Primary pancreatic paraganglioma: a case report and literature review

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Abstract

Background: Primary pancreatic paraganglioma is an extremely rare extra-adrenal paraganglioma.

Case presentation: We report a case of primary pancreatic paraganglioma undergoing middle segment pancreatectomy in a 42-year-old woman. Histological examination showed that the tumor was composed of well-defined nests of cuboidal cells separated by vascular fibrous septa, forming the classic Zellballen pattern. The chief cells showed positive staining to neuron-specific enolase, chromogranin A, synaptophysin, and the chief cells were surrounded by S-100 protein-positive sustentacular cells. The patient has remained tumor free for 12 months after surgery. A brief discussion about the histopathological features, clinical behavior, and treatment of primary pancreatic paraganglioma, and review of the relevant literature is presented.

Conclusions: Primary pancreatic paraganglioma is a rare clinical entity, its diagnosis mainly depends on histopathological and immunohistochemical examinations. Complete surgical resection is the first choice of treatment and close postoperative follow-up is necessary.

Keywords: Pancreas, Paraganglioma, Middle segment pancreatectomy

Background

Paragangliomas are rare neuroendocrine tumors (NETs) that arise from the extra-adrenal chromaffin cells of the autonomic nervous system, with an average annual incidence rate of only 2 to 8 per 1 million adults. Paragangliomas could derive from the extra-adrenal chromaffin cells of the sympathetic paravertebral ganglia of the thorax, abdomen, and pelvis, also arise from the parasympathetic ganglia located along the glossopharyngeal and vagal nerves in the neck and at the base of the skull. However, primary pancreatic paraganglioma is extremely rare. Herein, we present a case of primary pancreatic paraganglioma and review of the literature.

Case presentation

A 42-year-old woman presented in September 2014 with recurrent upper abdominal pain for 3 months. She had no history of hypertension, headache, and palpitation. A physical examination revealed slight upper abdominal tenderness. Laboratory test results including liver function, renal function, and blood glucose were within normal ranges. Serum levels of CEA, CA19-9, and CA125 were normal. The level of 24-h urinary norepinephrine excretion was also normal. Unenhanced computed tomography (CT) revealed a 5.2 cm × 6.3 cm, solid, low density tumor on the body of the pancreas. On contrast-enhanced CT, the tumor demonstrated marked enhancement in the arterial phase (Fig. 1). Dilatation of the pancreatic duct was noted at the tail of pancreas. No biliary dilation or liver lesions were detected. A diagnosis suspicion of a pancreatic neuroendocrine tumor was made before operation. The patient underwent middle segment pancreatectomy. The proximal pancreas was transected using a linear stapler and continuous suture using 4-0 prolene, the stump of the distal pancreas was anastomosis to the jejunum with duct-to-mucosa pancreaticojejunostomy. The two resection margins were frozen section to confirm tumor-free. During the operation, the patient's blood pressure remained stable. Histological examination showed that the tumor was composed of well-defined nests of cuboidal cells separated by vascular fibrous septa, forming the classic Zellballen pattern (Fig. 2a). The chief cells showed positive staining to neuron-specific enolase (NSE) (Fig. 2b),...
chromogranin A (CgA), synaptophysin (Syn) (Fig. 2c), but showed negative response to vimentin (Vim), endo-
ymysial (EMA), cytokeratin (CK), insulin, and glucagon. The chief cells were surrounded by S-100 protein-
positive sustentacular cells (Fig. 2d). The Ki67 labeling
index was 1 % where no mitoses were observed. Region
lymph nodes and the resected margins were free of
tumor cells. Taking the morphological and immunohis-
tochemical features into account, the diagnosis of pri-
mary pancreatic paraganglioma was confirmed. The
patient’s postoperative course was uneventful and dis-
charged on the 8th postoperative day. The patient re-
ceived no subsequent adjuvant treatment, and had
remained tumor free for 12 months after surgery.

Discussion
Primary paraganglioma that arises in the pancreas is
rare. Whether this tumor type is an extension of a retro-
peritoneal tumor of true visceral origin, derived from ec-
topic paraganglia, remains unknown. To the best of our
knowledge, only 21 cases of pancreatic paraganglioma
having been reported from 1943 to the present in the lit-
erature (Table 1) [1–18]. The mean age of the 21 cases
reported in the literature was 57.6 years ranging from 19
to 85 years. Of those patients, 16 were women and five
were men with the ratio of 3.2:1. The tumor was located
in the head of the pancreas in 15 patients, 2 in the body,
and 4 in the tail. The mean size of the tumors was
6.1 cm. Four cases were considered malignant, and six
cases showed functional activity. Herein, we presented a
42-year-old woman with primary pancreatic paragan-
glioma, which located in the body of the pancreas. The
patient had no symptoms of catecholamine excess, and
the blood pressure remained stable during the operation,
the norepinephrine levels was normal, therefore non-
functional pancreatic paraganglioma was diagnosed.
The location of pancreatic paragangliomas can usually be
identified by abdominal ultrasonography, CT, or magnetic
resonance imaging. In our current case, the pancreatic
paraganglioma appeared as a solid mass on the body of the
pancreas on CT scans, and marked enhancement was
found on contrast-enhanced CT. The preoperative diagno-
sis of pancreatic paraganglioma is difficult, especially in
nonfunctional cases. Functional cases are easier to diagnose
because having symptoms of catecholamine excess such as
hypertension, headache, and palpitation, and the urinary
catecholamines are elevated. The confirmed diagnosis of
paraganglioma mainly depend on histopathological and immunohistochemical findings as following (i) the classic Zellballen pattern composed of chief cells and sustentacular cells within the tumor; (ii) the chief cells showed positive staining to NSE, CgA, Syn, and negative for CK; and (iii) the sustentacular cells showed positive staining to S-100 or GFAP. Pancreatic paragangliomas are potential to be malignant [13–15], but factors predictive of malignant behaviors have not been well characterized. In general, malignant paragangliomas are defined as those that metastasize, recur, or show evidence of local invasion.

The first choice of treatment for primary pancreatic paraganglioma is complete surgical resection. Postoperative I\textsubscript{131}-metaiodobenzylguanidine (I\textsubscript{131}-MIBG) radiotherapy has been advocated in cases proven to be malignant [14], chemotherapy and novel biologically targeted drugs could be the other reasonable choice. Although pancreaticoduodenectomy or pylorus preserving pancreaticoduodenectomy is recommended for paraganglioma of the pancreatic head, and distal pancreatectomy for tumors of the pancreatic body or tail, simple tumor enucleation also showed an equally good outcome. In the present case, middle segment pancreatectomy was performed being the tumor located in the body of the pancreas. Middle segment pancreatectomy procedure has the advantage of preserving normal pancreatic parenchyma to the most extent and consequently long-term endocrine and exocrine pancreatic function. The patient had an uneventful postoperative course. Being have no evidence of tumor invasion and metastases, the patient received no subsequent adjuvant treatment, and has been tumor free for 12 months after surgery. The long-term outcome is still in follow-up.

**Conclusions**

We report a case of primary nonfunctional paraganglioma on the body of the pancreas. Middle segment pancreatectomy could be a reasonable procedure for such tumor. Pancreatic paraganglioma has malignant potential, and requiring close postoperative follow-up.

**Consent**

Written informed consent was obtained from the patient for publication of this Case Report and any accompanying images. A copy of the written consent form is available for review by the Editor-in-Chief of this journal.

**Abbreviations**

CgA: chromogranin A; CK: cytokeratin; CT: computed tomography; EMA: endomysial; MSP: middle segment pancreatectomy; NETs: neuroendocrine tumors; NSE: neuron-specific enolase; Syn: synaptophysin; Vim: vimentin.

### Table 1 Twenty-one cases of pancreatic paraganglioma in the literature

| Author        | Year | Age (y) | Sex | Location | Size (cm) | Cystic or Solid | Function | Malignant | Treatment | Survival |
|---------------|------|---------|-----|----------|-----------|----------------|----------|-----------|-----------|----------|
| Gooho [1]     | 1943 | 62      | M   | Body     | 1.5       | Solid         | No       | No        | –         | Autopsy  |
| Bartley [2]   | 1966 | 75      | F   | Tail     | Goose egg | Cystic        | Yes      | No        | DP        | NM       |
| Bartley [2]   | 1966 | 70      | F   | Head     | Walnut    | Cystic        | Yes      | No        | TR        | NM       |
| Cope [3]      | 1974 | 72      | F   | Head     | 13        | Cystic        | No       | No        | TR        | 2Y(A)    |
| Zamir [4]     | 1984 | 47      | M   | Body     | 10        | Cystic        | No       | No        | TR        | 6Y(A)    |
| Fujino [5]    | 1998 | 61      | M   | Head     | 2.5       | Solid         | No       | No        | PD        | 5Y(A)    |
| Parithivvel [6]| 2000 | 85      | M   | Head     | 6         | Cystic        | No       | No        | TR        | 3Y(A)    |
| Ohkawara [7]  | 2005 | 72      | F   | Head     | 4         | Cystic        | No       | No        | TR        | NM       |
| Perrot [8]    | 2007 | 41      | F   | Tail     | 4.2       | Solid         | Yes      | No        | TR        | 18 M(A)  |
| Tsukada [9]   | 2008 | 57      | F   | Head     | 2         | Solid         | No       | No        | TR        | 4Y(A)    |
| Kim [10]      | 2008 | 57      | F   | Head     | 6.5       | Solid         | No       | No        | PPPD      | NM       |
| Paik [11]     | 2009 | 70      | F   | Tail     | 4.2       | Solid         | No       | Yes       | DP        | NM       |
| He [12]       | 2011 | 40      | F   | Head     | 4.5       | Solid         | No       | No        | NM        | NM       |
| Higa [13]     | 2012 | 65      | F   | Head     | 2         | Solid         | No       | Yes       | PD        | 10 M(A)  |
| Al-Jiffry [14]| 2013 | 19      | F   | Head     | 9.5       | Solid         | Yes      | Yes       | PD        | 3Y(A)    |
| Zhang [15]    | 2014 | 50      | F   | Head     | 6         | Solid         | Yes      | Yes       | Laparotomy| 4Y(D)    |
| Zhang [15]    | 2014 | 63      | M   | Head     | 4         | Solid         | Yes      | No        | TR        | 3 M(A)   |
| Borgohain [16]| 2014 | 55      | F   | Tail     | 19        | Solid         | No       | No        | TR        | 10 M(A)  |
| Straka [17]   | 2014 | 53      | F   | Head     | 8.5       | Solid         | No       | No        | PPPD      | 49 M(A)  |
| Meng [18]     | 2015 | 54      | F   | Head     | 3         | Solid         | No       | No        | TR        | NM       |
| Meng [18]     | 2015 | 41      | F   | Head     | 6         | Solid         | No       | No        | TR        | NM       |

F female, M male, NM not mentioned, DP distal pancreatectomy, PD pancreaticoduodenectomy, TR tumor resection, PPPD pylorus preserving pancreaticoduodenectomy, Y years, M months, A alive, D dead
Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
XWD designed the study; LSR analyzed the data and drafted the manuscript; PL collected the data and presented the clinical features; LY, XWD, and LSR performed the operation; HS made the pathologic diagnosis. All authors have read and approved the final manuscript.

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