Somatostatinomas are rare functioning neoplasms usually arising in the pancreas and duodenum. They are seldom associated with typical clinical symptoms. Their diagnosis is confirmed only by histological and immunohistochemical studies and the presence of specific hormones. Two distinct clinicopathological forms of somatostatinoma exist: duodenal and pancreatic somatostatinomas. Clinically, compared to pancreatic somatostatinomas, duodenal somatostatinomas are more often associated with nonspecific symptoms and neurofibromatosis, but less often with somatostatinoma syndrome or metastasis. We report a case of somatostatin-producing duodenal carcinoma in a 45-year-old female with neither neurofibromatosis nor somatostatinoma syndrome. Abdominal computed tomography showed a 18-mm mass in the duodenum which had given rise to multiple lymph node metastases. Although the endoscopic biopsies were free of malignancy, the patient subsequently underwent Whipple’s operation for the duodenal mass. Immunohistochemical analysis confirmed the diagnosis of somatostatin-producing carcinoma.

Key words: somatostatin-producing, carcinoma, duodenum, diagnosis

INTRODUCTION

Somatostatinoma is a neuroendocrine tumor derived from the D cells of the APUD system. This tumor is very rare endocrine neoplasm, with an annual incidence of 1 in 40 millions. The pancreas is the most common site of somatostatinomas representing 68% of all tumors. Other sites of somatostatinomas include the duodenum (19%), the papilla of Vater (3%) the small intestine (3%), bronchus and liver. Unlike pancreatic somatostatinoma which generally produces a clinical syndrome (diabetes, steatorrhea, hypohidrosis, dyspepsia) duodenal somatostatinoma may be completely asymptomatic. In view of the rarity and the significance of the histologic diagnosis, we report a patient with malignant duodenal somatostatinoma with lymph node metastases that has been treated by surgery. The diagnostic challenges are highlighted in our case report.

THE CASE HISTORY

Clinical and radiological finding

The 45-year-old woman presented with nausea, vomiting and moderate epigastric pain. The general condition and the nutritional status at admission were good. Routine blood analysis showed only mild hyperglycemia (7.8 mmol/l) and elevated carcinoembryonic antigen: 8.9 ug/l (normal <5 ug/l). Other laboratory data and tumor markers (Alpha-fetoprotein, CA 19-9, CA 125) were within normal limits. Somatostatin levels were not measured before the operation because the patient did not have clinical presentation of the inhibitory syndrome (e.g. cholelithiasis, steatorrhea or weight loss). After ultrasonography, she was suspected to have a pancreatic tumor. An abdominal CT angiography showed three hypervascular lesions. The largest one 4.5 cm in diameter, confirmed to be under the visceral surface of the liver, medially to the head of pancreas and behind the inferior cava vein (Fig.1a). This tumor mass was lobulated, clearly demarcated from surrounding tissues and vessels and during the portal venous phase appeared inhomogenous and isodense with the surrounding tissue. The other two hypervascular lesions were smaller and one of them, 18 mm in diameter, seemed to be within the wall of the descending duodenum (Fig.1b). The third hypervascular lesion, 11 mm in diameter, was more caudomedial in comparison with the previously mentioned. CT scan also revealed a few enlarged perifocal lymph nodes, between 8 and 12 mm in size. The described features of the tumor lesions were suggestive of its neuroendocrine or even mesenchymal origin. There were no other important findings in the MDCT exploration of the abdomen and pelvis. Endoscopy did not
revealed dudenal tumor mass. Neither neurofibromatosis nor multiple endocrine neoplasms were detected. Following a colorectal multidisciplinary meeting, patient underwent pylorus-preserving Whipple’s procedure as well as regional lymph node dissection. A rounded mass arising from the pancreatic head was removed. The duodenum was involved by other smaller tumor. The rest of the abdomen was unremarkable. The patient had an uneventfull recovery after the tumor resection.

**PATHOLOGY AND IMMUNOHISTOCHEMISTRY**

On gross pathology, the largest tumor mass, 50 mm in diameter, was proven to be an incapsulated lymph node metastasis close to the uncinate process but without pancreatic involvement. There was one more lymph node metastasis in the peripancreatic adipose tissue which was dissected on the surgery. The specimen consisted of duodenum with attached solid 18x15x10 mm tumor, was proven to be a duodenal tumor which was 15 mm proximal to the papilla of Vater and did not invade adjacent tissues. On the cut surface the mass had granular structure and grayish color. Histopathology of the duodenal tumor revealed a dominant trabecular pattern with rare microlandular and insular microorganization, and without necrotic areas. The tumor cells were with a high degree of uniformity and ovoid/polygonal shapes. All of the resection margins were free of tumor involvement (Fig.2). The immunohistochemical profile of sections of the specimen revealed the presence of somatostatin. There was a significant cytoplasmic immunoexpression of neuroendocrine markers: Chromogranin A and Synaptophysin. There was strong somatostatin immunoreactivity in over 95% of the duodenal tumor cells. Some tumor cells coexpressed gastrin. Proliferative activity measured using Ki-67 protein labeling indices was less than 0.01. The final histo pathological diagnosis of somatostatin-producing neuroendo-

crine tumor of the duodenum was made in tumor stage: T2N1(2/9)MxL1V1. On follow-up, 18 months after the operation, the patient was asymptomatic and CT showed no signs of tumor recurrence and metastasis. Glycemic control also was normalized. Nevertheless, we have arranged 3-monthly follow-up in the outpatient department to monitor his progress.

**DISCUSSION**

Somatostatinomas may be sporadic (93,1%) or familial (6,9%) in association with neurofibromatosis type 1 (NF1), multiple endocrine neoplasia type 1 (MEN 1) and Von Hippel-Lindau syndrome. Unlike pancreatic somatostatinomas which are supposed to present with diabetes mellitus, cholelithiasis and steatorrhea also known as the "somatostatinoma syndrome", duodenal somatostatinomas produce local symptoms such as jaundice, abdominal pain and gastrointestinal bleeding or are asymptomatic. Only 1,2% of duodenal somatostatinomas presented with the inhibitory syndrome. Somatostatin supresses the release of growth hormone, thyrotropin, gastrin, VIP, cholecystokinin, secretin, gastric inhibitory polypeptide, insulin, glucagon and many others. Exocrine secretions (pancreatic, biliary, gastric, intestinal) and gallbladder contractility are also inhibited by somatostatin. Extrapancreatic somatostatinoma rarely secretes somatostatin and even when it does, the serum level of somatostatin is lower in comparison with its pancreatic counterpart. Thus, it is seldom associated with a recognizable somatostatin syndrome. The failure to detect a somatostatinoma syndrome may be explained by the very short biological half-life of somatostatin making it almost unable to affect its target cells via the circulation. Although somatostatin is the main secretory product, at least 10% of somatostatinomas produce other hormones as a gastrin, VIP and calcitonin. The clinical picture might depend on the effects of these secreted...
hormones. As most patients don’t have classic symptoms or physical findings, a preoperative diagnosis of duodenal somatostatinoma is very difficult and frequently impossible. In this case, the tumor originated from the duodenum and was smaller than 2 cm. The patient had only vague nonspecific symptoms. Even though a preoperative somatostatin level wasn’t detected, the histological results have clearly demonstrated that it is a duodenal somatostatinoma with two lymph nodes’ metastases. One of those lymph node metastases was larger in diameter than the primary tumor, and at first thought to be the original tumor. Even tumors with a diameter between 1 and 2 cm may show metastases in the paraduodenal lymph nodes as it was in our case. Because of their slow growth and nonspecific symptoms, the diagnosis is often late, and metastases have often been observed in 88% of cases of somatostatinoma. A modified analogue of octreotide labeled with indium 111, was shown to detect localised primary and metastatic somatostatinoma tumors. Scintigraphy positive for metastatic spread can obviate unnecessary surgery, similarly a negative scan can indicate that curative resection is a possibility. An adjuvant chemotherapy is not advocated after complete resection. For locally unresectable tumors or in metastatic disease chemotherapeutic agents have been used with moderate clinical responses. Although the prognosis of metastatic somatostatinomas had been proposed to be poor, there have been reported some cases of malignant duodenal somatostatinomas which had a relatively long survival.

In conclusion, this clinical case with nonspecific symptoms highlights the possibilities of preoperative diagnosis of duodenal somatostatinoma. Hypervascular tumors on CT imaging should increase clinicians’ awareness on neuroendocrine tumor.

REFERENCES