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Early massive accumulation of In-111 pentetreotide in a metastatic liver tumor of islet cell carcinoma

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A 62-year-old woman was examined with In-111 pentetreotide and Ga-67 citrate. She had undergone an operation to resect a neuroendocrine tumor of the pancreas and still had masses in the liver. One of her hepatic lesions had been biopsied and acinar cell carcinoma was suspeted. Fluid in the cyst of the tumor, however, contained a high concentration of gastrin and the tumor was strongly suspected of being a metastasis from the neuroendocrine tumor of the pancreas. The hepatic tumors quickly accumulated In-111 pentetreotide immediately after the injection, but there was no Ga-67 citrate uptake in the tumor. Five months after pentetreotide scintigraphy, her hepatic tumors were resected and histologically proven to be metastasis of islet cell carcinoma. In-111 pentetreotide provides information of the somatostatin-receptor status on the tumor and supports the diagnosis made by hormonal survey.

Key words: neuroendocrine tumor, In-111 pentetreotide, somatostatin, gastrin

INTRODUCTION

In-111 PENTETREOTIDE is a new pharmaceutical agent to use in diagnosing somatostatin-receptor bearing tumors.[1–4] European multi-center trials[5] yielded successful results on positive imaging not only of apudomas, but of other somatostatin-receptor positive tumors such as lymphoma, astrocytoma, breast cancer and so on. Similar results from other institutes have followed.[6–14] These articles describe the agent as sensitive especially for neuroendocrine gastro-enteropancreatic tumors and the scintigraphy often detects unknown lesions missed by other conventional methods.[8,10,15]

The optimal time for imaging of the scintigraphy has been discussed. Many articles recommend late imaging because of high background in the early stages of imaging.[15,16] Several series, however, described early accumulation of the tumors.[15,17]

We examined a patient with metastatic liver tumors which had not been diagnosed as neuroendocrine tumors at the initial biopsy. Dynamic images showed high vascularity and the somatostatin-receptor status was clearly shown immediately after the injection on In-111 pentetreotide scintigraphy. The radioactivity in the tumors was retained for at least 48 hours after the injection.

CASE REPORT

The patient was a 62-year-old woman. She had undergone an operation one year previously when an endocrine pancreatic tumor had been resected together with the spleen along with tumor thrombi in the portal vein and the splenic vein. The pancreatic tumor was histologically proven to be neuroendocrine in type because the specimen had been found to strongly stain positive for neuron specific enolase and focally positive for gastrin and other gastrointestinal hormones. She had a huge hepatic tumor (approximately 8.5 × 7 × 8 cm) and another small tumor (approximately 2 × 3.5 × 4 cm) lying close to it. Contrast angiography showed that they were hypervascular tumors. Although the biopsy specimen of the liver tumor suggested acinar cell carcinoma, the tumor was strongly suspected to be metastasis of the neuroendocrine pancreatic primary because the gastrin level of the fluid in the hepatic cyst was extremely high (16,800 pg/m*l*). Blood gastrin activity remained high (401–918 pg/m*l*, normal range 30–140 pg/m*l*) after the initial operation on the pancreas.

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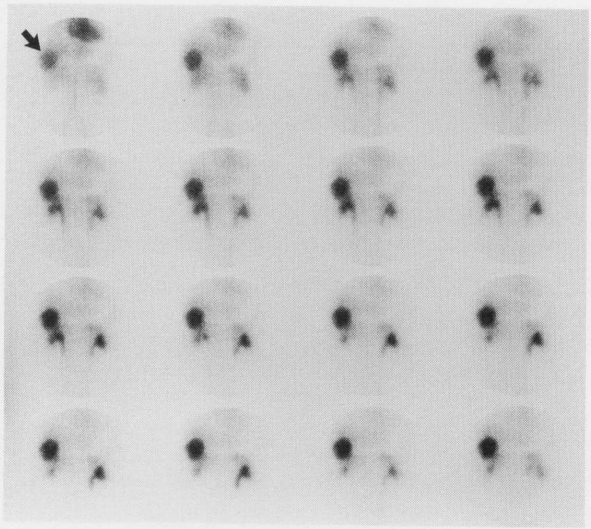

Fig. 1 Sequential images of every two minutes of the abdomen following the injection with In-111 pentetreotide. Marked accumulation of the tracer in the hepatic tumor (arrow) is noted immediately after the injection.

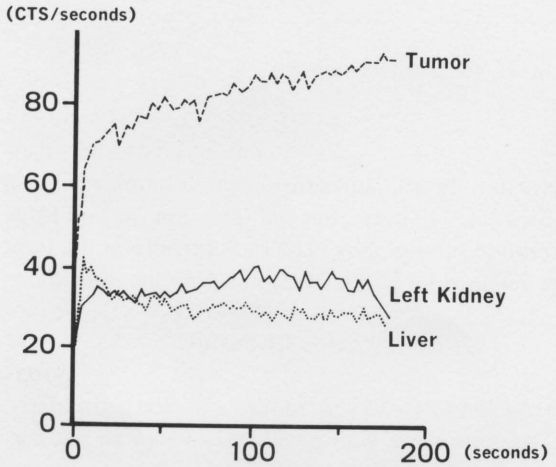

Fig. 2 Time activity curves of the tracer in the tumor, normal liver and left kidney for the first 30 minutes. Rapid increase of the radioactivity in the tumor is shown.

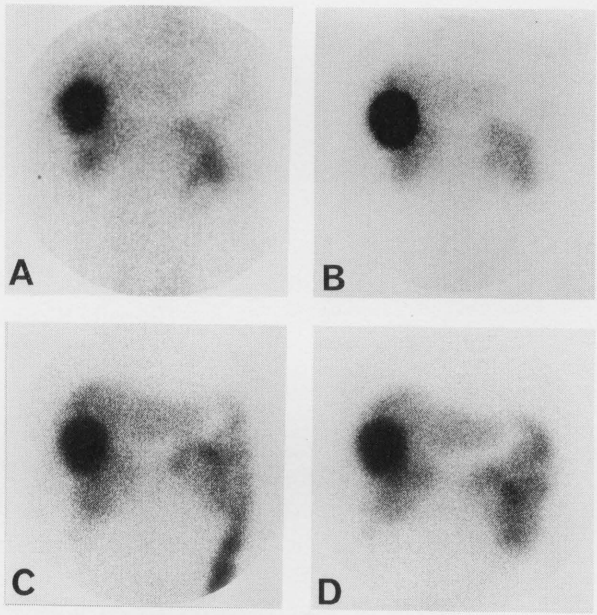

Fig. 3 Images of the abdomen at 30 minutes (A), 4 hours (B), 24 hours (C) and 48 hours (D) after the injection. Marked accumulation of the tracer (arrow) in the hepatic tumor is retained for 48 hours after the injection.

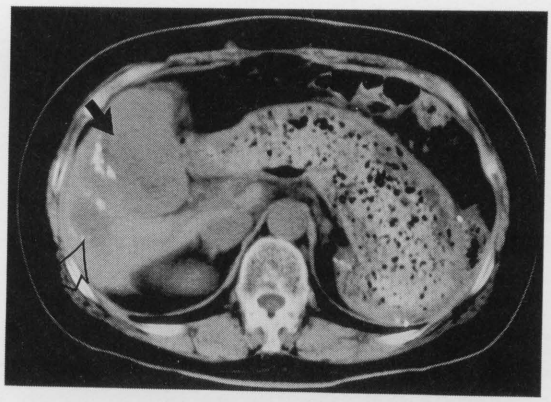

Fig. 4 CT scan shows a huge tumor (arrow) and another small tumor (open arrow) lying close to it.

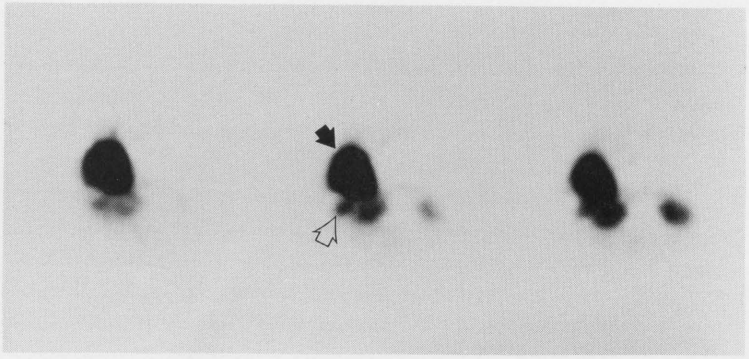

Fig. 5 Massive uptake in the tumors consistent with those shown on CT scan is demonstrated on SPECT with In-111 pentetreotide.

To evaluate the localization and nature of the tumors, In-111 pentetreotide scintigraphy was performed. The patient gave written informed consent approved by Ethical Committee of Hokkaido University School of Medicine before the examination. Sequential images of 120 seconds/frame of the abdomen were taken for 30 minutes immediately after the intravenous injection of 111 MBq of In-111 pentetreotide (Mallinckrodt Medical Co., Ltd.) with a GE Maxicamera 400AC/T equipped with a medium energy parallel-hole collimator. Marked accumulation of the tracer in the lesion was shown immediately post injection (Fig. 1) and the time-activity curve of the tumor showed a rapid increase in radioactivity (Fig. 2). This marked accumulation was evident on planar images at 30 minutes, 4 hours, 24 hours and 48 hours after the injection (Fig. 3). Tumor to normal liver ratios at 30 minutes, 4 hours, 24 hours and 48 hours were 4.9, 9.8, 7.1, and 6.9 and tumor to left kidney ratios at 30 minutes, 4 hours, 24 hours and 48 hours were 3.5, 7.5, 5.3, and 5.2 respectively. Whole body images at 24 hours and 48 hours showed consistent findings in the liver, but no other lesion was demonstrated. SPECT of the liver was performed 24 hours (Fig. 5) and 48 hours after the injection. Massive uptake in the huge tumor and a part of the small tumor beside it was demonstrated and localization was consistent with that of the tumors shown on CT scan (Fig. 4). Ga-67 scan was performed 1 month after the pentetreotide scintigraphy, but no abnormal uptake in the liver was shown.

Five months after the scintigraphy, the patient underwent an operation and the hepatic tumors were resected. They were histologically diagnosed as metastatic islet cell carcinoma.

DISCUSSION

In the present case In-111 pentetreotide was well accumulated in the tumor. This strongly supported the diagnosis of metastatic neuroendocrine tumor which was suggested by the high gastrin level in the cystic fluid. In-111 pentetreotide does not replace the histologic examination, but it can clearly characterize the tumor by demonstrating its somatostatin-receptor status. The negative Ga-67 scan suggested that there was little possibility of Ga-67 positive tumors such as hepatoma, lymphoma and granuloma[4,14] although lymphoma and granuloma had been reported to accumulate In-111 pentetreotide. Finally, post resection, the tumors were histologically proven to be metastatic islet cell carcinoma, whereas they had been suspected of being acinar cell carcinoma at the initial biopsy.

The sequential images of the first 30 minutes showed marked accumulation of the tracer in the tumors as early as 2 minutes post injection which persisited for 48 hours. The early accumulation suggests high vascularity of the tumor, where the persistent activity may reflect high density of the somatostatin receptors. Because of high background radioactivity on early images, previous reports[1,5,16] recommended imaging at 24 hours and 48 hours, especially for tumors with low somatostatin-receptor density in the abdomen. In our patient, however, the tumor was most clearly demonstrated at 4 hours after the tracer administration. The tumor to normal liver ratio was the highest at 4 hours and gradually decreased afterwards, mainly due to a gradual increase in the radioactivity in the normal liver. Joseph[15] et al. reported that all neuroendocrine pancreatic tumors in their study were visible as soon as 4 hours. Bajc[17] et al. also reported 3 cases in whom early scintigrams best showed neuroendocrine tumors. A high somatostatin-receptor density permits an intense accumulation of the tracer with high-tumor-background activity. Furthermore, an enriched blood flow enables accumulation of the tracer on the early images. Early imaging may be useful in obtaining clear demonstration of hypervascularized tumors. Westlin et al.[10] however, showed a false positive accumulation of the tracer in an inflammatory lesion at 4 hours which disappeared at 24 hours, probably due to increased vascularity but no receptor density. In this respect, the combined imaging at 4 hours and 24 hours is preferable to assess receptor density and perfusion and thus to avoid false positive results.

In conclusion, In-111 pentetreotide scintigraphy is useful in characterizing the metastatic islet cell carcinoma and supporting the diagnosis suggested by the hormonal survey. Early imaging is valuable in clearly visualizing of the tumors when they are hypervascularized.

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