Cystic Pancreatic Neuroendocrine Neoplasms with Uncertain Malignant Potential: Report of Two Cases

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Abstract

Neuroendocrine tumors of the pancreas (NETP) represent only 1%–2% of all pancreatic neoplasms. They can be classified as functioning or non-functioning, respectively, according to the presence or absence of paraneoplastic syndrome. Case 1 concerned a 70-year-old woman with a cystic lesion of the pancreatic head and body. All tumor markers were negative. The patient underwent a distal pancreatectomy. The histology revealed a well-differentiated endocrine tumor with uncertain malignant potential. Case 2 was a 61-year-old man with chronic polyserositis. The serum tumor markers were negative, while he was strongly positive for intracystic tumor markers carcinoembryonic antigen, carbohydrate antigen (CA) 19-9, and CA 125. The patient underwent a cephalo-pancreatic duodenectomy. The preoperative differential diagnosis of cystic NETP is still a challenge due to the high rate of the nonfunctional variant. Although cystic NETPs are well differentiated, they are still tumors with a malignant potential, and therefore an early diagnosis and radical surgical resection could be associated with a better long-term survival.

Key words Pancreas · Neuroendocrine neoplasm · Uncertain malignant potential · Chromogranin · Synaptophysin

Introduction

Neuroendocrine tumors of the pancreas (NETP) form a small subgroup of tumors characterized by a biological behavior that varies with hormone production and the degree of differentiation. Based on their clinical presentation, NETPs are classified as either functioning or nonfunctioning. Functioning tumors are characterized by a clinical endocrinopathy caused by inappropriate hormone secretion. Nonfunctioning NETPs are histologically similar to functioning NETP, but do not produce any clinical syndromes. Non-functioning tumors may, however, coincide with high hormone levels in blood tests and immunoreactivity in the histological specimens. The lack of clinical signs is thought to be due to inadequate hormone secretion, the secretion of a hormone in inactive form, or the fact that the hormone being released causes a clinical syndrome that has yet to be defined.

The World Health Organization (WHO) has revised its classification of NETPs to better reflect the variable prognosis of these tumors. The histological criteria adopted for their classification includes the degree of differentiation, tumor size, necrosis, the presence or absence of vascular invasiveness, perineural invasion, and the proliferation index. Neuroendocrine tumors of the pancreas usually appear radiologically as solid tumors, though on rare occasions they manifest as cystic lesions of the pancreas. Cystic NETPs are often impossible to differentiate preoperatively from other cystic pancreatic tumors, such as intraductal papillary mucinous neoplasms (IPMN), mucinous cystic neoplasms (MCNs), serous cystic neoplasms (SCNs), solid pseudopapillary neoplasms (SPPNs), and non-neoplastic cysts, which is why they pose a diagnostic challenge.

The treatment options for NETP have evolved over the past decade and the optimal treatment for all such lesions is a radical surgical resection whenever possible. This report describes two cases of cystic pancreatic endocrine tumors while also reviewing the pertinent literature. Written consent was obtained from the patients for the publication of this study.
Case Reports

Case 1

A 70-year-old woman was referred to the Surgery Unit for a cystic pancreatic lesion. She had a history of continuous pain in the epigastric area, with no fever or other symptoms. A thorough series of laboratory analyses, including serum amylase and lipase concentration tests, were within the normal range. Moderate pressure pain was documented in the upper right abdomen during a physical examination. About a year before admission, the patient had experienced diffuse abdominal pain and cramps.

Ultrasonography (US) revealed a cystic lesion located in the pancreatic head and body measuring 2.9 × 3.3 cm. The lesion was apparently larger than had been documented on previous US scans. Two simple biliary cysts were detected on the VI and VII hepatic segments. A computed tomography (CT) scan identified an expansile growth (3.6 cm in diameter) between the pancreatic head and body (Fig. 1a). This lesion had the features of a cyst containing fluid of variable density and a single solid formation in the middle of the posterior wall of the cyst. Magnetic resonance imaging (MRI) confirmed the presence of the lesion in the cephalic portion of the pancreas (Fig. 1b). The lesion appeared to be rounded, with a thin wall, and it contained a proteinaceous material. The MRI scan also showed a small solid token about 1 cm in size located on the posterior wall of the cyst, characterized by contrast enhancement.

Tumor markers were all within the normal range: carbohydrate antigen (CA) 19-9, 4.6 U/ml (reference range: 0–39 U/ml); carcinoembryonic antigen (CEA), 1.83 ng/ml (reference range: 0–4.3 ng/ml); CA 125, 6.8 U/ml (reference range: 0–35 U/ml); CA 72-4, 1.1 U/ml (reference range: 0–6.9 U/ml); and CA 15–3, 23.5 U/ml (reference range: 0–25 U/ml). P-chromogranin A was 17 ng/ml (reference range: 2–18 ng/ml) and neuron-specific enolase (NSE) was 7.9 μg/ml (reference range: 0–17 μg/ml). The patient underwent endoscopic ultrasonography (EUS) in association with fine-needle aspiration (FNA) of the liquid contained in the pancreatic lesion. Cytology showed small cell nests with an epithelial appearance: the cells appeared to be cylindrical, with focal mucus secreting characteristics; there was no evidence of any atypical nuclei. These results were consistent with those of a mucinous cystic lesion.

A well-encapsulated cystic mass was found during a laparotomy. No extrapancreatic involvement or enlarged intra-abdominal lymph nodes were observed. Therefore, a spleen-preserving distal pancreatectomy was performed. The histological diagnosis was a well-differentiated endocrine tumor with uncertain malignant potential. The histology of the pancreatic specimen showed an unusual-looking cystic lesion on a fibrotic wall (Fig. 2). The lesion consisted of monomorphic cells with rounded nuclei, pronounced nucleoli, overfilled basophilic cytoplasm and solid trabecular growth (Fig. 3). Immunohistochemical tests were positive for cytokeratin (MNF116), chromogranin, synaptophysin (Fig. 3), progestin receptors, and CD56/NCAM, and negative for estrogen receptors. The cytoproliferation rate (measured by MIB-1) was 2% and the mitotic index was 2 × 10 mitoses per high-power field (HPF). There was no evidence of vascular invasion or tumor necrosis.