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Usefulness of asialoglycoprotein receptor imaging for the evaluation of liver metastasis of neuroblastoma

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Neuroblastoma, derived from the neural crest ectoderm, is the most common type of solid abdominal mass seen in infancy. The diagnosis, staging, and follow-up of neuroblastoma are often performed using metaiodobenzylguanidine (MIBG) imaging. However, the evaluation of liver metastasis by this method is complicated by the normal physiological uptake of MIBG by the liver. The asialoglycoprotein receptor is a hepatic cell-surface receptor specific for galactose-terminated glycoprotein, and ^{99m}Tc-DTPA-galactosyl human serum albumin (GSA) accumulates selectively in hepatic cells. Here, we report a case of congenital neuroblastoma with liver metastasis in which GSA scans were useful for differentiation between normal and metastatic sites in the liver.

Key words: neuroblastoma, liver metastasis, MIBG, GSA, asialoglycoprotein

INTRODUCTION

METAIODOBENZYLGUANIDINE (MIBG) imaging is often used in the diagnosis, staging, and follow-up of neuroblastoma (NB).[1–4] However, the liver shows MIBG uptake under normal physiological conditions. Therefore, the diagnosis of hepatic neuroblastoma is difficult due to the inability to differentiate between abnormally increased tracer deposition and normal hepatic activity. The asialoglycoprotein receptor is a hepatic cell-surface receptor specific for galactose-terminated glycoprotein.[5,6] We performed hepatic receptor imaging using ^{99m}Tc-DTPA-galactosyl human serum albumin (^{99m}Tc-GSA) to facilitate differentiation between normal and metastatic sites in the liver.

CASE REPORT

A boy, born after a 38-week gestation and weighing 3.4 kg at birth, showed marked hepatomegaly, and a chest roentgenogram revealed a right upper mediastinal mass. Levels of urinary vanillylmandelic acid and homovanillic acid excretion were elevated, supporting a diagnosis of neuroblastoma. The baby's respiratory condition deteriorated, requiring tracheal intubation and ventilatory support at age 14 days. Therefore, radiotherapy was planned, with 8 Gy for the mediastinal tumor and 10 Gy for whole liver (1 Gy per fraction, 1 fraction per day). However, at the point of 2 Gy for the mediastinal tumor and 3 Gy for the liver, the baby's general condition recovered, and the radiotherapy was concluded. CT scan one week after the radiotherapy showed mild regression of hepatomegaly, but the size of the right upper mediastinal mass did not show any definite change.

About one month after the radiotherapy, MIBG and GSA scans were performed with a double-head gamma camera (E-cam, Siemens, Erlangen, Germany). MIBG planar images were obtained 6 and 24 h after intravenous (i.v.) injection of ^{123}I-MIBG (3.7 MBq/kg of body weight). In addition, single-photon emission computed tomography (SPECT) images were acquired 6 h after injection. After an interval of two days, GSA scans were performed. The patient was injected i.v. with ^{99m}Tc-GSA (3.7 MBq/kg of body weight). The dynamic data were acquired for 15 minutes after injection, and planar and SPECT images were obtained 15 minutes after injection.

MIBG planar images demonstrated hepatomegaly and diffuse liver uptake (Fig. 1-A, B). MIBG SPECT showed

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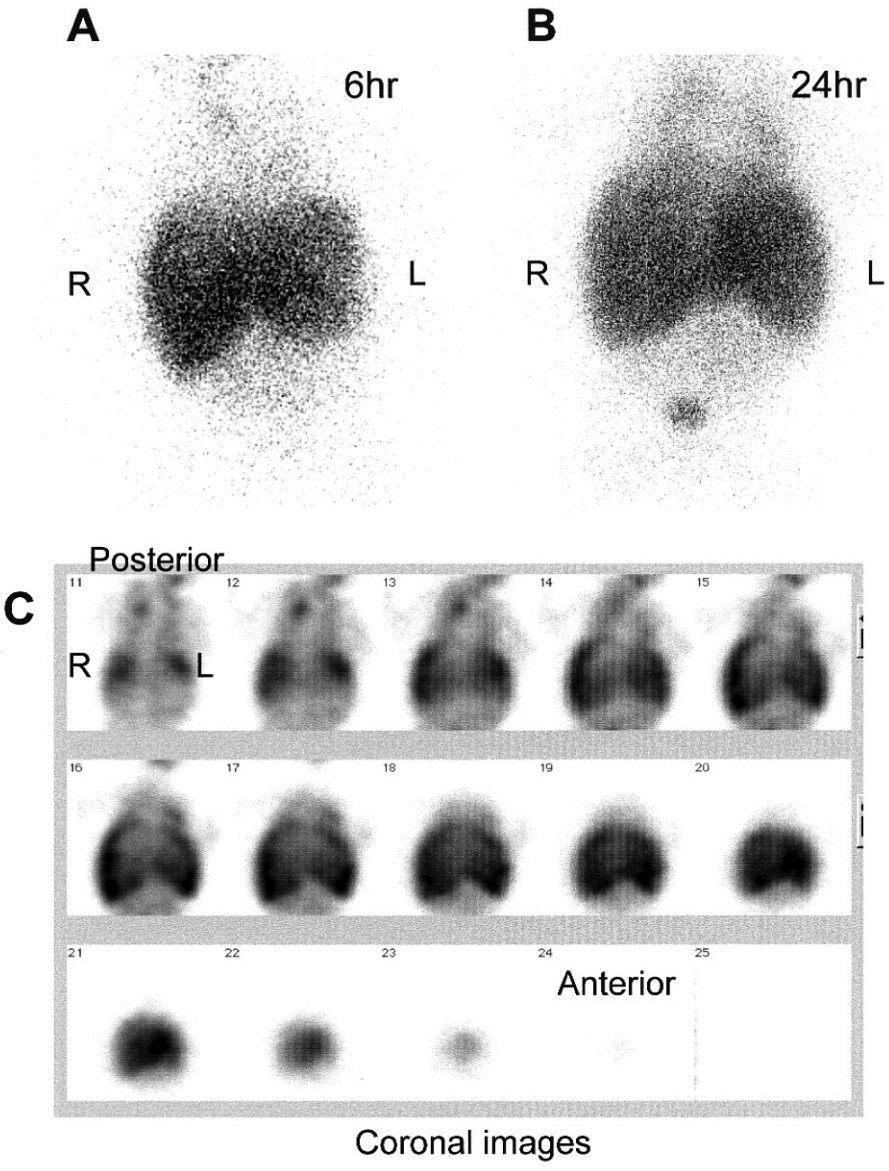

Fig. 1 MIBG images. A: Anterior planar image 6 h after injection. B: Anterior planar image 24 h after injection. Increased uptake was seen in the posterior right mediastinum and the liver. C: SPECT 6 h after injection. SPECT showed relatively increased liver uptake peripherally. However, this pattern is often seen in non-attenuation corrected SPECT images, and it is hard to detect the border between normal liver and metastases.

decreased uptake in the center of the liver (Fig. 1-C). GSA planar images demonstrated apparently inhomogeneous uptake in the liver (Fig. 2-A, B). GSA SPECT also showed inhomogeneous uptake, and the liver uptake determined by MIBG and GSA SPECT seemed complementary (Fig. 2-C).

The indices for blood clearance and liver accumulation were evaluated periodically based on the dynamic data for 15 minutes after ^{99m}Tc-GSA injection. HH15, the ratio of the heart count at 15 minutes to that at 3 minutes after injection, was obtained as an index of blood clearance, and LHL15, the ratio of liver count to the liver plus heart count at 15 minutes after injection, were obtained as indices of accumulation in the liver. In this patient, HH15 and LHL15 were 0.637 and 0.901, respectively, indicating mild hepatic reserve failure.

DISCUSSION

Most congenital NBs are characterized by favorable clinical and biological characteristics.[5–13] As reported previously, congenital NBs generally show frequent metastasis to the liver,[12] and many cases of congenital NBs with liver metastases are associated with stage IVs disease.[5–7,9–13] In

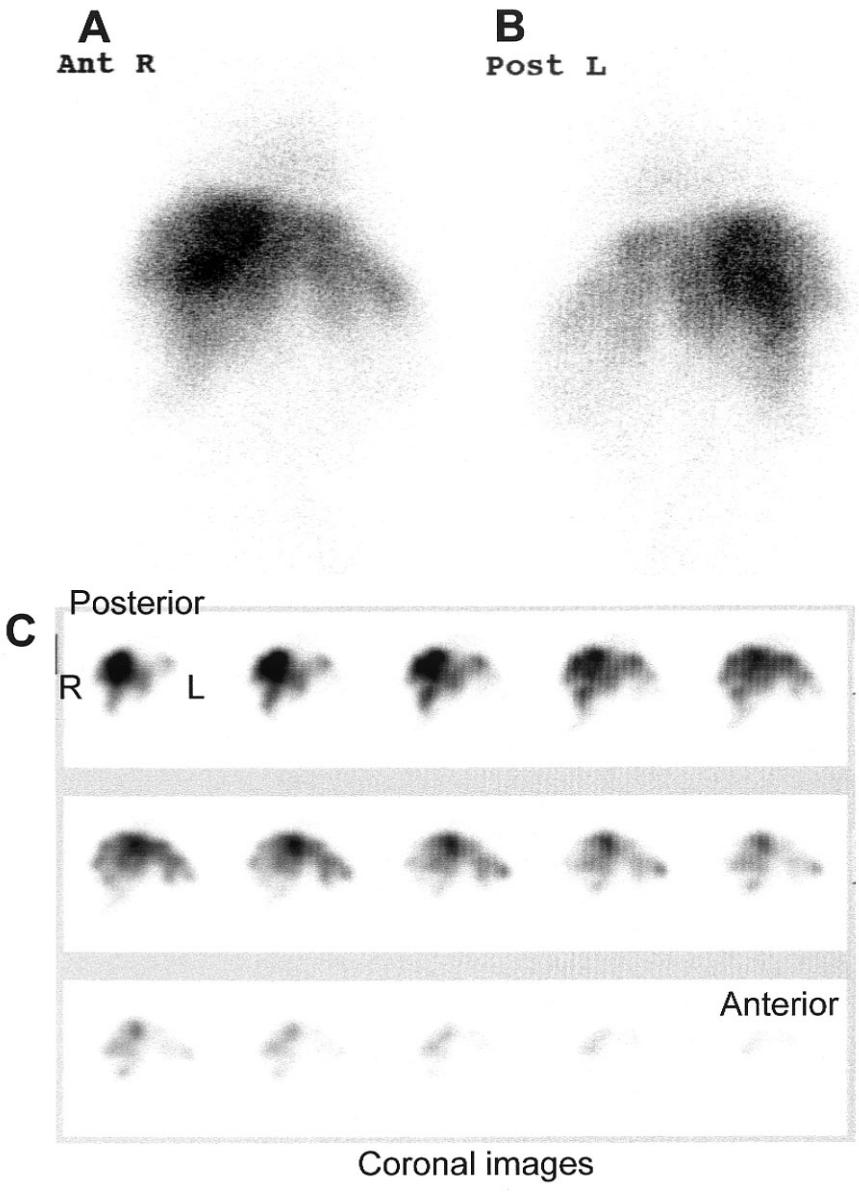

Fig. 2 GSA images. A: Anterior planar image. B: Posterior planar image. C: SPECT. GSA planar and SPECT images showed a marked inhomogeneous liver uptake, which has an increasing tendency at the upper inner part. The peripheral sites of decreased GSA uptake in the liver indicate lack of hepatic cells, representing liver metastases.

contrast, some patients with congenital NB have stage III or IV disease and show rapid progression with poor outcome.[5–7,10,14] Metaiodobenzylguanidine (MIBG) imaging is often used in the diagnosis, staging, and follow-up of neuroblastoma. However, some previous studies demonstrated difficulties in differentiating between liver metastases and physiological uptake in the liver[15,16] with a general false-negative rate of 8–10% on MIBG scintigraphy.[3,15]

In the case described here, MIBG planar images showed diffuse liver uptake indicating hepatomegaly. MIBG SPECT showed marked increases in peripheral uptake and a slight increase in central uptake in the liver. However, the border was unclear. Moreover, this relatively decreased MIBG uptake in the inner part might be influenced by attenuation.

Liver scans using GSA can be used to measure the hepatic function, called *functional hepatic reserve*, both directly and quantitatively. A number of reports have described the usefulness of assessment of functional hepatic reserve by GSA scans in various physiological and pathological hepatic conditions.[17–19] In the present case, the GSA planar and SPECT images clearly showed inhomogeneous uptake in the liver with an increasing

tendency at the upper inner part. The decreased sites of uptake in the liver represent the absence of hepatic cells, because of the presence of metastatic lesions derived from the neuroblastoma. These sites corresponded to the regions showing markedly increased uptake on MIBG SPECT. Therefore, the peripheral regions with increased MIBG uptakes and decreased GSA uptakes in liver indicate liver metastases of neuroblastoma. The indices for blood clearance and liver accumulation, such as HH15 and LHL15, may reflect not only functional hepatic reserve, but also the status of liver metastasis or efficacy of therapy. However, further studies to clarify these points are required.

Liver CT scans with or without contrast enhancement were performed in this case. However, CT images showed almost homogeneous density in liver, and provided no additional information except for hepatomegaly. For evaluating the distribution of liver metastases, additional functional images using GSA or MIBG are thought to be useful.

This study had the limitation that both MIBG and GSA scans were performed after radiation therapy. However, we do not think that the decreased MIBG or GSA uptakes are caused by radiation necrosis, which might be seen as matched decreasing of both MIBG and GSA uptakes.

In conclusion, MIBG scans are very useful for evaluating sites of both primary and metastatic neuroblastoma lesions. However, for the evaluation of liver metastasis, additional GSA scans provide clearer and more easily distinguishable images as compared to MIBG.

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