Brain metastasis from malignant pancreatic somatostatinoma

Case report

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Somatostatinomas are rare endocrine tumors that are located primarily in the pancreas. Metastases are seen most frequently in the liver and lymph nodes. The authors present the case of a 63-year-old man who had a malignant somatostatinoma of pancreatic tail origin that metastasized to the brain 10 years after diagnosis of the primary tumor. The metastatic brain lesions were totally removed and the patient is alive without tumor recurrence 12.3 years after the initial diagnosis. To our knowledge, this case represents the first documentation of brain metastasis from a malignant somatostatinoma, as well as the longest survival time of a patient with a somatostatinoma.

KEY WORDS • somatostatinoma • pancreas • brain • metastasis • long-term survival

Somatostatinomas are rare endocrine tumors that were first described in 1977; few cases have been reported. Somatostatinomas are located mainly in the pancreas, but they can also present in extrapancreatic organs such as the duodenum. Metastases or local invasion are seen most frequently in the liver and lymph nodes. Other sites of metastasis include the peritoneum, skin, bone, kidney, ovary, adrenal gland, and thyroid gland. To our knowledge, metastasis from a pancreatic somatostatinoma to the brain has not been previously described. We report a case of a malignant somatostatin-producing endocrine tumor of the pancreatic tail that metastasized to the brain 10 years after diagnosis of the primary tumor.

Case Report

History. This 63-year-old, right-handed man was admitted to our hospital for evaluation of left-leg motor weakness of 1 month’s duration. Ten years prior to this admission, the patient had been evaluated and treated at another hospital after presenting with hepatomegaly and an 8-kg weight loss over a 4-year period. Abdominal computerized tomography (CT) scanning performed at that time had revealed tumors in the liver and the pancreatic tail (Fig. 1). The tumors were removed en bloc via resection of the left lobe of the liver combined with a complete resection of the spleen and the body and tail of the pancreas. The pancreatic mass was 4 × 3.5 cm and the hepatic mass was 10 × 9 cm in size. Histological examination of specimens from these masses suggested a diagnosis of malignant somatostatinoma of pancreatic tail origin with metastasis to the brain.
liver metastasis (Fig. 2). Preoperatively, the patient’s plasma somatostatin concentration was 95 pg/ml (normal 1.0–12.2 pg/ml) and the somatostatin content of tumor tissue was more than 64,000 ng/g wet weight. There were no symptoms or signs to suggest somatostatinoma syndrome, such as diabetes mellitus, gallstones, steatorrhea, or hypochlorhydria. The plasma somatostatin concentration decreased to 6.8 pg/ml by the 35th postoperative day. After the 20th postoperative day, 4 mg of mitomycin C and 20 mg of adriamycin were administered three times per week for a total of eight doses. At the same time, oral administration of six capsules Tegafur (100 mg) and uracil (224 mg) was begun, and the patient remained healthy for 10 years after surgery. Repeated abdominal CT scans demonstrated no recurrence or lymph node metastases.

The patient had no family history of cancer or hepato-biliary disease.

**Examination.** The patient was afebrile and had a normal blood pressure of 130/80 mm Hg, with a regular pulse rate of 60 beats/minute and regular respirations of 18 breaths/minute. Examination of the skin, heart, and lungs was normal. An abdominal examination revealed a well-healed surgical scar with no tenderness or palpable mass. Neurological examination revealed an alert and oriented man whose cranial nerves were intact. Motor and sensory functioning in the extremities was intact except for a mild left-sided motor weakness. The results of cerebellar testing were normal.

Routine laboratory data were within normal ranges except for a mildly increased plasma somatostatin concentration (14 pg/ml). Cranial CT scanning demonstrated a heterogeneous, contrast-enhancing, hyperdense mass in the right temporal lobe, with extensive surrounding edema. Magnetic resonance (MR) imaging demonstrated a large well-defined mass (4 cm in diameter) attached to the dura mater in the right temporal lobe (Fig. 3) and a small homogeneous, contrast-enhancing mass in the right frontal lobe. Cerebral angiograms showed avascular lesions in the right temporal and frontal lobes. No other lesions were revealed by skull and chest roentgenograms, an upper gastrointestinal series, chest and upper abdominal CT scans and a $^{67}$Ga citrate tumor scan.

**First Operation.** A right temporal craniotomy was performed. The mass was well-defined, solid, and soft gray in

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**Fig. 2.** Photomicrographs obtained during the patient’s first admission 10 years previously. *Left:* Tumor cells in the pancreatic tail are elliptical or spindle-shaped and line the numerous capillaries in the tumor. H & E, original magnification × 150. *Right:* Immunohistochemical examination reveals that the tumor cells are positive for somatostatin. Original magnification × 1300.

**Fig. 3.** Axial magnetic resonance images obtained during the current hospital stay. *Left:* A $T_1$-weighted image demonstrating a hypointense mass with a few hyperintense lesions in the right temporal lobe. *Center:* Contrast-enhanced, $T_2$-weighted image showing a well-defined, large, heterogeneous enhancing mass. *Right:* A $T_2$-weighted image demonstrating a slightly hypointense mass with an irregular hyperintense core and extensive surrounding edema.
appearance. It was removed en bloc by microdissection of the tumor border. There were no adhesions to the dura mater. Gross examination revealed a mushroom-shaped tumor measuring $4.5 \times 4.0 \times 4.0$ cm, with a hemorrhagic center.

First Postoperative Course. The patient’s immediate postoperative course was uneventful. Four months later, cranial CT scanning demonstrated an enlarged, homogeneous, contrast-enhancing mass in the right frontal lobe (Fig. 4) and the patient was readmitted. At that time, the patient’s plasma somatostatin concentration (11 pg/ml) was normal.

Second Operation. A right frontal craniotomy was performed and a transcortical ultrasound study revealed a hyperechogenic mass located 0.5 cm below the cortical surface. This soft and dark red intraaxial mass was removed piecemeal.

Second Postoperative Course. The patient was discharged without neurological deficits on the 14th postoperative day. He had no abdominal or neurological complaints at his most recent clinic follow-up visit in June 1995, 12.3 years after his first presentation.

Pathological Examination. Microscopic examination of specimens from the tumors in his right temporal and frontal lobes revealed similar findings to those in the previously excised pancreatic somatostatinoma. The tumor consisted of a relatively homogeneous proliferation of polygonal cells with spindle-shaped, hyperchromatic nuclei and eosinophilic cytoplasm (Fig. 5 left). The tumor cell nests were separated by a thin, delicate, vascular stroma. The tumor had not invaded the dura mater.

Immunohistochemical staining for somatostatin and chromogranin A revealed a large number of immunoreactive tumor cells (Fig. 5 right). The somatostatin content of freshly prepared conditioned medium from the somatostatinoma was 30 pg/ml. The proliferative potential of the tumor, determined by immunostaining with the monoclonal antibody MIB-1 (Immunotech, S.A., Marseille, France), was estimated to be 6.8%.
Electron microscopy of a brain tumor specimen revealed many round, densely cored secretory granules, measuring 250 to 300 nm in diameter, resembling those of normal D cells (Fig. 6). Ultrastructures similar to those in the primary pancreatic tumor also were observed.

Discussion

Neuroendocrine neoplasms of the pancreas were classified in 1974 on the basis of a cell’s ability to take up and decarboxylate amine precursors. Tumors of D cells within the pancreatic islets secrete excessive amounts of somatostatin and are therefore called somatostatinomas. A somatostatinoma is a rare neuroendocrine tumor of the pancreas that has not previously been described in association with brain metastasis. The measurement of plasma somatostatin concentrations is thought to be useful in the diagnosis and follow-up care of patients with somatostatinomas. In our patient, the primary lesion caused an elevated plasma somatostatin concentration and an increased somatostatin content in tumor tissue. Although the metastatic brain lesion was a large mass that produced a high somatostatin content in freshly prepared condition medium, the plasma somatostatin concentration was almost normal. This suggests that determining the plasma somatostatin concentration may not be of significant value in the diagnosis of brain metastasis from a somatostatinoma.

The MIB-1 proliferative cell index of metastases from a malignant pancreatic somatostatinoma is a more useful indicator. In our patient, the proliferative cell index (determined by MIB-1 immunostaining) of the metastatic brain lesion was 6.8%, indicative of a neoplasm with a high proliferative potential. Harris, et al., have reviewed the length of survival in 31 patients with somatostatinomas and have reported that four patients (13%) survived for 5 years or more. The longest previously reported survival time was 12 years. Although several patients have been suspected of having a pancreatic tumor for as long as several years prior to diagnosis, the length of survival has been defined as the time from first presentation to the time the case was reported. In our patient, a pancreatic somatostatinoma metastasized to the brain 10 years after diagnosis of the primary tumor; nevertheless, the brain metastatic lesions were totally resected and he is currently alive without abdominal or neurological complaints, 12.3 years after initial diagnosis. To our knowledge, this case represents the first documentation of brain metastasis from a malignant somatostatinoma and the longest survival time of a patient with somatostatinoma.

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References


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