Annals of Nuclear Medicine Vol. 5, No. 3, 103–107, 1991

Detection of complications after liver transplantation by technetium-99m mebrofenin hepatobiliary scintigraphy

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Fifty-five hepatobiliary scintigraphic studies using ^{99m}Tc-Mebrofenin were performed in 52 orthotopic liver transplant patients to evaluate suspected biliary complications, namely biliary extravasation and extrahepatic obstruction. Final diagnosis was made by analysis of the clinical course and other procedures.

Three out of three studies of biliary leak and four out of five studies of biliary obstruction were detected. There were no false positives in either complication. The sensitivity, specificity and accuracy were 100, 100, 100% for ectravasation and 80, 100, 98% for obstruction, respectively.

Hepatobiliary scintigraphy appears to be an accurate means of detecting biliary leak and obstruction associated with the transplanted liver.

Key words: technetium-99m-Mebrofenin, hepatobiliary scintigraphy, liver transplantation

INTRODUCTION

ORTHOTOPIC LIVER TRANSPLANTATION (OLTX) has acquired an important role as a treatment of end-stage liver disease in the USA; more than 2,000 OLTXs were performed in our university hospital.[1-3] However, it is attended with many kinds of complications, including rejection, hepatic artery and/or portal vein obstruction, biliary obstruction or leak, gastrointestinal bleeding, infections owing to immunosuppression and side effects of the immunosuppressive drugs themselves.

Biliary complications occur in 12 to 25% of the patients after OLTX[4-7] and have been one of the critical problems which usually require immediate surgical intervention. It must be detected quickly and differentiated from other medical complications. An inaccurate choice of therapy could lead to a serious outcome. Therefore, a reliable and non-invasive test for the early detection and differentiation of these problems is needed. Despite the fact that hepatobiliary scintigraphy (HBS)[8,9] is well recognized for evaluating biliary complications after other types of biliary surgery (non-OLTX),[10] there are only a few articles in the literature[8,11-13] related to its use following OLTX.

The purpose of this study is to evaluate the ability of HBS to detect biliary complications after OLTX by means of a new radiopharmaceutical, Tc-99m 3-bromo-2,4,6-trimethyl iminodiacetic acid (^{99m}Tc-Mebrofenin).

MATERIALS AND METHODS

Sixty-two consecutive hepatobiliary scintigraphic studies were performed in 59 orthotopic liver transplant (OLTX) patients having suspected biliary complications. Of these, 52 OLTX patients' clinical data (55 HBS) were obtained from the patients' charts and subjected to review. There were 28 males (30 HBS) and 24 females (25 HBS), whose ages ranged from 6 to 66 years old with a mean of 44.3±13.0 yr (mean±SD). The time interval between OLTX and

Received February 13, 1991, revision accepted June 7, 1991.

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HBS ranged from 3 days to 5 years, with a mean of 3.5 months [40 studies (73%) were performed within 2 months].

HBS was performed after intravenous administration of 185 MBq (5 mCi) [74 MBq (2 mCi) in a child] of ^{99m}Tc-Mebrofenin (CHOLETEC, SQUIBB, New Jersey, USA). Patients were scanned in a supine position; anterior data were acquired with a gamma camera (Raytheon, Technicare, USA) equipped with a low energy, all purpose, parallel-hole collimator and interfaced to a computer (VAX11, Siemens, USA). Soon after injection, the first set of the serial data was obtained every second for one minute into a 64×64 matrix. The second set of consecutive data was collected every 1.5 minutes for 54 minutes (36 images) into a 128×128 matrix. When clinically necessary, 3-, 6- and 24-hour delayed images were added. Biliary images were evaluated visually both with films and in the cine mode on the computer.

RESULTS

Results are summarized in Tables 1 and 2. Fifty-five HBS were reviewed to evaluate the biliary complications. Three out of three leaks and four out of five biliary obstructions (repeat study was performed in patient 42) were detected without false positives. Although the other 47 HBS were negative for leak or obstruction, 17 cases with OLTX rejection, 8 with hepatitis (3 had both), 5 with sepsis or abscess, one with hepatic artery occlusion and one with "reserve injury" (defective liver at surgery) showed various degrees of uptake and excretion abnormalities; 9 who had extrahepatic problems and 9 who had a minimal increase of liver function tests (LFT) or mild clinical symptoms also showed various degrees of hepatic function, i.e., normal to moderately impaired uptake and/or excretion.

Sensitivity, specificity and accuracy were 100, 100 and 100% for leak and 80, 100 and 98% for obstruction, respectively.

Case Reports

Case 1 A sixty-two-year-old male patient (patient 26) underwent hepatobiliary scintigraphy two weeks after liver transplantation primarily due to liver cirrhosis related to hepatitis B. The indication for hepatobiliary scintigraphy was suspicion of biliary complications, since his serum bilirubin was increasing. Extraluminal bowel radionuclide activities appeared in a 23 minute image and became prominent in a 60 minute image (Fig. 1). Cine-mode display was helpful in differentiating intra- from entra-luminal bowel radionuclide activity. The patient underwent surgery, in which disruption of the anterior wall of the choledochojejunostomy with biliary leak was found. The patient's LFT and clinical conditions improved after successful repair surgery and subsequently the patient was discharged.

Case 2 A fifty-five-year-old male patient (patient 52) underwent hepatobiliary scintigraphy on the third day after orthotopic liver transplantation with choledochojejunostomy primarily due to chronic active hepatitis B. The indication for the test was an increase in serum bilirubin level. Twenty and forty-five minute images show mild to moderately delayed hepatic extraction and retention of radionuclide activity in the common bile duct. No small bowel activity was seen. (A 3-hour delayed image also showed the same findings.) These findings are compatible with the obstruction at the anastomotic site of the choledochojejunostomy. The patient received repair surgery the next day, in which invagination of the jejunum by the choledochus was demonstrated.

DISCUSSION

^{99m}Tc-Mebrofenin is a relatively new radiopharmaceutical (one of the imino-diacetic acid [IDA] compounds), and has high hepatic extraction and low renal excretion even in the presence of hyperbilirubinemia, when compared with other IDA compounds such as ^{99m}Tc-diisopropyl IDA (DISIDA).[9,14] Since many of the post-OLTX patients who require HBS have impaired liver function, ^{99m}Tc-Mebrofenin may be more suitable for HBS. In our study, HBS with ^{99m}Tc-Mebrofenin provided good image quality even in patients with hyperbilirubinemia and with moderately to severely impaired liver function, and the renal excretion did not interfere with the diagnosis.

The HBS appeared to be very sensitive for biliary leak (all of the three detected), and also very specific (no false positives). Cine mode display was very helpful in discriminating extraluminal bowel from intraluminal bowel radionuclide activity, i.e., the former continue to increase, whereas the latter moved through the small bowel. Delayed images were also helpful in comfirming the leak which was emphasized by radionuclide activity around the liver, duodenum or proximal jejunum. All three of our leak patients were immediately taken to surgery. However, if the amount of leakage was minimal and conservative therapy selected, the approximate amount of leakage could be assessed by comparing the radionuclide counts in the region of the leak with the counts in the region of the bowel (the radioactivity which passed through the portion where leakage occurred). This might be helpful in monitoring the amount of leak and for comparison in follow up HBS.

The HBS detected four out of five biliary obstruc-

Table 1 Results of the 55 hepatobiliary scintigraphy

Patient No.	Year	Sex	Interval	Obstruct	Leak	Final diagnosis
1	24	F	4 w	n	n	rejection
2	62	M	6 w	n	n	sepsis
2	62	M	3 m	FN	n	bile duct stricture
4	37	M	4 w	n	n	pancreas-small bowel fistula
5	30	F	6 w	n	n	rejection
6	29	M	1 w	n	n	hepatic artery occulusion
7	54	M	6 m	n	n	hepatitis B
8	32	M	1 w	n	n	rejection
9	38	F	4 w	n	n	adhesion
10	34	M	1 w	n	n	rejection
11	66	M	4 m	n	n	hepatitis, pneumonia
12	31	M	2 w	n	n	rejection
13	38	F	3 m	n	n	pancreatitis
14	42	M	4 m	n	n	hepatitis B
15	41	F	4 w	n	n	rejection
16	57	M	1 w	n	n	gastroinestinal bleeding
17	42	M	6 w	n	n	pneumonia
18	66	M	4 m	n	n	sepsis
19	48	F	4 w	n	n	negative
20	38	M	1 w	n	n	negative
21	37	M	2 w	n	n	rejection
21	37	M	3 m	n	n	negative
23	21	F	17 m	n	n	cholangitis
24	50	M	4 w	n	n	negative
25	50	M	5 y	n	n	rejection, hepatitis
26	62	M	2 w	n	TP	leak
27	38	F	4 w	n	n	negative
28	53	F	1 w	n	n	sepsis
29	53	M	4 w	n	n	esophageal ulcer
30	26	M	2 w	n	n	gastrointestinal bleeding
31	31	M	2 w	n	n	abscess
32	35	F	1 w	n	n	negative
33	63	M	2 w	n	n	rejection
34	33	F	1 w	n	n	rejection
35	42	F	4 w	n	n	rejection
36	19	F	4 w	n	n	hepatitis
37	33	M	5 m	n	n	negative
38	40	M	18 m	n	n	hepatitis
39	39	M	5 m	n	n	rejection
40	43	F	4 w	n	n	rejection
41	55	M	4 w	n	n	rejection, hepatitis
42	55	F	2 w	TP	n	obstruction at anastomosis
42	55	F	4 w	TP	n	bile duct stricture
44	47	F	1 w	n	n	mild reservation injury
45	54	M	12 m	n	n	rejection, hepatitis
46	53	F	2 w	n	TP	leak, pancreatitis, sepsis
47	55	F	7 m	n	n	rejection
48	46	M	2 m	n	n	rejection
49	36	F	3 m	n	n	bile duct-artery fistula
50	47	F	2 m	n	n	negative
51	49	F	2 w	n	n	negative
52	55	M	3 d	TP	n	obstruction at anastomosis
53	48	F	4 w	n	n	sepsis
54	61	F	2 m	TP	n	obstruction at anastomosis
55	6	F	2 m	n	TP	leak at T-tube site

Interval: between OLTX and HBS, d: day, w: week, m: month, y: year, n: negative, FN: false negative, TP: true positive

tions (all three of the complete obstructions and one of the two strictures). Delayed images were usually required to differentiate biliary obstruction from severely impaired parenchymal function, which showed slow extraction and slow excretion. Since the resolution of the HBS was not sufficient to detect the stenosis itself, and in some cases the bile ducts could not be visualized, this might be a limitation in visual detection of the partial obstruction. Non-visualization of the bile ducts may have been caused by delayed excretion itself and/or relatively rapid flow of the bile. However, this can be seen in normal cases. Quantitative HBS (Q-HBS)[15–18] may be helpful in diagnosing partial obstruction. Q-HBS may also be very useful in monitoring transplanted liver function, since bilirubin production is one of the simplest and most reliable indexes of the liver function and no other imaging method can assess this.

In conclusion, HBS is outstanding in detecting biliary leaks and biliary obstructions after liver transplantation.

Table 2 Results of the 55 hepatobiliary scintigraphy

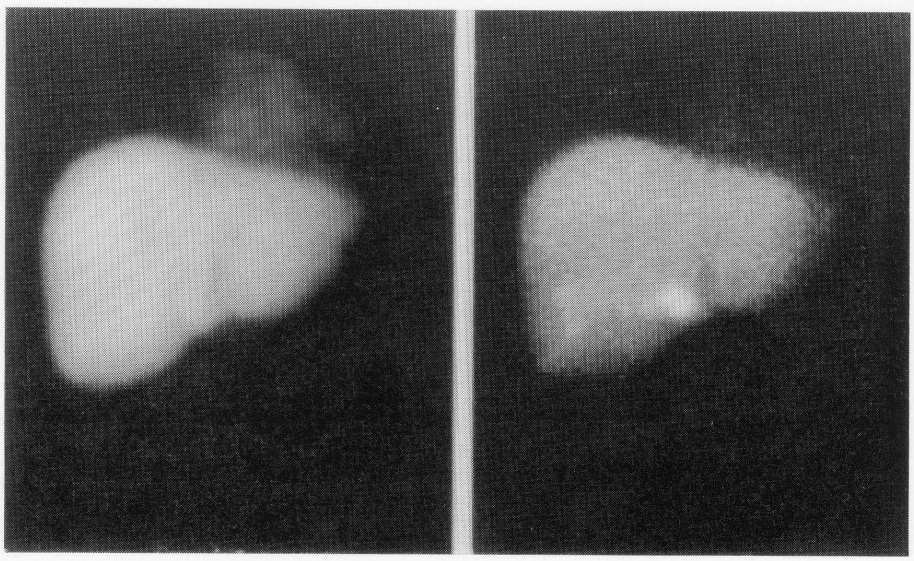
	Scintigraphic finding					
	Leak			Obstruction		
	+	−			+	−
Final diagnosis						
Leak +	3	0	Obstruction +		4	1
Leak −	0	52	Obstruction −		0	50

ACKNOWLEDGMENT

The authors gratefully acknowledge the assistance of

5 min 23 min 65 min

Fig. 1 Case 1 (patient 26). Representative hepatobiliary scintigram of a patient with biliary leak (arrows) after liver transplantation.



20 min 45 min

Fig. 2 Case 2 (patient 52). Representative hepatobiliary scintigram of a patient with biliary obstruction.

Ms. Judith K Holden in preparing the manuscript.

This work was presented in part at the 38th Annual Meeting of the Society of Nuclear Medicine, Cincinnati, Ohio, USA, in June, 1991.

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