

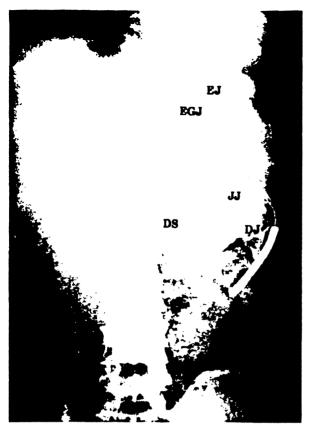


FIG 20-6.

Abdominal film showing surgical anastomoses as seen in Figure 20-1.A. The suture lines are seen as tiny rows of metal surgical bowel staples. The nasogastric tube is down through the esophagojejunostomy (*EJ*) or esophagogastrojejunostomy (*EGJ*) into the efferent jejunal simb even beyond the duodenojejunostomy (*DJ*). *JJ* = jejunojejunostomy; *DS* = duodenal stump; *IC* = ileocolostomy.

cross-table lateral, and erect films are helpful so that after iodized contrast material has filled the gastrointestinal tract, nonfilled pockets of gas may well indicate an abscess. Extraluminal contrast indicates an anastomotic leakage and the relationship of the contrast to the surgical bowel staples should be carefully assessed to determine whether one is dealing with a partially filled small bowel segment or an extraluminal leakage. Contrast material injected per rectum should be performed very slowly with multiple spot films and particular attention given to localizing the bowel staples before the contrast is injected. Anastomotic leakage is extremely uncommon in these cluster patients.

Leakage from the duodenal stump may be assessed by a Gastrografin and upper GI series as demonstrated in Figure 20–7, although there are many times when the duodenum will not fill through the duodenojejunal anastomosis. Technetium 99m mebrofenin can be used to fill the extrahepatic bile ducts which shows as a collection of enlarging radioactivity at the site of the duodenal stump (Fig 20–7, B and C). On this view, the duodenum was normally contractile and propulsive, whereas the site of leakage was adynamic.

The postoperative assessment of the liver in patients with known malignancy is the same as that of nonneoplastic patients with several notable exceptions.

Focal intrahepatic or infrasplenic areas of diminished tissue density suggest ischemia, infection, metastatic disease, or cyclosporine-induced hepatic lymphoma. Focal inhomogeneity of the liver detected either by ultrasound or CT is highly suggestive of hepatic artery thrombosis.¹⁶ The intrahepatic finding, particularly when associated with leakage of contrast material from the biliary tree, is significant and frequently indicates occlusion of the hepatic artery. Most bile leaks occur in the hilar or juxtahilar regions with the intrahepatic peripheral sites being less frequent.^{17, 18} Angiography is diagnostic for arterial occlusion.

Extrahepatic lymph node enlargement can be due to metastatic tumor, a lymphoproliferative disorder associated with cyclosporine administration, and, on rare occasions, infection. Lymphoproliferative disorders ¹⁹ are most commonly seen in enlarged abdominal, mediastinal, or hilar lymph nodes, as well as masses identified within the lung, pleura, or in the gastrointestinal tract or liver.²⁰

Because of the proximity of masses next to major vessels, particularly near surgical anastomoses, psuedoaneurysms may simulate matted lymph nodes. In a series of 15 patients reported by Tobben et al.,²¹ 8 occurred with arterial anastomoses and 7 were nonanastomotic including intrahepatic low- or mixed-attenuation lesions. Bolus CT and duplex sonography are appropriate although it must be appreciated that neither CT nor US is valuable when the pseudoaneurysm is small. Arteriography was diagnostic in all 15 patients.

The CT and US findings in the abdomen in the upper abdominal exenteration patients are understandably different from the findings in nonexenteration patients. Except for the presence or absence of the pancreas, the findings are the same in the exenteration patients.

There is almost always a left upper quadrant extrahepatic fluid collection, which can be quite large. To determine whether this is infected or not is very difficult and fine-needle aspiration with or without catheter drainage is diagnostic. Left upper quadrant bowel gas, whether opacified with contrast material or not, is jejunum. In those patients in whom the jejunum is properly opacified, noncontrast-filled gas is highly suggestive of abscess. A fluidfilled structure near the pancreatic head may be fluid within the duodenal loop, which will frequently not fill with contrast material given orally or through the nasogastric tube in the ileum. The duodenal sweep near the pancreas or the anastomosis with the bile duct in pancreatic patients is frequently dilated.

There have been several instances in which marked dilatation of the patient's ileum occurred in which the ileum fills with fluid but is not obstructed. The cause of this is not apparent.





FIG 20-7.

A, duodenal stump (DS) leak (*black arrow*) with Gastrografin seen extending beyond the DS staple line (*open arrow*). Same patient as in Figure 20–6. **B**, ^{99m}Tc mebrofenin with a small early collection of isotope (*arrow*) which becomes much larger (**C**). Utilizing cine, the large pocket was felt to be the same leak through the DS as shown in **A**.

CONCLUSIONS

The radiologist is an important consultant in the postoperative period after liver transplantation. Infection remains the most serious complication. Thirteen of 38 patients treated by upper abdominal exenteration and liver or liver-pancreas transplantation were septic. Eleven patients died. Every available imaging modality has been used to attempt to find a localized abscess that can be drained either by needle, catheter, or open surgical intervention. This is a never-ending challenge.

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