Case Report

Long-Term Survival of a Patient with Jejunal Somatostatin-Producing Tumour and Liver Metastases

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Abstract

Extrapancreatic somatostatinomas are uncommon neuroendocrine tumours. Information related to its long-term prognosis is scarce. The prognosis of patients with advanced somatostatinoma is expected to be poor, but some tumours show low malignant potential and long-term survival rates have been described, even in the presence of metastases. We present a case of a 30-year-old patient, diagnosed with jejunal somatostatinoma. Multiple liver metastases were present at diagnosis. The primary tumour was removed and somatostatin analogues were prescribed. The patient survived for 12 years, with acceptable quality of life, although he suffered from repeated episodes of abdominal pain, diarrhea and vomiting along with severe hyperglycaemia followed by hypoglycaemia. Finally, he died because of severe ascitis and dyspnea due to tumour progression.

Keywords: Neuroendocrine tumour, somatostatinoma, survival, liver metastases.

Introduction

Neuroendocrine tumours arise from enterochromaffin cells of the gastrointestinal tract and other organs. Somatostatin-producing tumours are relatively rare neuroendocrine tumours, with an estimated annual incidence of 1 in 40 million. After the first description of two pancreatic somatostatinomas in 1977, fewer than 200 cases have been reported. The clinical presentation includes nonspecific symptoms such as abdominal pain, nausea, diarrhea and weight loss. Typical somatostatin syndrome, first described in 1979, consists of diabetes, cholelithiasis and steatorrhea and is caused by excess somatostatin released from the...
tumour. However, this classic triad is present in only a small proportion of patients.

Somatostatinomas arise more frequently in the pancreas, followed by the duodenum; the ampulla of vater and the jejunum are infrequent locations. Extrapancreatic somatostatinomas are malign tumours, but they are generally smaller and less often associated with metastases than pancreatic somatostatinomas. However, only limited information about the long-term prognosis of patients with advanced somatostatinoma has been reported.

**Case Report**

We are presenting a case of a male patient diagnosed with somatostatinoma when he was 30 years old. The patient was admitted to Badajoz University Hospital (Spain) because of repeated episodes of abdominal pain, nausea, vomiting and diarrhea with steatorrhea, preceded by sweating and flushing, during the previous year.

The laboratory tests revealed a blood glucose level of 128 mg/dl as well as abnormal liver enzymes. Multiple metastatic masses appeared on the ultrasound. Abdominal computed tomography confirmed the liver enlargement due to innumerable liver metastases (Figure 1). A liver biopsy showed a low-grade neuroendocrine tumour with a proliferation index Ki-67 lower than 1%. Immunohistochemical staining demonstrated a diffuse positivity for neuron-specific enolase, chromogranin A, synaptophysin and somatostatin (Figure 2). The serum somatostatin level was 724 pg/ml (normal range: 17-80 pg/ml). Serum gastrine level was in the normal range.

![Figure 1. Abdominal Computed Tomography Showing Liver Enlargement and Multiple Focal Liver Metastases. Black Arrows Show the Location of Liver Metastasis](image-url)
The patient was operated and a 1.5 cm tumour located in the second portion of the jejunum was removed. The pathological examination showed a grade 1 neuroendocrine tumour. Liver metastases were confirmed and infiltration in four lymph nodes was found (T4N1M1). Immunohistochemistry showed strong staining with somatostatin and weak staining with gastrin. Although the somatostatin receptor scintigraphy failed to show any somatostatin receptor tissue (Figure 3), after surgery the patient was treated with the long-acting release formulation of octreotide, a somatostatin analogue. The somatostatin receptor scintigraphy was repeated several times during follow-up, showing similar results.

The patient survived for 12 years, with stable metastatic hepatic lesions and he enjoyed a good quality of life. Serum somatostatin levels increased after 6 years of follow-up, probably reflecting tumoral progression, although they were not checked again afterwards (Figure 4).
Nevertheless, the patient experienced, from diagnosis, twice a month episodes of abdominal pain, diarrhea with steatorrhea and vomiting. No symptoms of cholelithiasis were shown. During these episodes, blood glucose rose to 400 mg/dl and, without administration of any insulin at that moment, it rapidly decreased to severe hypoglycaemia (< 30 mg/dl). In two of these episodes, the patient suffered from hypoglycaemic coma that recovered with intravenous glucose infusion. Seven years after the diagnosis, the glycosilated hemoglobin was 9.3%, so the patient was treated with insulin glargine (0.13 U/kg).

The tumour was stable on somatostatin analogs for 10 years. Then, the tyrosine-kinase inhibitor sunitinib was prescribed for one year due to symptoms persistence and progression; as the symptoms showed no improvement, sunitinib was later changed to the mTOR inhibitor everolimus. No improvement in the symptoms, biochemistry levels or radiological images was found in response to sunitinib or everolimus.

Finally, the patient died 12 years after diagnosis because of severe ascitis and dyspnea due to tumour progression.

Discussion

Even in presence of liver metastases at diagnosis, surgical removal of primary somatostatin-producing tumours is recommended, as it may lead to improved survival or quality of life. Somatostatin analogues may reduce tumour secretion and retard tumour growth1.

An overall 5-year survival rate of 40-60% for patients with somatostatinoma has been reported. In the presence of liver metastases, the reported survival rate is 40%. Many patients with duododenal or pancreatic somatostatinomas have advanced disease at diagnosis, but long-term survival rates have been observed after surgical treatment. The size of the tumour appears to be the critical risk factor for the development of metastases, whereas other factors, such as age, gender, location of the tumour and histological

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characteristics have demonstrated no
relation to metastases. The risk of
metastases seems to increase significantly
with tumours larger than 2 cm. Therefore,
the prognosis of patients with advanced
somatostatinoma is perhaps not as poor as
previously reported, with an average
survival period of 1-2 years. The reported
long-term survivals, up to 30 years, suggest
that duodenal malignant somatostatinomas
potentially have a low malignant potential
and slow growth. Indeed, primary location
in jejunum is very rare and the information
related to the long-term prognosis of
jejunal somatostatinomas is scarce.

Several causes may lower tumor
detectability in somatostatin receptor
scintigraphy studies, such as presence of
unlabeled somatostatin resulting from
production by the tumor itself, different
somatostatin receptor subtypes with
different affinities for the radioligand and
variable tumor differentiation and receptor
expression.

Hypoglycemia in somatostatinomas has
been reported in very few cases and its
mechanism remains unclear. Somatostatin
may inhibit the secretion of glucagon and
other hormones that can increase the
glucose level.

Systemic therapy for somatostatin-
producing tumours includes somatostatin
analogs, cytotoxic chemotherapy and
molecular targeted therapy, such as
tyrosine-kinase inhibitors (sunitinib and
sorafenib) and mTOR inhibitors
(everolimus). In our patient, the tumour
was stable on somatostatin analogs for 10
years but showed to response to sunitinib
or everolimus.

In summary, we report a case of a low-
grade malignancy jejunal somatostatinoma
in a 30-year-old man, with liver metastases
at diagnosis, treated with surgical resection
and somatostatin analogues. The patient
presented a long-term survival, with
acceptable quality of life but with repeated
episodes of gastrointestinal symptoms.

References

Ganda, O. P., Weir, G. C., Soeldner, J. S., Legg,
M. A., Chick, W. L., Patel, Y. C., Ebeid, A. M.,
"Somatostatinoma: A Somatostatin-
Containing Tumor of the Endocrine
Pancreas," The New England Journal of
Medicine, 28; 296(17) 963-7.

Garbrecht, N., Anlauf, M., Schmitt, A.,
Henopp, T., Sipos, B., Raffel, A., Eisenberger,
C. F., Knoefel, W. T., Pavel, M., Fottner, C.,
Musholt, T. J., Rinke, A., Arnold, R., Berndt,
U., Plöckinger, U., Wiedemann, B., Moch,
H., Heitz, P. U., Komminoth, P., Perren, A. &
Klöppel, G. (2008). "Somatostatin-
Producing Neuroendocrine Tumors of the
Duodenum and Pancreas: Incidence, Types,
Biological Behavior, Association with
Inherited Syndromes, and Functional
Activity," Endocrine-related Cancer, 15(1)
229-41.

House, M. G., Yeo, C. J. & Schlock, R. D.
(2002). "Periampullary Pancreatic
Somatostatinoma," Annals of Surgical
Oncology, 9(9) 869-74.

Kim, J. A., Choi, W. H., Kim, C. N., Moon, Y. S.,
Somatostatinoma: A Casereport and
Review," The Korean Journal of Internal
Medicine, 26(1) 103-7.

Koc, O., Duzkoylu, Y., Sari, Y. S., Bektas, H.,
"Duodenal Somatostatinoma: A Case
Report and Review of the Literature,"
Journal of Medical Case Reports, 25;7(1)
115.

Krejs, G. J., Orci, L., Conlon, J. M., Ravazzola,
M., Davis, G. R., Raskin, P., Collins, S. M.,
Mccarthy, D. M., Baetens, D., Rubenstein, A.,
"Somatostatinoma Syndrome. Biochemical,
Morphologic and Clinical Features," The
New England Journal of Medicine, 9;301(6)
285-92.

