Reversal of Intrapulmonary Shunting in Cirrhosis After Liver Transplantation Demonstrated by Perfusion Lung Scan

Daniel P. Levin, Cesar F. Pison, Mary Brandt, Andre Weber, Khazal Paradis, Jean-Martin Laberge, and Herve Blanchard

Division of Nuclear Medicine, Department of Gastroenterology, and Department of Surgery, Hôpital Ste-Justine, Montreal, Quebec, Canada

A young girl with biliary atresia leading to cirrhosis developed respiratory complications with hypoxemia. Intrapulmonary shunting was diagnosed with a ^{99m}Tc-MAA perfusion lung scan, which showed marked systemic activity. The shunting resolved after liver transplantation. The perfusion lung scan offers an efficient method to screen patients with cirrhosis in whom intrapulmonary shunts are suspected and to follow their progress.

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Intrapulmonary shunting is an occasional complication of severe liver disease (*1*). Right-to-left shunting may reach proportions of 20%–70% of cardiac output and result in incapacitating respiratory compromise. Shunts in these patients have been demonstrated by perfusion lung scanning with ^{99m}Tc-labeled macroaggregates of albumin (MAA) (*2,3*). The functional nature of these shunts and their potential reversibility also have been shown (*4*). More recently, cases of improvement and resolution of intrapulmonary shunting after liver transplantation have been documented with ^{99m}Tc-MAA (*5*) and other shunt evaluation methods (*6*).

The purpose of our report is to present another case of resolution of intrapulmonary shunting after liver transplantation in a patient with cirrhosis with a discussion of the role of nuclear medicine therein. This patient had excellent clinical recovery of pulmonary function within months of the operation. Lung perfusion scanning before the transplant demonstrated right-to-left shunting. No shunt was found after transplantation.

CASE REPORT

The patient was born in 1976 with extrahepatic biliary atresia for which a Kasai procedure was performed at age 3 mo. She had several episodes of cholangitis in the first year after the operation and over the following years developed progressive cirrhosis. She was followed at Hôpital Ste-Justine, Montreal, Canada, and in November 1987, at age 11, she complained of shortness of breath with effort and limited exercise tolerance. She was noted to have cyanosis of the buccal membranes, lips and hands, and clubbing of the fingers. Vital signs were normal, the lungs were clear, and there were normal heart sounds with no murmur. The liver was palpable 2.5 cm below the right costal margin, and the spleen could be felt 5 cm below the left costal margin. Spider nevi were present on her cheeks, shoulders, and chest.

On admission for further investigation, Hb was 16.8 g/dl, and all liver function tests were elevated, with the exception of LDH. Evidence of portal hypertension, with a small, irregular liver and splenomegaly, were noted on liver-spleen scan and at abdominal ultrasound. Chest x-ray was normal and EKG showed evidence of right ventricular strain. All lung volumes and flow rates were within normal limits on pulmonary function testing, with a mild decrease in transfer factor (DLCO). Table 1 summarizes results of blood gases and measurements of oxygen saturation at this time and during the progression of her illness. Many of the blood gases were analyzed on capillary specimens due to the patient's age. Of note was the great decrease in oxygen saturation when the patient was upright as compared to when she was supine.

Perfusion and ^{67}Ga lung scans were obtained to further characterize the pulmonary abnormality. Technetium-99m-MAA was prepared with a standard kit preparation (Frosstimage MAA Kit, Merck Frosst, Quebec, Canada). Chromatography of the MAA product showed a greater than 95% labeling and the distribution of particles was normal in other patients imaged with the same preparation that day. Technetium-99m-MAA (111 MBq) was injected in an antecubital vein while the patient was supine and images were obtained with an Ohio Nuclear LFOV gamma camera and a low-energy, parallel-hole collimator in six projections with the patient upright. Three hundred thousand counts were obtained in the anterior projection and the remaining images were of equal time. The perfusion lung scan showed a relatively normal perfusion pattern with no perfusion defects. Marked systemic activity was noted, demonstrated on these images by the presence of intense renal uptake (Fig. 1). Neither bladder activity nor hepatic uptake was present. The ^{67}Ga scan (74 MBq ^{67}Ga-citrate) demonstrated normal pulmonary activity, and a small liver and an enlarged spleen were noted.

Echocardiography did not demonstrate an intracardiac abnormality, and the pulmonary vasculature was normal on pulmonary

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For reprints contact: Daniel P. Levin, MD, Division of Nuclear Medicine, Health Sciences Center, 820 Sherbrook Ave., Winnipeg, Manitoba, Canada R3A 1R9.

TABLE 1
Blood Gases and Oxygen Saturation Before and After Liver Transplantation

Date	Sample type	FiO_2 or Rate*	Position	pO_2	O_2 SAT %	pCO_2	pH
07/25/87	CAP	RA	SUP	46.8	89.3	27.8	7.44
11/10/87	ART	0.10	SUP	98.5	97.8	30.9	7.45
05/18/88	ART	RA	SUP	44.8	80.7	33.1	7.40
		TRANSPLANT 09/10/88					
10/05/88	ART	RA	SUP	37.8	71.8	36.2	7.40
11/16/88		6	UPR		66		
		RA	UPR		48		
		RA	SUP		62		
12/14/88	CAP	RA	UPR	40.3	76.7	31.7	7.42
05/29/89		RA	UPR		89		
		RA	SUP		98		

* O_2 Flow Rate, l/min.
Abbreviations: CAP = capillary; ART = artery; RA = room air; SUP = supine; and UPR = upright.

angiography with no evidence of intracardiac shunting. All hemodynamic parameters were normal.

Approximately 1 yr later, during which time the cirrhosis had progressed and the pulmonary status had deteriorated further, the patient underwent orthotopic liver transplantation. Four months after the transplant, the patient's respiratory status had improved markedly, with no further cyanosis, decreased clubbing, and O_2 saturation of 98% on room air. The decrease in hypoxemia was gradual, and changes in oxygen saturation with position were still present 8 mo after the operation (see Table 1). No systemic activity was evident on a lung scan done 6 mo post-transplant (Fig. 2). Within the year, the patient had no limitation of activity and no further dyspnea with exercise.

DISCUSSION

Intrapulmonary shunting and other mechanisms are considered to cause hypoxemia in up in 28% of patients with cirrhosis or hepatitis. Shunting is the main cause of severe pulmonary complications in cirrhosis (*1*), and severe hypoxemia due to shunting is considered a relative contraindication to liver transplantation (*7*). The present case, as well as other recent reports (*5,6*), demonstrate that these channels are not anatomically fixed and resolution of the shunt can occur. Resolution also has been demonstrated previously in a patient with chronic alcoholic liver disease by perfusion lung scanning (*4*), and improvement coincident with recovery of hepatic function has been noted in other patients with severe liver disease (*8,9*).

Multiple arteriovenous anastomoses, more numerous at the lung bases, have been demonstrated at autopsy in patients with cirrhosis (*10*). These communications are likely responsible for the diffuse nodular pattern with basal predominance which may be seen on chest x-ray (*9*). However, the x-ray may be normal. The anastamoses may be seen as a spongy vascular blush on pulmonary angiography, although this study also may be normal. A humoral effect on the pulmonary vascular bed, possibly due to a circulating vasoactive substance which is normally metabolized by the liver, has been proposed as promoting the development of these channels. True shunting through arteriovenous anastamoses as well as decreased oxygenation of the blood in the center of dilated precapillary vessels are proposed mechanisms for the hypoxemia (*11,12*).

These patients tend to have platypnea (dyspnea while upright which improves when recumbent), presumably because of redistribution of blood to the predominantly basal dilated vessels while upright. The lung scan images show increased basal perfusion, but the pattern cannot be distinguished from the normal distribution. Closure of the arteriovenous anastamoses is a gradual process, but the earlier clinical improvement and the absence of a demonstrable shunt (Fig. 2) show their decreasing impact. It is not known how long these abnormal pathways persist or if they ever completely resolve.

Contrast-enhanced two-dimensional echocardiography has been recommended as the preferred method to demonstrate shunting, because of both its sensitivity and its ability to determine whether the shunting is intracardiac or intrapulmonary (*12*). Transthoracic echocardiography, however, may have difficulty differentiating shunted contrast from turbulence in the atrium. Transesophageal studies may be necessary, but this requires esophageal intubation and instrumentation, and the expertise and equipment may not be available in all centers. Pulmonary and

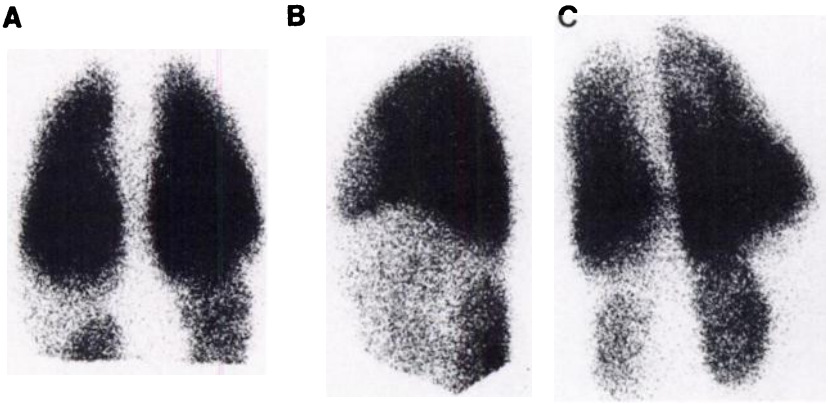

FIGURE 1. There is intense renal and abdominal activity on the perfusion lung scan indicative of right-to-left shunting. The projections are (A) posterior, (B) left lateral, and (C) right posterior oblique.

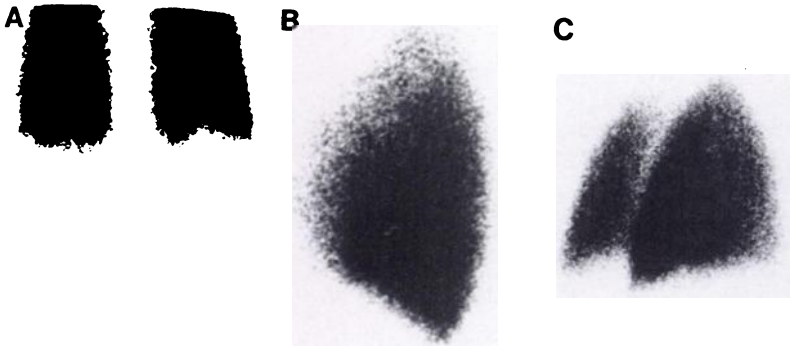

FIGURE 2. Six months after liver transplantation no systemic activity is demonstrated. The projections correspond to those in Figure 1.

cardiac angiography can assess the pulmonary vasculature and look for intracardiac causes of shunt, but the invasiveness and risk of the procedure limits it use in this situation.

Lung perfusion scanning elegantly demonstrates the presence or absence of right-to-left shunting, although it cannot indicate the site of the shunt. A flow study may be useful for localization. The lung scan is a simple, nonoperator-dependent, noninvasive, and inexpensive method to investigate pulmonary dysfunction in patients with chronic liver disease. The scan appears to be the most efficacious method as a screening test, and it may detect shunting in patients before it is clinically apparent. Shunt quantification methods can provide early evidence of progression of the shunt. The demonstration of increasing shunt in a candidate for transplantation may increase the urgency of the operation.

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