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Gallium-67 scintigraphy in patients with hemochromatosis treated by deferoxamine

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Gallium scintigraphy was performed as an aid for determining the presence or absence of malignant neoplasm in two patients with hemochromatosis treated by deferoxamine. However, gallium scan images could not be obtained. So gallium scintigraphy was performed once more to investigate the cause of low activity. Both patients had heavy urinary excretion of gallium in the first 24 hrs after the injection, and activity was very low on the day of examination. This phenomenon may be attributed to the effect of deferoxamine which is highly bound to the gallium.

Key words: Gallium scintigraphy, Deferoxamine, Hemochromatosis, Urinary excretion

INTRODUCTION

DEFEROXAMINE is a well known specific iron-chelating agent and is usually used for the treatment of iron overload.[1–3] In addition, deferoxamine has high affinity for gallium as well as iron.[4,5] So the distribution of gallium is significantly affected by administration of deferoxamine.[5–7] In previous human studies, deferoxamine has been confirmed to accelerate the excretion of Ga-67 from the blood by Ga-67 activity counts of venous blood samples.[8] But these scintigraphic images and Ga-67 activity in the urine were not reported. We report on the scintigraphic images and the urinary excretion of Ga-67 citrate in two patients who received deferoxamine.

CASE REPORTS

Case 1

A 54-year-old man was admitted with a history of sideroblastic anemia persisting for the past two years. The patient had received blood transfusions 5 times during this period. A diagnosis of liver dysfunction was made on admission. A diagnosis of secondary hemochromatosis was made and the deferoxamine was administered, 4,000 mg per day, for 30 days.

The skin showed generalized brown hyperpigmentation all over the trunk. The liver was palpable 6 cm below the right costal margin and the spleen was not felt. Examination of the blood showed a decreased red cell count of $273 \times 10^4/mm^3$, a depressed hemoglobin of 10 g/d*l*, an increased serum iron of 256 g/d*l* and a depressed UIBC of 68 g/d*l*. The other studies were normal. Computed tomography (CT) of the upper abdomen (Fig. 1) revealed a marked increase in density of the liver parenchyma (CT number is 100 H.U.).

Gallium scintigraphy was performed to evaluate the effect of deferoxamine during the administration of this drug (the 25th day). After the intravenous administration of 3 mCi of Ga-67 citrate, a study using gamma camera (MaxiCamera 400T, General Electric Co.) was done. Fig. 2 shows anterior and posterior whole body images at 6 hrs after the injection. Activity in the kidneys and the bladder is noted. Fig. 3 shows sequential posterior views of the abdomen, and rapid decrease of the activity in the bilateral kidneys and the body is noted.

Case 2

A 53-year-old woman was admitted with a six-month history of general fatigue and right epigastric pain. Hepatomegaly was noted but pigmentation was not. Examination of the blood showed a normal red cell count of $360 \times 10^4/mm^3$, a depressed hemoglobin of

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10.8 g/dl, an increased iron of 199 g/dl and a decreased UIBC of 8.0 g/dl.

CT of the abdomen (Fig. 4) revealed increased density in the liver parenchyma (CT number is 105 H.U.). Liver biopsy by laparoscopy verified hepatic hemochromatosis, so she was treated with 2,000 mg of deferoxamine per day for 14 days.

Gallium scintigraphy was performed on the 12th

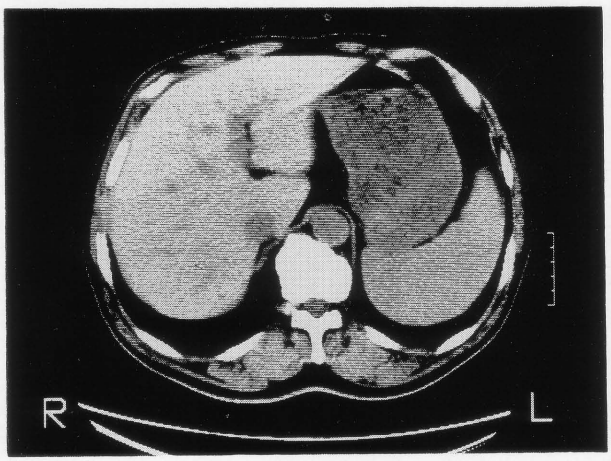

Fig. 1 (case 1)
Abdominal CT reveals marked increased density of liver parenchyma (CT number is 100 H.U.).

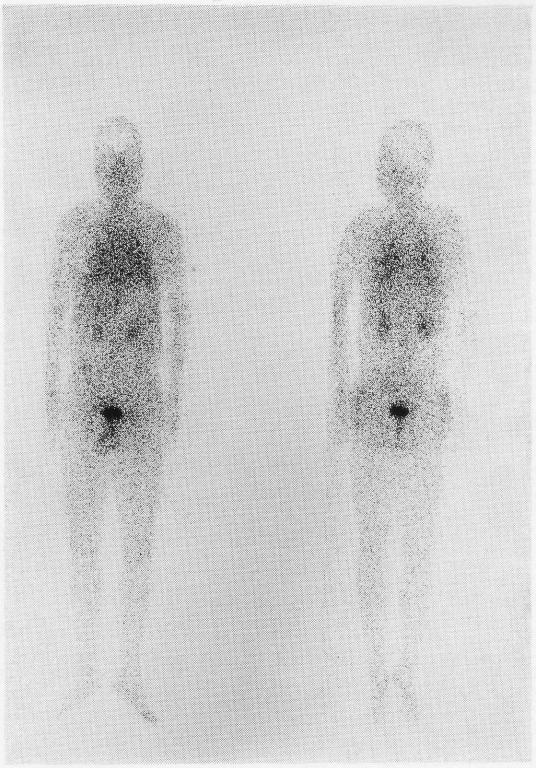

Fig. 2 (case 2)
Whole body images at 6 hrs after injection showing high activity in kidneys and bladder.

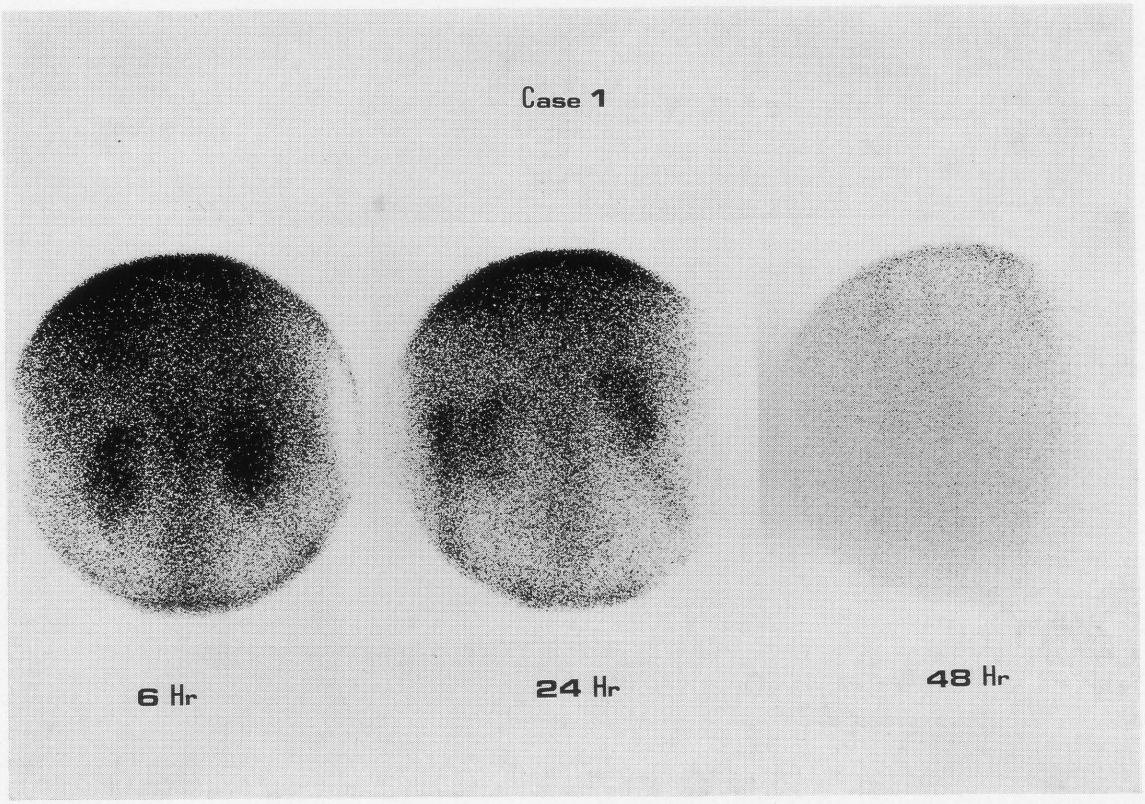

Fig. 3 (case 1)
Sequentional images in posterior view at 6, 24, 48 hrs after injection. High uptake is noted in bilateral kidneys and subsequently decreased within 48 hrs.

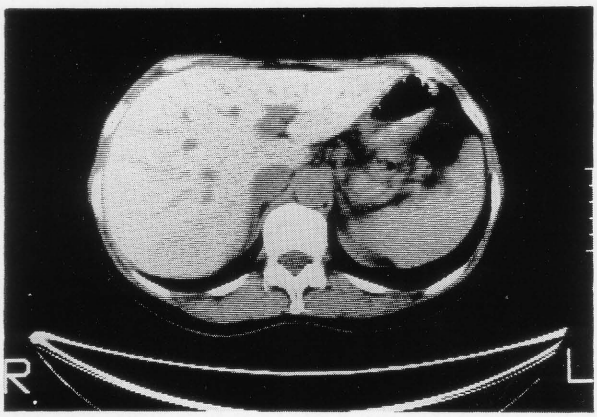

Fig. 4 (case 2)
Abdominal CT reveals increased density of liver parenchyma (CT number is 105 U.H.).

day of the administration of deferoxamine, revealing high activity in both kidneys in the posterior view of the abdomen (Fig. 5), and rapid decrease of activity was noted.

Figure 6 shows the time activity curve of the abdominal region in case 1 and case 2. Activity was rapidly decreased. Activity on the 3rd day after the injection was about 8% of the activity at 6 hrs in case 1 and about 30% in case 2. Fig. 7 shows urinary excretion of gallium in case 1 and case 2. High excretion was found during the first 24 hrs.

DISCUSSION

Gallium scintigraphy was performed for the two patients with hemochromatosis. However, the imaging was unsuccessful because of the rapid urinary excretion of Ga-67 citrate. Both patients had been treated with deferoxamine as an iron-chelating agent. Activity in the control case was reduced to half on the third day. On the other hand, the patient having deferoxamine as a treatment for hemochromatosis showed rapidly decreased activity on the first day following the injection of Ga-67 citrate. Case 1 with a high dosage (4,000 mg/day) of deferoxamine showed about 5% activities on the third day, and case 2 with a low dosage (2,000 mg/day), about one-third. Rapid excretion of Ga-67 citrate into the urine was found in the first 24 hrs in both cases. This was especially prominent in case 1.

Two factors were considered for these rapid excretions. The first is UIBC and the second is deferoxamine.

Several studies have shown that transferrin is one

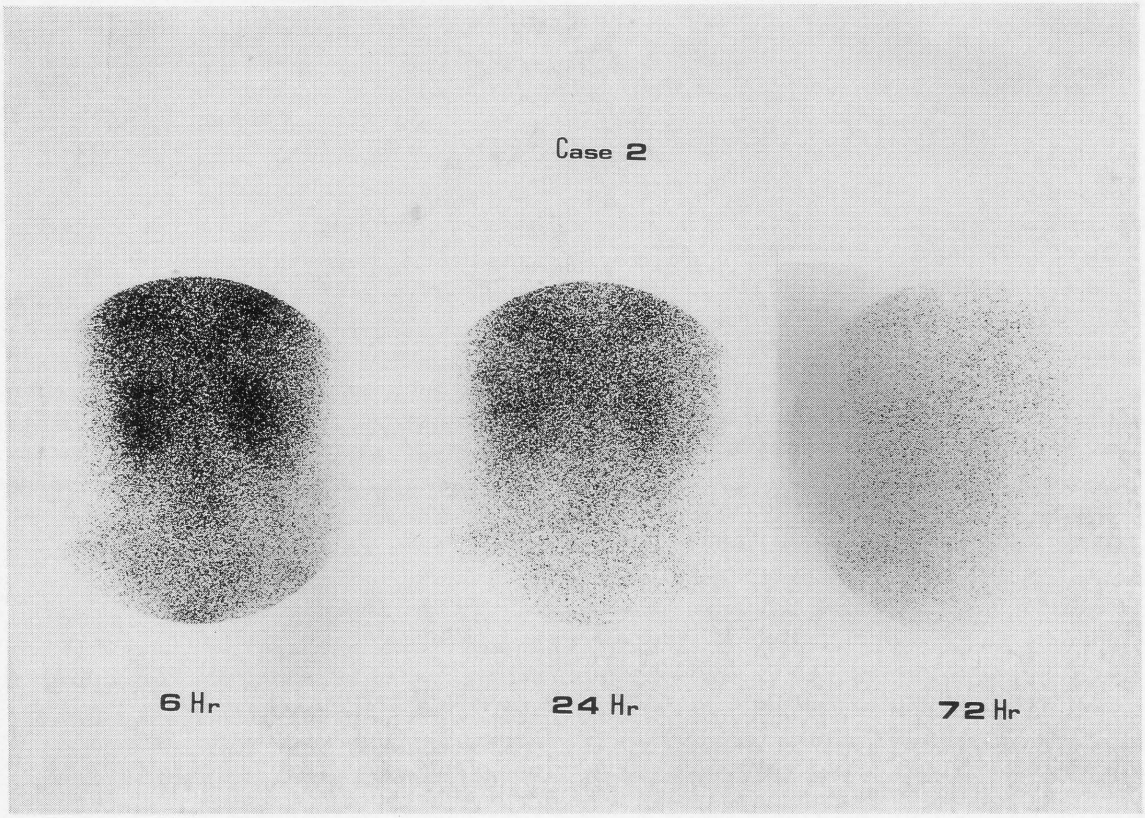

Fig. 5 (case 2)
Sequentional images in posterior view at 6, 24, 72 hrs after injection. High uptake is noted in bilateral kidneys and decreased rapidly.

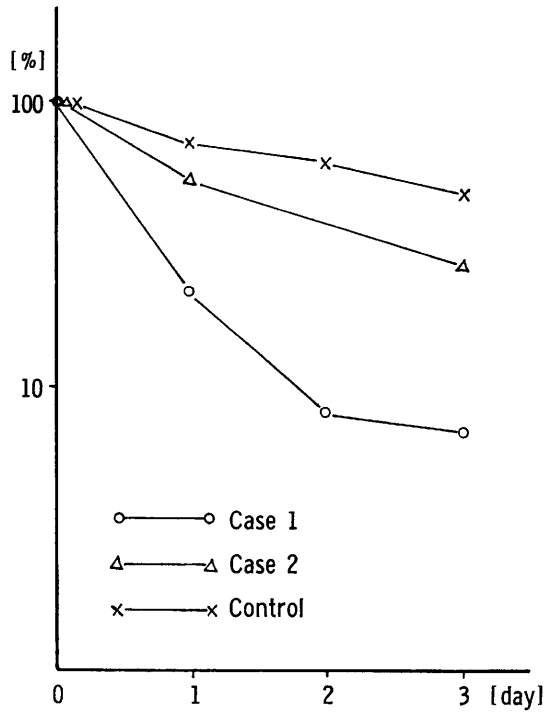

Fig. 6 Time activity curves after injection of Ga-67 citrate. Deferoxamine was given 4,000 mg/day in case 1 and 2,000 mg/day in case 2. Activity in body decreased rapidly.

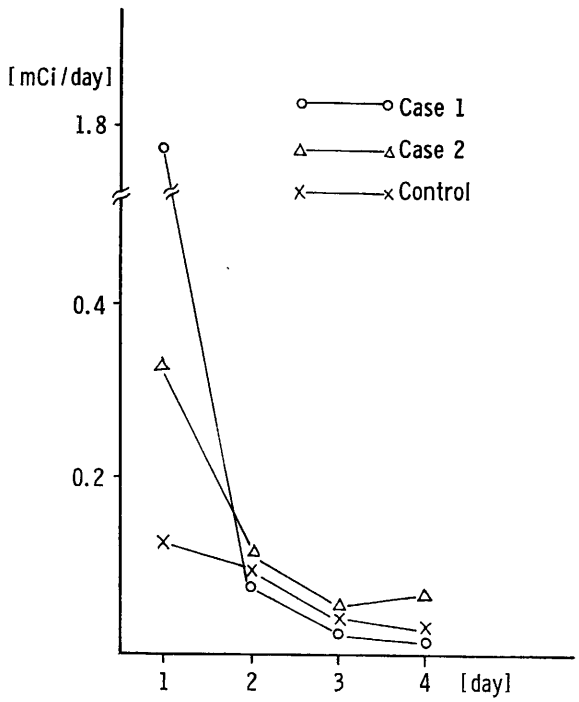

Fig. 7 Urinary excretion of Ga-citrate is remarkable in first 24 hrs.

of the major carrier proteins for Ga-67 citrate in plasma.[9–12] So the biodistribution of Ga-67 citrate is significantly affected by the serum iron level and UIBC.[13–16] When the serum iron level is elevated and UIBC is low, urinary excretion of Ga-67 citrate increases and normal accumulation is prevented. This process has been confirmed experimentally.[15] Examination of the blood in both our cases showed increased serum iron and decreased UIBC, so Ga-67 citrate was prone to be excreted from the body. However, marked change was seen in case 1 whose UIBC was higher than case 2. Therefore, the main factor for poor images in our Ga-67 scintigraphy was not considered to be UIBC.

The second factor is the effect of deferoxamine. This drug is widely used for treating various iron storage diseases because of its very high affinity for iron.[1–3] Besides, this drug forms a stable complex with Ga-67 citrate[4–6] and accelerates the Ga-67 blood clearance by increasing urinary excretion.[6,7] Thus it lowers Ga-67 activities in all organs. Although deferoxamine lowers Ga-67 activities in tumors and abscesses, the tumor-to-blood ratio[5,17] and abscess-to-blood ratio[4,6,7] increase with the use of this drug. So, deferoxamine could be used to improve diagnostic imaging by increasing the target-to-non-target ratio in an animal experiment.[4–8,17] However, its enhancement effect on tumor imaging was shown to be insufficient in human studies.[8]

In our cases, urinary excretion of Ga-67 was remarkable in the patient given high-dose deferoxamine (case 1). So the dose-dependent effects of deferoxamine must be considered. This drug may be clinically used for tumor enhancement under optimal conditions.

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