Course Before and After Treatment of a Patient with Budd-Chiari Syndrome Monitored by Iodine-123-Iodoamphetamine Scintigraphy per Os and per Rectum

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A 55-yr-old woman with Budd-Chiari syndrome was treated by percutaneous transluminal angioplasty with a balloon catheter. Before and after treatment, portal scintigraphy was performed by the administration of [^{123}I]iodoamphetamine per os and per rectum. An enteric capsule was used for the oral administration. Before treatment, the portal shunt index via the superior mesenteric vein was 40.5%; two weeks after treatment, it was 50.2%; and five months after treatment, it was 41.2%. Before treatment, the portal shunt index via the inferior mesenteric vein was 86.0%; two weeks after treatment, it was 87.6%; and five months after treatment, it was 21.8%. The treatment improved the portal circulation through the inferior mesenteric vein only, with little effect on the portal circulation through the superior mesenteric vein.

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Percutaneous transluminal angioplasty is used to treat patients with Budd-Chiari syndrome (*1,2*). The changes in portal systemic circulation after angioplasty in Budd-Chiari syndrome have not been reported. To estimate the portal circulation before and after angioplasty, an enteric capsule containing [^{123}I]iodoamphetamine can be given per os and the same radionuclide can be given per rectum simultaneously for portal scintigraphy. Principles of the method are as follows. In healthy subjects, the radionuclide is absorbed in the rectum and passes through the inferior mesenteric vein to the liver via the portal vein; much of the radionuclide accumulates in the liver, and little accumulates in the lungs. The iodoamphetamine in the enteric-coated capsule is absorbed in the small intestine, entering the superior mesenteric vein and reaching the liver via the portal vein. A smaller proportion accumulates in the lungs than by the per rectal route; little accumulates in the lungs. Collateral circulation in the inferior mesenteric vein increases the portal shunt index via the rectum; collateral circulation in the superior mesenteric vein increases the index via the small intestine. Both are seen as increased accumulation of the radionuclide in the lungs, and decreased accumulation in the liver (*3*). We used this method to examine a patient with Budd-Chiari syndrome before and after treatment.

CASE REPORT

A 55-yr-old woman consulted a neighborhood physician with the complaint of edema of the legs. The results of clinical tests showed mild anemia and abnormalities in liver function, and physical examination showed esophageal varices. She was referred to our hospital with suspected Budd-Chiari syndrome.

At the time of hospitalization, the patient was of moderate build and was well-nourished. The liver was palpable on the right midclavicular line 3 cm below the ribs and veins in the abdominal region were dilated. At the time of admission, red blood cells were 359 × 10^4/mm^3, hemoglobin was 10.3 g/dl, total bilirubin was 0.9 mg/dl, aspartate aminotransferase was 23 IU/liter, alkaline phosphatase was 12.2 KAU/liter, γ-glutamyltranspeptidase was 110 IU/liter, and serum cholinesterase was 0.40 ΔpH. An inferior venocavogram showed occlusion of the inferior vena cava and a large patent right hepatic vein; venous pressure was 290 mm H_2O. The region of obstruction was dilated with a balloon catheter, after which venous pressure decreased to 70 mm H_2O (Fig. 1). Five months after treatment, the anemia and liver function tests had improved, and the esophageal varices had healed.

Once before and twice after treatment, portal scintigraphy was done by simultaneous administration of an enteric capsule containing [^{123}I]iodoamphetamine by mouth and by rectum. The portal shunt index via the small intestine (the shunt index of portal circulation via the superior mesenteric vein) and the per-rectal portal shunt index (the shunt index via the inferior mes-

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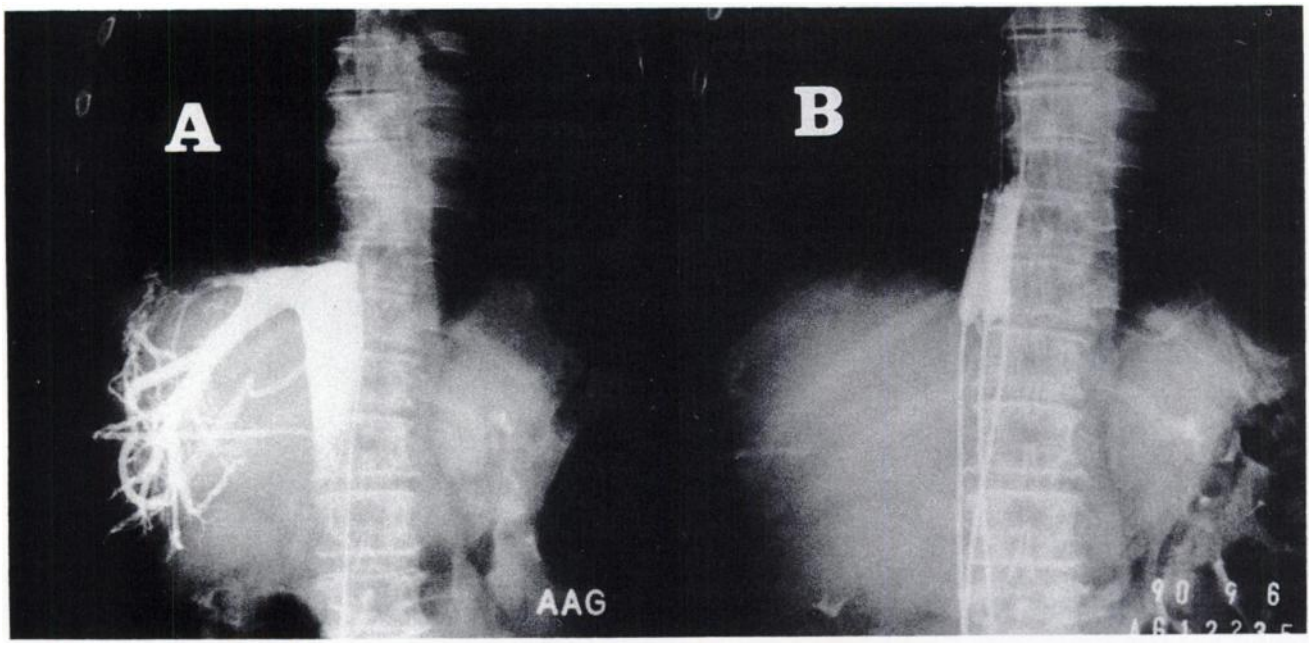

FIGURE 1. (A) Inferior venocavogram showing occlusion of the inferior vena cava and the presence of a large patent right hepatic vein. (B) Obstruction being dilated with a balloon catheter.

enteric vein) were calculated. In healthy volunteers (n = 5), the shunt index via the small intestine was 11.6% ± 6.8%, and that via the rectum was 10.4% ± 5.7%. In patients with chronic hepatitis (n = 12), the index via the small intestine was 18.1% ± 10.1%, and that via the rectum was 15.7% ± 9.0%. In cirrhotic patients without varices (n = 12), the index via the small intestine was 39.4% ± 6.7%, and that via the rectum was 42.9% ± 27.0%. In cirrhotic patients with varices (n = 14), the index via the small intestine was 42.7% ± 12.7%, and that via the rectum was 85.4% ± 13.1% (*3*).

Before treatment, the index via the small intestine was 40.5%. Two weeks after treatment, it was 50.2%, and five months after treatment, it was 41.2% (Fig. 2). Before treatment, the index via the rectum was 86.0%. Two weeks after treatment, it was 87.6%, and five months after treatment, it was 21.8% (Fig. 3).

DISCUSSION

In Japan, Budd-Chiari syndrome arises because of a membranous web in the vena cava in 80% of reported cases; in the United States, this etiology is rare (*4*). Our patient had such a membranous web, and so treatment could readily be done by percutaneous transluminal angioplasty. Koizumi et al. (*5*) reported that the venous pressure of the inferior vena cava decreased and the collateral circulation of this vein improved immediately after treatment of three patients. Ohtomo et al. (*6*) found that esophageal varices disappeared five months after the treatment of a patient with Budd-Chiari syndrome. This suggests that improvement in portal circulation, including changes in esophageal varices, does not begin immediately. The findings for subjects with Budd-Chiari syndrome who are examined by conventional static radiocolloid scintigraphy are of central localization of the radiocolloid in most cases and of patchy uptake in a smaller proportion of cases (*7–9*). Such findings reflect a complication that may or may not develop. For definite diagnosis of the syndrome, examination of the vena cava is needed. The portal shunt index reflects abnormalities in the portal circulation that arise in all cases of this disease. The method is relatively noninvasive and can be done in the outpatient clinic for diagnosis or before and after treatment in patients with Budd-Chiari syndrome. Radionuclide venography has been used to diagnose this syndrome (*10,11*). With this method, collaterals of the inferior vena cava can be seen simply and relatively noninvasively, but the degree of portal collateral circulation cannot be measured.

We used a radionuclide method to measure changes in the portal systemic circulation after treatment of a patient with Budd-Chiari syndrome. The portal shunt index via the small intestine and that via the rectum had both increased slightly 2 wk after angioplasty. Five months after angioplasty, only the index via the rectum had improved greatly. Most of the portal collateral circulation drained into the inferior vena cava, which may explain why the shunt indices rose transiently when the pressure in the inferior vena cava decreased immediately after angioplasty. The finding that only the portal shunt index via the rectum had greatly improved 5 mo after treatment showed that angioplasty improved only the portal circulation via the inferior mesenteric vein, with little effect on the portal circulation via the superior mesenteric vein.

This method permits assessment in a noninvasive way of portal hemodynamics and is clinically useful.

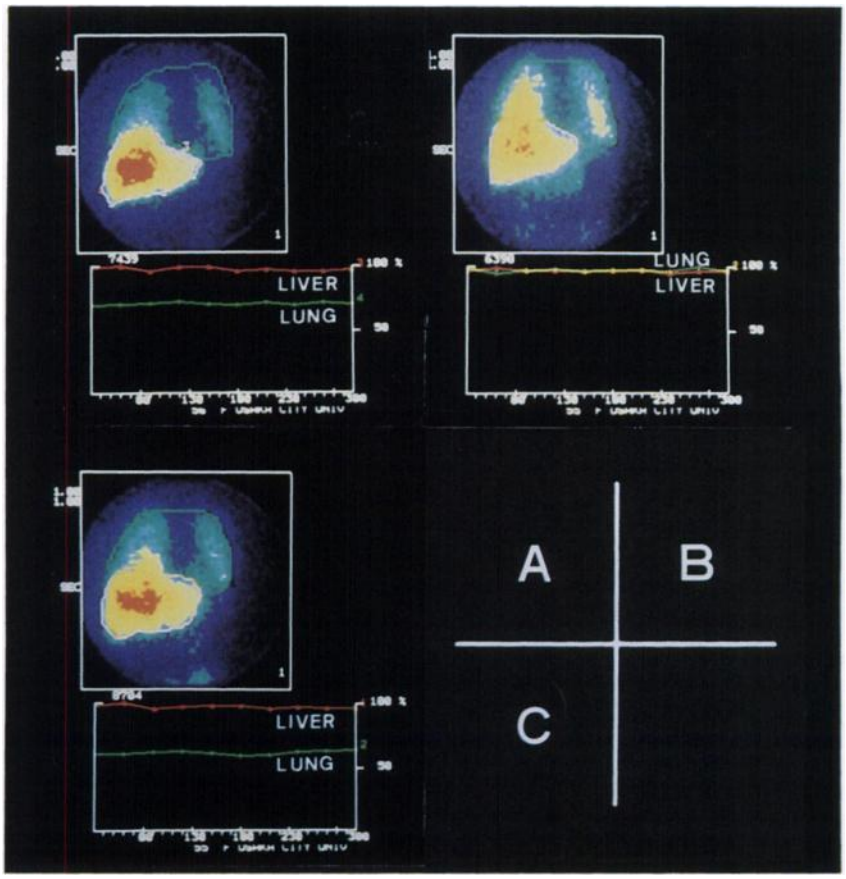

FIGURE 2. (A) Portal scintigram via the small intestine and time-activity curves over the liver and lungs before treatment. (B) Portal scintigram via the small intestine and time-activity curves over the liver and lungs 2 wk after treatment. (C) Portal scintigram via the small intestine and time-activity curves over the liver and lungs 5 mo after treatment.

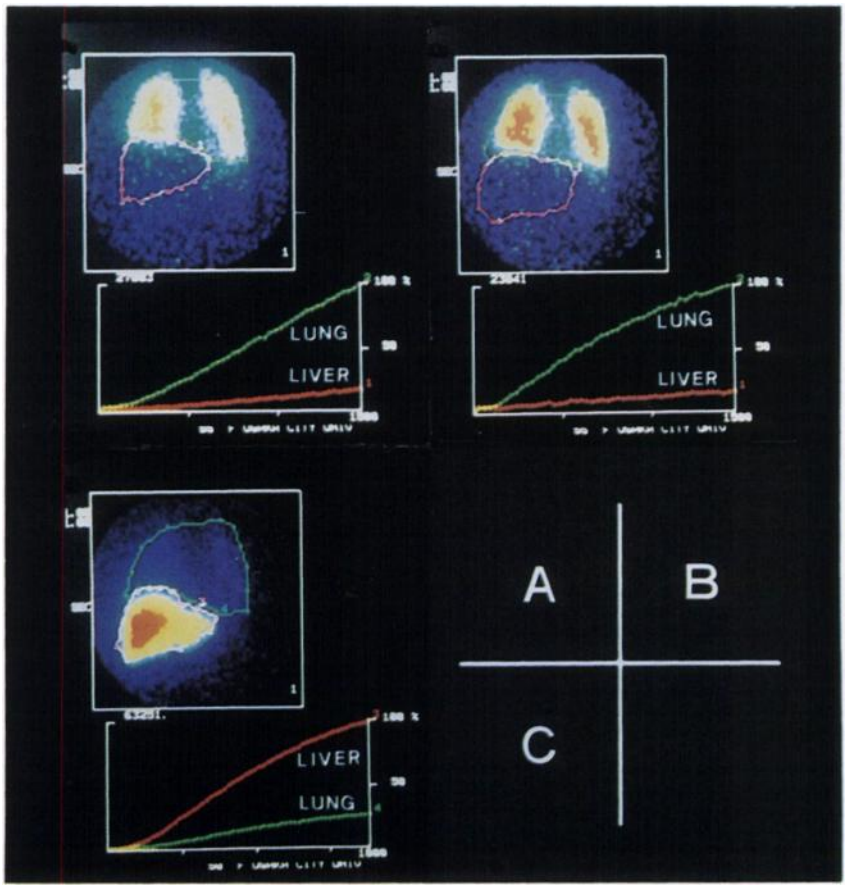

FIGURE 3. (A) Portal scintigram via the rectum and time-activity curves over the liver and lungs before treatment. (B) Portal scintigram via the rectum and time-activity curves over the liver and lungs 2 wk after treatment. (C) Portal scintigram via the rectum and time-activity curves over the liver and lungs 5 mo after treatment.

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SELF-STUDY TEST
Skeletal Nuclear Medicine
ANSWERS

ITEM 1: "Flare" Phenomenon

ANSWER: A

The term "flare phenomenon" was originally used by Gillespie et al. to describe the increase in activity seen on ^{87m}Sr bone scans during treatment of patients with metastatic disease who were responding to chemotherapy. This phenomenon was further characterized by Rossleigh et al. in patients undergoing ^{99m}Tc MDP bone scintigraphy for evaluation of therapy for breast cancer metastases. They defined the "flare response" as: (1) an increase in tracer uptake or in the apparent size of known metastatic lesions and/or the appearance of new lesions within 6 mo of commencing therapy, in the absence of increasing bone pain (in practice, however, pain occurs in some patients responding to therapy); and (2) subsequent decreased uptake in these lesions, without a change in therapy, on repeat scintigraphy within 2–3 mo. In this series, ten patients showed a healing "flare response" 6 wk to 6 mo after therapy. Five of the ten patients showed increased uptake in previously demonstrated lesions. In the other five patients, new lesions were identified that previously were undetected. In all of the patients, therapy was not altered during the course of the serial studies, there was a reduction in bone pain or objective tumor responses in other sites, and later follow-up studies showed decreased uptake in the known lesions. In only one of the patients was a radiographic change (sclerosis of a lytic lesion) seen in association with the healing flare. The "flare phenomenon" has been seen in patients with prostate carcinoma and other tumors, as well. It also may occur locally in regions undergoing irradiation for metastatic disease. The likelihood of observing the "flare phenomenon" depends on the type of tumor, the type of therapy, the interval after onset of treatment, and the frequency of bone scintigraphy.

The "extended pattern" seen with primary bone tumors in long bones is not related to the "flare phenomenon." Patients with primary bone tumors may show increased activity in adjacent joints or along the entire extremity. This increase in activity is usually mild to moderate in degree and is thought to be due either to generalized increased blood flow to the extremity or to a change in the patient's gait. The "extended pattern" is one reason that bone scintigraphy may overestimate the extent of osseous involvement by a primary bone tumor. Similar "extended" findings also occur with inflammatory lesions of the long bones.

When Paget's disease involves long bones, the process may involve the entire bone or it may extend from one end of the bone for a variable length into the diaphysis. Radiographically, the leading edge of the lytic phase of Paget's disease in a long bone has been described as a "flame-like" rarefaction. This also has been characterized as a "blade of grass" appearance.

The persisting minimal uptake seen in regressing metastases is not the "flare phenomenon." This uptake likely reflects continued remodeling of bone after the local tumor deposit has been reduced or eradicated.

On oblique scintigrams of the skull, an area of increased activity in the anterior temporoparietal region is occasionally seen. This has been called a calvarial flame and probably is due to the increased bone thickness of the lateral orbital ridge or the pterion viewed on end in this projection.

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ITEM 2: Mechanisms of Radiopharmaceutical Uptake in Osseous Lesions

ANSWER: E

Bone-seeking radiopharmaceuticals are accumulated in greater degree at skeletal sites where there is increased blood flow (thus exposing that bone to more tracer for chemisorption over any given time), and also in sites of new bone formations where there is an increase in the surface area of hydroxyapatite crystals per unit volume of bone. Newly forming hydroxyapatite crystals are of smaller size than mature crystals and provide a relatively greater surface area for chemisorption of the tracer. Although both increased blood flow and new bone formation (with associated increase in crystal surface area) are important, several studies have shown that the magnitude of the change in blood flow is insufficient to account for the substantially increased tracer accumulation in epiphyseal plates, metastatic lesions, and healing fractures.

A large mass of compact bone with normal blood flow and hydroxyapatite deposition will not necessarily have increased uptake; e.g., bone islands are not usually noticeably "hot" by scintigraphy.

The organic matrix has rather low affinity for the ^{99m}Tc diphosphonate agents when compared with hydroxyapatite crystals. There is little experimental evidence that alkaline phosphatase activity bears a relationship to the localization of bone-seeking radiopharmaceuticals.

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