

## Inexplicable suppression of hepatic uptake of gallium-67, a case report

Tadaki NAKAHARA, Hirofumi FUJII, Kayoko NAKAMURA, Jun HASHIMOTO and Atsushi KUBO

*Department of Radiology, Keio University School of Medicine*

We describe here a case report of a patient with acute lymphocytic leukemia in whom hepatic gallium-67 (Ga-67) uptake was suppressed. The patient was hospitalized with increasing dyspnea. In Ga-67 scintigraphy, there was no hepatic uptake, although other physiological uptake was clearly observed. In addition, the scintigraphy showed increased accumulation in the right lung consistent with infection. We considered possible reasons for these findings. The patient had no history of chemotherapy or blood transfusion, and his iron metabolism was almost normal. He was not receiving any medication which might reduce hepatic blood flow. Blood chemistry suggested normal hepatic and renal function. The patient died from pneumonia 6 weeks later. The autopsy revealed extensive infiltration of the right lung with *Bacillus cereus* (*B. cereus*). Metabolic acidosis and/or iron utilization of *B. cereus* may induce both increased Ga-67 accumulation in the infected lesion and suppressed uptake in the liver, but these mechanisms could not explain normal physiological uptake in the other organs. This case warranted the further study of the hepatic Ga-67 uptake mechanism.

**Key words:** gallium-67 scintigraphy, hepatic uptake, physiological uptake

### INTRODUCTION

THE MECHANISM of gallium-67 (Ga-67) uptake by certain tumors and the liver has been extensively investigated.<sup>1</sup> There have been previous reports of patients with poor hepatic uptake of Ga-67 due to chemotherapy or transfusion.<sup>2-6</sup> We discuss a patient with an unexplained reduction in hepatic uptake of Ga-67.

### CASE REPORT

A 72-year-old man was admitted to our hospital in May 1999, complaining of shortness of breath. His medications included pilsicainide hydrochloride, digoxin, aspirin, rebamipide, oxethazaine, cefcapene pivoxil hydrochloride, carbocysteine and tiaprofenic acid. There was no

history of previous blood transfusion. Previous routine blood tests were normal.

On admission his complete blood count showed granulocytopenia and anemia. Serum iron, transferrin and total iron binding capacity were almost normal. Serum alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, and creatinine were within normal limits. Blood gas analyses performed on admission and a week after admission showed normal blood pH. Chest x-ray showed infiltrates in the right middle lung field. Analysis of bone marrow aspiration was consistent with acute lymphocytic leukemia (ALL).

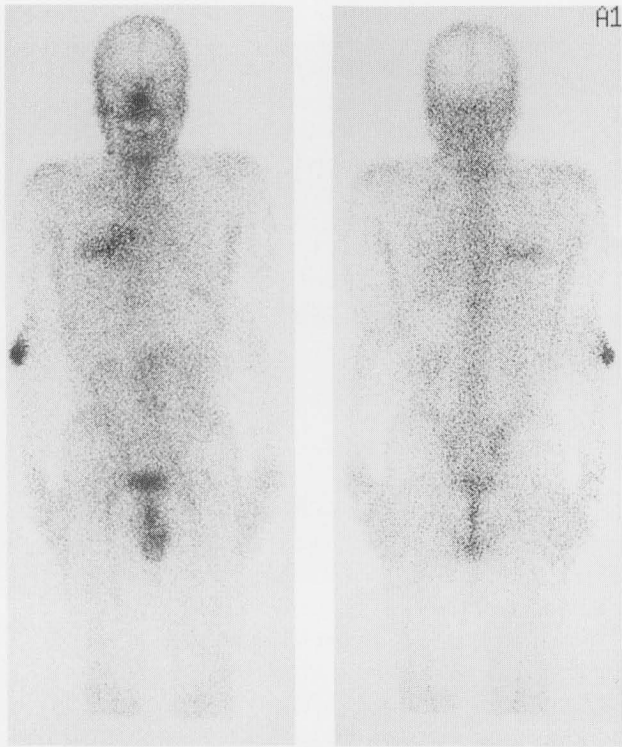
Ga-67 scintigraphy was performed 2 weeks after admission. Ga-67 imaging showed an area of increased accumulation in the middle portion of the right lung and noticeably reduced hepatic uptake (Fig. 1). Cardiac and renal uptake was barely visible. Physiological uptake was observed in the spine, nasal cavity and scrotum. Chest and abdominal CT scans, performed after the Ga-67 scan, indicated pneumonia in the right lower lobe and a small hepatic cyst.

Despite subsequent treatment with antibiotics and chemotherapy the patient died from overwhelming

Received December 18, 2000, revision accepted April 27, 2001.

For reprint contact: Tadaki Nakahara, M.D., Department of Radiology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, JAPAN.

E-mail: n-tadaki@snu.ne.jp



**Fig. 1** Anterior (left) and posterior (right) views of gallium-67 scintigraphy image in our patient. These images show an area of increased accumulation in the middle portion of the right lung and markedly reduced hepatic uptake. Focal intense accumulation around the right elbow indicates the leak of the tracer under the skin.

pneumonia within four weeks. Autopsy revealed *Bacillus cereus* (*B. cereus*) infection of the right lung.

## DISCUSSION

We have described here a case report of a patient presenting with ALL and pneumonia, and with unexplained suppression of normal hepatic uptake of Ga-67. Hepatic uptake of Ga-67 is usually ascribed to transferrin-dependent mechanisms as it is reduced after chemotherapy or transfusion.<sup>2-6</sup> In such cases, physiological accumulation in other organs (e.g., the nasal cavity and scrotum) is also reduced, and Ga-67 scintigraphy resembles bone scintigraphy. As shown in Figure 1, Ga-67 uptake by organs other than the liver is clearly seen, which was quite different from bone scintigraphy-like images. The patient had no history of chemotherapy or blood transfusion. It would therefore not appear that Ga-67 hepatic uptake was suppressed by the usual transferrin-dependent mechanisms in this case.

To our knowledge, only one mechanism can explain why hepatic uptake was suppressed but normal physiological uptake was observed in the other organs. Reduced hepatic blood flow can suppress hepatic uptake of

Ga-67 because local blood perfusion is related to Ga-67 uptake in the corresponding area. Some drugs can reduce hepatic blood flow,<sup>7</sup> although our patient had not received such drugs. Portal and/or sinusoidal infiltration of tumor cells sometimes occurs in patients with hematological malignancies,<sup>8,9</sup> which can cause a decrease in hepatic blood flow. Nevertheless, such tumor involvement was unlikely to occur in our patient because his blood tests showed normal liver function, and an abdominal CT scan showed no sign of reduced hepatic blood flow (e.g., hepatic venous thrombosis). Moreover, since Ga-67 generally accumulates in leukemic lesions, the absence of hepatic Ga-67 uptake might reflect no hepatic involvement of acute lymphocytic leukemia.

Increased Ga-67 accumulation in the infectious lesion is suggested by two mechanisms. In an acidic condition, Ga-67 binds to lactoferrin rather than transferrin.<sup>10,11</sup> This is the explanation given for the localization of Ga-67 in infectious lesions—due to local acidosis and the presence of abundant lactoferrin in the lesions. Although the patient's blood gas analyses were performed only two times as mentioned above, and showed normal blood pH, his severe illness might have resulted in a systemic metabolic acidosis. This can lead to reduced transferrin-dependent hepatic uptake of Ga-67. In addition, *B. cereus* utilizes hemoglobin and the hemoglobin-haptoglobin complex rather than transferrin-bound iron as a source of iron,<sup>12,13</sup> suggesting that *B. cereus* may also take up Ga-67 irrespective of whether it is bound to transferrin or not. Without physiological uptake by organs, these suggestions can also explain suppression of transferrin-dependent hepatic uptake.

In summary, we had not yet clarified the cause of the unusual Ga-67 scintigraphy findings in this patient. This case warranted further study of the hepatic Ga-67 uptake mechanism.

## REFERENCES

1. Hoffer P. Gallium: mechanisms. *J Nucl Med* 1990; 21: 282-285.
2. Weiner RE, Spencer RP, Dambro TJ, Klein BE. Gallium-67 distribution in a man with a decrease in both transferrin and hepatic gallium-67 concentration. *J Nucl Med* 1992; 33: 1701-1703.
3. Sohn M-H, Jones BJ, Whiting JH, Datz FL, Lynch RE, Morton KA. Distribution of gallium-67 in normal and hypotransferrinemic tumor-bearing mice. *J Nucl Med* 1993; 34: 2135-2143.
4. Sawada A, Yoshida S, Kamiike O, Morita M, Nishioka M, Inomata T, et al. Study on suppressed uptake by the liver in Ga-67 scintigraphy. *Radioisotopes* 1986; 35: 473-477.
5. Englestad B, Luk SS, Hatner RS. Altered Ga-67 citrate distribution in patients with multiple red blood cell transfusions. *AJR* 1982; 139: 755-759.
6. Loesberg AC, Martin WB. Altered biodistribution of Ga-67 citrate in an iron-overloaded patient with sickle cell disease. *Clin Nucl Med* 1994; 19: 157-159.

7. Bomber P, McCready R, Hammersley P. Propranolol hydrochloride enhancement of tumor perfusion and uptake of gallium-67 in a mouse sarcoma. *J Nucl Med* 1986; 27: 243–245.
8. Walz-Mattmuller R, Horny HP, Ruck P, Kaiserling E. Incidence and pattern of liver involvement in haematological malignancies. *Pathol Res Pract* 1998; 194: 781–789.
9. Weidmann E. Hepatosplenic T cell lymphoma. A review on 45 cases since the first report describing the disease as a distinct lymphoma entity in 1990. *Leukemia* 2000; 14: 991–997.
10. Carver FJ, Frieden E. Factors affecting the adenosine triphosphate induced release of iron from transferrin. *Biochemistry* 1978; 17: 167–172.
11. Morgan EH. Studies on the mechanism of iron release from transferrin. *Biochem Biophys Acta* 1979; 580: 312–326.
12. Sato N, Kurotaki H, Watanabe T, Mikami T, Matsumoto T. Use of hemoglobin as an iron source by *Bacillus cereus*. *Biol Pharm Bull* 1998; 21: 311–314.
13. Sato N, Ikeda S, Mikami T, Matsumoto T. *Bacillus cereus* dissociates hemoglobin and uses released heme as an iron source. *Biol Pharm Bull* 1999; 22: 1118–1121.