A case of glucagonoma with high uptake on F-18 fluorodeoxyglucose positron emission tomography

Shuhei Nishiguchi,* Susumu Shiomi,** Hirotaka Ishizu,** Yoshinori Iwata,* Hiroko Kurooka,* Shin Minamitani,* Daiki Habu,* Joji Kawabe** and Hironobu Ochi**

> *Third Department of Internal Medicine and **Division of Nuclear Medicine, Osaka City University Medical School

Glucagonomas are relatively rare, and can be difficult to differentiate from other pancreatic tumors. A 62-year-old woman who had suffered from diabetes mellitus was hospitalized for further evaluation of a space-occupying lesion in the head of the pancreas and tumors in the liver. F-18 fluorodeoxyglucose positron emission tomography revealed accumulation of isotope corresponding to a tumor of the pancreas with a standardized uptake value of 4.3, and tumors in the liver with standardized uptake values of 2.4 and 2.8. The serum glucagon level was high (1,170 pg/ml) and the secretin tolerance test was negative. She was diagnosed with glucagonoma with a high serum glucagon level and clinical findings. It is suggested that glucagonoma may be one of the tumors which show high uptake of F-18 fluorodeoxyglucose.

Key words: FDG, glucagonoma, pancreatic carcinoma, positron emission tomography

INTRODUCTION

GLUCAGONOMA is a relatively rare pancreatic neuroendocrine tumor, for which a close correlation exists between tumor size and malignancy. Small glucagonomas (diameter less than 3 cm) are usually asymptomatic and benign, but most large tumors (diameter greater than 5 cm) are malignant and have metastasized to distant organs. The most common location for distant metastases is the liver.¹

Positron emission tomography (PET) with C-11-labeled L-dihydroxyphenylalanine (L-DOPA)² and hydroxytryptophan (5-HTP)³ has been used for the diagnosis of pancreatic neuroendocrine tumors. With these techniques, however, uptake of isotope by non-functioning neuroendocrine tumors is in many cases low, and such techniques often fail to identify such tumors.³ F-18 fluorodeoxyglucose (FDG)-PET is designed to diagnose tumors based on their glucose metabolism,⁴ and it ensures establishment of a

E-mail: shiomis@med.osaka-cu.ac.jp

diagnosis even for non-functioning neuroendocrine tumors. Nevertheless, reports of the usefulness of FDG-PET for the diagnosis of glucagonoma are few in number,^{5,6} and no study has evaluated the usefulness of this technique for patients with glucagonoma and liver metastasis. We report a case of glucagonoma with liver metastasis in which FDG-PET revealed high uptake of isotope.

CASE REPORT

A 62-year-old woman had been treated for diabetes mellitus by a neighborhood physician for ten years. She was referred to our hospital because of general fatigue and liver function test abnormality. Abdominal ultrasonography revealed a space-occupying lesion in the head of the pancreas, and she was hospitalized.

On admission, the patient was emaciated. The liver was not palpable and there was no ascites. The red blood cell count was 348×10^4 /mm³, total bilirubin concentration 4.1 mg/dl (direct bilirubin, 2.6 mg/dl), aspartate aminotransferase activity 327 IU/l, alkaline phosphatase activity 2,106 U/l, fasting blood sugar concentration 124 mg/dl, HbA_{1C} 6.3%, carcinoembryonic antigen concentration 7 ng/ml, carbohydrate antigen 19-9 concentration

Received December 14, 2000, revision accepted March 5, 2001.

For reprint contact: Susumu Shiomi, M.D., Division of Nuclear Medicine, Osaka City University Medical School, 1–4–3 Asahimachi, Abeno-ku, Osaka 545–8585, JAPAN.



Fig. 1 Percutaneous transhepatic cholangiography revealed dilatation of common bile duct, which was obstructed in the region of the head of the pancreas.

43 U/ml, serum glucagon concentration 1,170 pg/ml, and seum gastrin concentration 2,230 pg/ml. The serum gastrin level decreased from 3,140 to 2,670 pg/ml 30 minutes after intravenous injection of 2 U/kg of secretin.

Percutaneous transhepatic cholangiography revealed dilation of the common bile duct, which was obstructed in the region of the head of the pancreas (Fig. 1). Contrast computed tomography revealed a tumor in the head of the pancreas (Fig. 2A) and tumors in the liver (Fig. 3A). FDG-PET revealed accumulation of isotope corresponding to the tumor in the pancreas with a standardized uptake value (SUV) of 4.3 (Fig. 2B), and tumors in the liver with SUVs of 2.4 and 2.8 (Fig. 3B). The patient was diagnosed with glucagonoma with diabetes mellitus, anemia, marked weight loss, a high serum level of glucagon, and a negative secretin tolerance test.⁷



A



B

B Fig. 3 A: Contrast computed tomography revealed tumors in the liver (arrow). B: FDG-PET revealed accumulation of isotope corresponding to the tumors (arrow), with SUVs of 2.4 and 2.8.

Fig. 2 A: Contrast computed tomography revealed a tumor in the head of the pancreas (arrow). B: FDG-PET revealed accumulation of isotope corresponding to the tumor (arrow), with SUV of 4.3.

DISCUSSION

McGavran et al.⁸ reported that glucagonomas are rare pancreatic tumors that arise from α islet cells. Mallison et al.⁹ noted that patients with glucagonoma usually presented with "glucagonoma syndrome," which is characterized by mild non-ketotic diabetes mellitus, weight loss, normochromic normocytic anemia, and narcoleptic migratory erythema. Subsequently, with increased use of immunological measurement of hormones, reports of cases of glucagonoma have become sporadic, but these tumors must still be considered rare. Neuroendocrine neoplasms originating in the pancreas may be classified into gastrinomas, glucagonomas, insulinomas, and VIPomas, depending on the type of hormone secreted. Our patient had high blood levels of both gastrin and glucagon. In the secretin tolerance test, however, the serum gastrin level had decreased from 3,140 to 2,670 pg/ ml, ruling out gastrinoma. Cases of glucagonoma in which the serum gastrin level is higher are not rare.⁷ Our patient was therefore diagnosed with glucagonoma with diabetes mellitus, anemia, marked weight loss, a high serum level of glucagon and a negative secretin tolerance test.7

PET has recently been used to diagnose various type of tumors,⁴ and FDG-PET is considered useful in the diagnosis of pancreatic carcinomas.^{10,11} PET with L-DOPA and 5-HTP is useful for establishing the diagnosis of pancreatic neuroendocrine tumors, but may sometimes fail to identify non-functioning neuroendocrine tumors. FDG-PET can yield the correct diagnosis even for the latter tumors. High glucose concentrations may alter FDG uptake because they compete for the glucose transport system, and diabetes may cause false-negative results.¹² Caution is therefore required in interpreting negative FDG-PET results in patients with typical glucagonoma syndrome. In our patient, FDG-PET revealed an accumulation of isotope with a SUV of 4.3, because the glucose concentration decreased to within the normal range on treatment for diabetes mellitus. Bares et al.¹² reported that the best differentiation between malignant and benign tumors was achieved with use of on a SUV of 3.5, and Zimny et al.¹⁰ reported that the best cut-off value for SUV was 2.9 for distinguishing malignant lesions from pancreas tumors.

In our case, accumulation of FDG was noted even at the sites of metastasis in the liver. FGD-PET is not useful for the diagnosis of hepatocellular carcinoma, since accumulation of FDG is sometimes not high in such tumors,¹³ but higher levels of FDG accumulation are observed in many cases of metastatic liver tumor. Iwata et al.¹⁴ reviewed the differential diagnosis of 68 patients with tumor lesions in the liver, and reported 90% accuracy in the diagnosis of metastatic liver tumor by FDG-PET, a rate higher than that for enhanced CT. Nakamoto et al.¹⁵ reported that the accuracy of diagnosis of liver metastasis from pancreatic

cancer by FDG-PET was 90%, a rate comparable to those of urtrasonography and computed tomography.

Tumor resection is the only radical treatment available for glucagonoma, but most (60 to 80%) large glucagonomas (greater than 5 cm) are malignant. By the time of diagnosis, they have penetrated the tumor capsule and have invaded regional lymph nodes or metastasized to distant organs.¹ Since radical resection should be avoided in patients with metastases, PET may become useful for preoperative detection and staging of glucagonomas, but further studies of large numbers of patients are required to determine the precise role of this imaging technique in the evaluation of glucagonomas.

REFERENCES

- 1. Boden G. Glucagonoma and insulinomas. *Gastroenterol Clin Nor Am* 1989; 18: 831-845.
- Bergström M, Eriksson B, Öberg K, Sundin A, Ahlström H, Johan K, et al. *In vivo* demonstration of enzyme activity in endocrine panceatic tumors: Decarboxylation of carbon-11-DOPA to carbon-11-dopamine. *J Nucl Med* 1996; 37: 32–37.
- Alström H, Eriksson B, Bergström M, Bjurling P, Långström B, Öberg K. Pancreatic neuroendocrine tumors: Diagnosis with PET. *Radiology* 1995; 195: 333–337.
- Strauss LG, Conti PS. The applications of PET in clinical oncology. J Nucl Med 1991; 32: 623–648.
- Yasuda S, Shohtsu A, Tomioka K. F-18 fluorodeoxyglucose positron emission tomography imaging in ectopic nonfunctioning glucagonoma. *Clin Nucl Med* 1998; 23: 474– 478.
- Femández-Represa JA, Rodríguez DF, Contin MJP, Peña ML, Martinez-Sarmiento J, Carreras JL, et al. Pancreatic glucagonoma: Detection by positron emission tomography. *Eur J Surg* 2000; 166: 175–176.
- Lo CY, van Heerden A, Thompson GB, Grant CS, Soreide JA, Harmsen WS. Islet cell carcinoma of the pancreas. *World J Surg* 1996; 20: 878–884.
- McGavran MH, Unger RH, Recant L, Polik HC, Kilo C, Levin ME. A glucagonoma-secreting alpha-cell carcinoma of the pancreas. *New Engl J Med* 1966; 274: 1408–1413.
- 9. Mallinson CN, Bloom SR, Warin AP, Salmon PR, Cox B. A glucagonoma syndrome. *Lancet* 1974; ii: 1–5.
- Zimny M, Bares R, Faß J, Adam G, Cremerius U, Dohmen B, et al. Fluorine-18 fluorodeoxyglucose positron emission tomography in the differential diagnosis of pancreatic carcinoma: A report of 106 cases. *Eur J Nucl Med* 1997; 24: 678–682.
- Keogan MT, Tyler D, Clark L, Branch MS, McDermott VG, Delong DM, et al. Diagnosis of pancreatic carcinoma: Role of FDG PET. *AJR* 1998; 171: 1565–1570.
- Bares R, Klever P, Hauptmann S, Helling D, Fass J, Cremerius U, et al. F-18 fluorodeoxyglucose PET *in vivo* evaluation of pancreatic glucose metabolism for detection of pancreatic cancer. *Radiology* 1994; 192: 79–86.
- Torizuka T, Tamaki N, Inokuma T, Magata Y, Yonekura Y, Tanaka A, et al. Value of fluorine-18 FDG-PET to monitor hepatocellular carcinoma after interventional therapy. J

Nucl Med 1994; 35: 1965-1969.

- Iwata Y, Shiomi S, Sasaki N, Jomura H, Nishiguchi S, Seki S, et al. Clinical usefulness of positron emission tomography with fluorine-18 fluorodeoxyglucose in the diagnosis of liver tumors. *Ann Nucl Med* 2000; 14: 121–126.
- Nakamoto Y, Higashi T, Sakahara H, Tamaki N, Kogire M, Imamura M, et al. Contribution of PET in the detection of liver metastases from pancreatic tumors. *Clin Radiol* 1999; 54: 248–252.