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# Primary non-functional pancreatic paraganglioma: A case report and review of the literature

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**Abstract**

Primary pancreatic paragangliomas are rare. They are mainly non-functional tumours that lack typical clinical manifestations. Definite diagnosis relies on histopathology and immunohistochemistry, and the main treatment is surgery. We report here a case of primary, non-functional, pancreatic paraganglioma in a 49-year-old woman. The tumour was approximately 5.0 × 3.2 × 4.7 cm in size and located in the pancreatic neck and body. We undertook 3D laparoscopic complete resection of the tumour. The patient developed a pancreatic fistula (biochemical leak) post-surgery, but she recovered and was discharged from hospital 11 days after surgery. We describe this case study and briefly summarize previous related reports.

**Keywords**

Pancreatic paraganglioma, pancreatic tumour, paraganglioma, pancreas

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## Introduction

Pheochromocytomas (PCCs) and paragangliomas (PGLs) are rare neuroendocrine tumours and are collectively called pheochromocytoma/paraganglioma (PPGL).[1] Pheochromocytomas are located in adrenal medulla, whereas paragangliomas are formed outside the adrenals, commonly near nerves.[1] All PPGL exhibit a malignant potential.[1] In a population-based setting, standardized incidence rates of PPGL

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were reported to have increased almost five-fold from 1977 to 2015.[2] The authors suggested that the increase was due to newly diagnosed patients (>50 years) and incidentally discovered PPGLs of small size (<4 cm). However, it could also be due to improved detection of PPGLs due to an increase in imaging.[3] The tumours are slightly more common in women than men with a prevalence of 51–57%, and median age of diagnosis has been estimated to be between 48–55 years.[3] Most PPGLs are discovered following signs and symptoms suspected to be related to catecholamine excess (i.e., paroxysmal hypertension and the classic triad of headaches, sweating and palpitations).[3] However, only one fifth of patients show the classic triad, and some patients are completely asymptomatic.[3]

The incidence of PGLs is low and estimated to occur in approximately 2–8 cases/million people, and the tumours can arise in sympathetic and parasympathetic nervous systems.[4] The parasympathetic PGLs are often located in the head and neck, and are mostly non-functional.[3,4] The sympathetic PGLs are often located in the abdomen, followed by the chest and pelvis.[5] Abdominal PGLs can produce, store, and secrete catecholamines; and they can produce typical signs and symptoms such as hypertension, palpitations, dizziness, anxiety, blushing, headaches, and sweating.[6]

Pancreatic PGLs are extremely rare and to the best of our knowledge, only 53 cases have been reported worldwide over the past 50 years. We present here a case of primary, non-functional, pancreatic PGL and briefly summarize and discuss related reports.

## Case Report

A 49-year-old woman presented with a complaint of intermittent epigastric pain which had lasted for one month. The patient had undergone cholecystectomy for gallstones five years previously and had no history of chronic diseases (e.g., hypertension or diabetes). Her personal and family histories were unremarkable. On abdominal examination the patient had abdominal tenderness in the epigastrium.

Routine blood examination, liver, renal, and coagulation function tests, and tumour marker levels (i.e., alpha-fetoprotein, carbohydrate antigen 15-3, carbohydrate antigen 19-9, carbohydrate antigen 72-4, carbohydrate antigen 125, and carcinoembryonic antigen) were within the normal range. Other parameters (i.e., cortisol; angiotensin II; renal activin A; aldosterone; dopamine; adrenaline; noradrenaline) were judged by an endocrinologist, to be within the normal range.

Abdominal computed tomography (CT) showed a pancreatic body tumour approximately $4.6 \times 2.9$ cm in size and oval in shape with a slightly low-density shadow and clear boundary. Edge enhancement was obvious in the arterial phase and inward-filling enhancement in the portal vein phase. An ectopic pheochromocytoma and splenic arteriovenous compression were considered (Figure 1).

To further define the lesion, magnetic resonance cholangiopancreatography (MRCP) was performed. This showed irregularly long T1 and T2 signal shadows behind the pancreatic body. The diffusion weighted imaging (Dw1) sequence showed a strong signal. Enhancement scanning was uneven, the size was estimated to be $4.3 \times 2.7 \times 3.9$ cm and it was considered a benign neoplastic lesion; the main pancreatic duct was not dilated, and the splenic artery and vein were compressed (Figure 1). Following consultation with endocrinologists and imaging physicians, the final diagnosis was non-functional PGL of the pancreas

The patient was prescribed oral phenbenzylamine 10 mg bd for a month to keep her hormones stable and prevent her blood pressure from increasing during intraoperative tumour removal. On re-examination

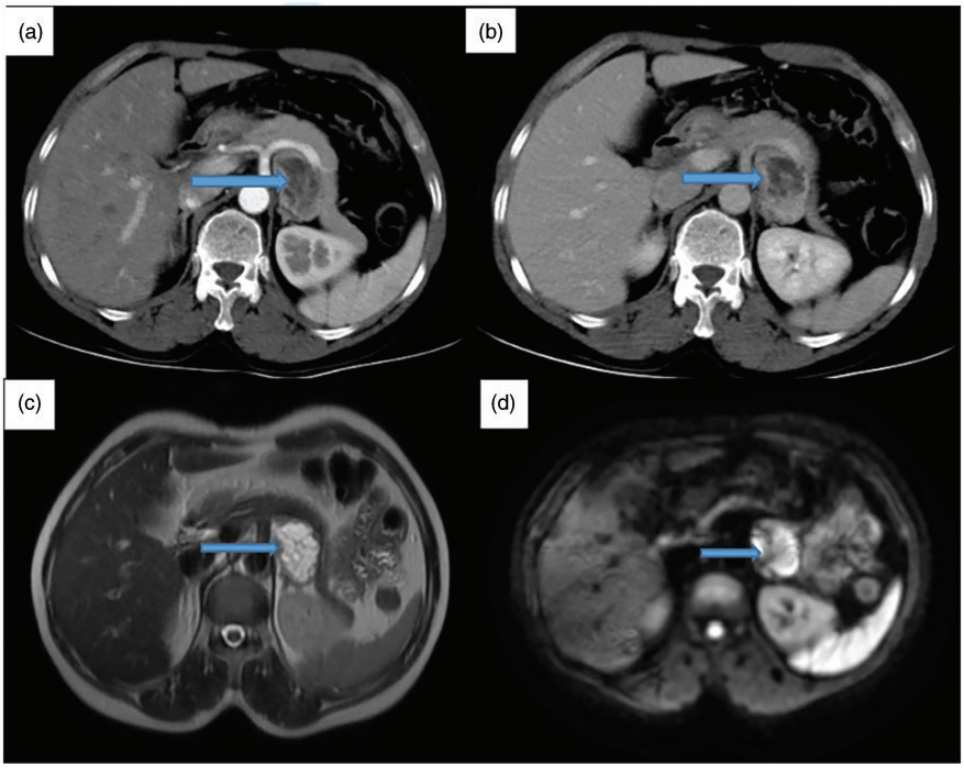


**Figure 1.** Computed tomography (CT) and magnetic resonance image (MRI) of the tumour: (a) From the CT image, the mass (blue arrow) showed obvious inhomogeneous enhancement in the enhanced arterial phase, (b) From the CT image the mass (blue arrow) showed continuous enhancement in the portal vein stage, (c) An oval, cystic, solid mass (blue arrow) with equal T2 signal in wall and septum, with multiple long T2 hyperintense cystic changes was shown on MRI and (d) The diffusion weighted imaging (Dw1) sequence of the mass (blue arrow) showed a strong signal.

four weeks later, her levels of methoxy epinephrine, methoxy norepinephrine and 3-methoxytyramine were within normal ranges. The patient then underwent 3D laparoscopic complete resection of the pancreatic mass. During the operation, the soft resected mass was located behind the junction of the pancreatic body and neck and was closely related to the pancreas; the size was approximately $5.0 \times 3.2 \times 4.7$ cm and it was adjacent to the left side of the abdominal aorta, in front of the left renal vein, between the splenic artery and vein (with obvious compression), and close to the confluence of the splenic and portal veins (Figure 2). On the third day post-surgery, a pancreatic fistula (biochemical leak) was detected which was treated conservatively. The patient fully recovered and was discharged from hospital 11 days post-surgery.

Histological examination post-surgery showed that the tumour cells were separated by capillary nests, forming the classic Zellballen pattern (Figure 3). Immunohistochemistry reports showed SYN (+), CGA (+), CD56 (+), Ki-67 ($\leq$2%), S-100 (−), Sox-10 (+), p53 (−), ERG (−), CD31 (+), CD34 (+), NSE (+),

GFAP (+), AE1/3 (−), Cam5.2 (−), GATA3(+). These findings were consistent with the characteristics of PGL Although the patient had no symptoms of hypertension or palpitations, and her blood catecholamine hormones were within normal levels, the postoperative pathological results were consistent with a PGL. Following consultation with endocrinologists and pathologists, the patient was diagnosed as having a non-functional pancreatic PGL. According to the grading system for adrenal PCC and PGL, the total score for this patient was 1, indicating a low-risk grade.[7] Six months following hospital discharge there was no recurrence or evidence of metastasis.

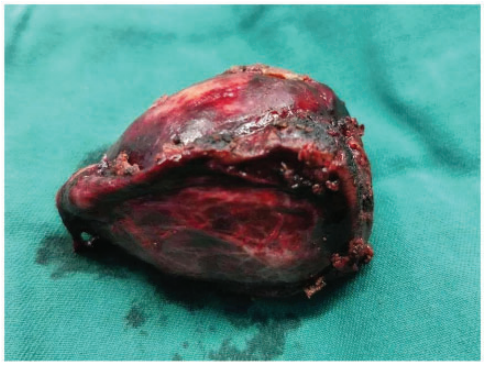

**Figure 2.** Gross examination of the surgical specimen showed the tumour was approximately 5.0 × 3.2 × 4.7 cm in size with a rough texture.

The case study was approved by Ethics Committee of Qinghai Provincial People's Hospital (2021-wjzdx-18) and signed informed consent was obtained from the patient for publishing her anonymised data. The reporting of this study conforms to CARE guidelines.[8]

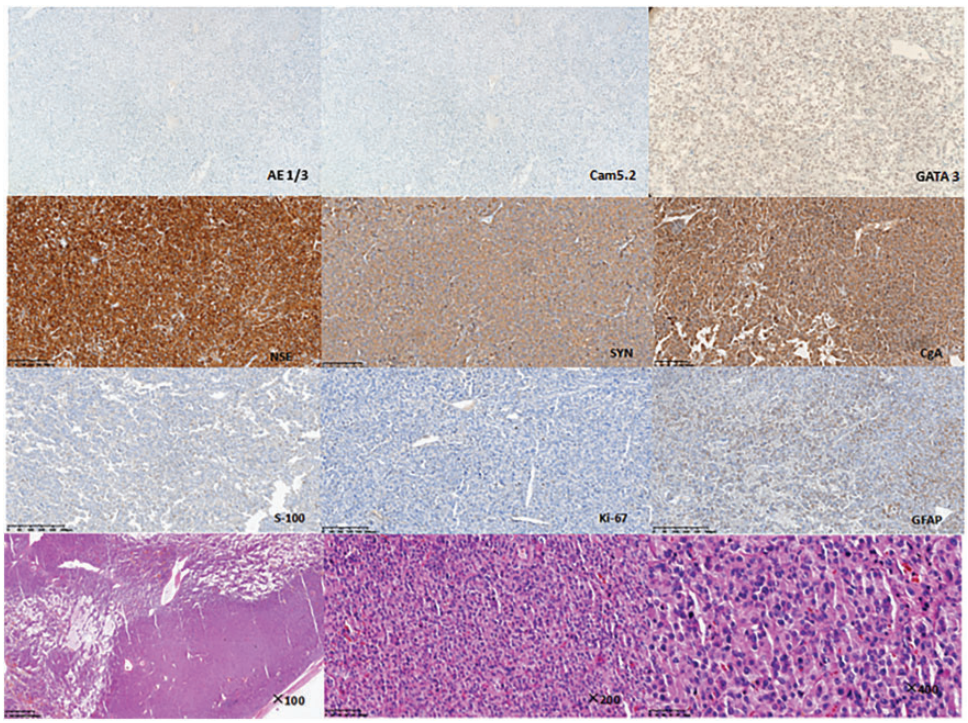


**Figure 3.** Postoperative histological and immunohistochemical examinations of the resected tumour. Typical "Zellballen" cell nests and lymphocytes were observed.

## Discussion

Primary pancreatic PGL is rare and according to our literature review, only 53 cases have been reported worldwide from 1974 to 2021 (Table. 1).[4,9–48] Across the 16 men and 37 women the average age was 52 years (range 19–85 years). Of the 53 cases, 28 cases presented with abdominal pain, low back pain, constipation or dyspepsia, 20 were found on physical examination, and only five cases presented with hypertension, palpitation, headache, or fatigue. Twenty-five cases were located in the pancreatic head (including the uncinate process), one in the pancreatic head, neck and body, one in the pancreatic head and neck, two in the pancreatic neck, twelve in the pancreatic body, two in the pancreatic body and tail, eight in the pancreatic tail, and two in the peripancreatic area. Tumour markers did not show any significant abnormalities (data not shown). Six cases were diagnosed as PGL following examination of fine-needle aspiration (FNA) or frozen section (FS)[20,27,48] Of the 53 cases, eight had been diagnosed as pancreatic PGL before surgery,[13,20,24,27,47,48] twenty-five had been diagnosed as pancreatic neuroendocrine neoplasm (pNEN),[4,10–12,15,20,23,29–38,40,41,44–46] and five had been diagnosed as other diseases (i.e., pancreatic cystadenoma,[9] insulinoma,[14] pancreatic cancer,[16] pancreatic pseudocyst,[20] and gastrointestinal stromal tumour (GIST).[42] Forty-seven cases underwent surgery (15 tumour local resection (TLR),[9,11,13,15,20,21,25,27,28,38–40,42,47] one case of TLR + splenectomy,[30] 10 cases of pancreaticoduodenectomy (PD),[10,19,20,22,23,29,31,45,46] one case of PD and hepatectomy,[24] three cases of pylorus preserving pancreaticoduodenectomy (PPPD),[14,26,34] one case of PPPD + distal pancreatectomy (DP) + left adrenalectomy (L-ADX),[37] seven cases of DP,[4,20,41,43] one case of DP + L-ADX,[16] one case of DP + splenectomy,[33] three cases of resection of the pancreas head (RPH),[12,18,44] three cases of central pancreatectomy (CP)[32,35,36] and one case of surgery radiotherapy.[17] Six cases did not specify the surgical procedure. Of the 24 studies that specified follow-up times, the range was 1–60 months; only six tumours were reported as functional,[13,24,27,43,46] and seven had definite metastases (data not shown).[17,20,24,27]

Our present case report of a typical, primary, non-functional PGL is consistent with previous findings in that the patient was female and over 40 years of age.[27] In addition, our patient sought medical treatment because of the common PGL symptom of abdominal pain. Although tumour markers were within the normal range and we did not perform an FNA, we made a correct diagnosis before the operation based on typical imaging features and the differential diagnosis for similar diseases. During surgery, we located the tumour behind the pancreatic neck, between the splenic artery and vein, and close to the pancreatic parenchyma. We carefully removed the tumour which was both cystic and solid and approximately $4.5 \times 4.7 \times 5.1$ cm in size. The patient developed a pancreatic fistula (biochemical leak) post-surgery suggesting that the pancreas had been damaged during the procedure. However, she fully recovered following conservative treatment and was discharged from hospital 11 days post-surgery. Pathology and immunohistochemical analysis post-surgery confirmed the diagnosis.

Due to the rarity of the condition, and the fact that most pancreatic PGLs are non-functional and lack typical clinical manifestations, the misdiagnosis rate can be high. Therefore, to improve the understanding of PGL, we have summarized its clinical features and compared them to those of other rare pancreatic tumours (i.e., PPGL, pNEN, serous cystadenoma [SCN], mucinous cystadenomas [MCN], and intraductal papillary mucinous tumour [(IPMN]) (Table 2).[49–51] Currently, there is no clear consensus

**Table 1.** Summary of reported cases of pancreatic paraganglioma from the literature (1974 to 2021).

| No. | Reference | Sex | Age y | Signs/symptoms | Imaging features | Location*/size, cm | FNA/FS | Preoperative diagnosis | Treatment | Functional | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Cope et al. 1974 [9] | F | 72 | Physical findings | US: low echo | Head, neck and body; 13 × 11 × 7 | FS: benign | PCN | TLR | no | 48m |
| 2 | Fujino et al. 1998[10] | M | 61 | Abdominal pain | CT: solid mass; MRI: T1 and T2 equal signals | Uncinate process; 2.5 × 4.2 × 1.8 | – | pNEN | PD | no | 60m |
| 3 | Parithivel et al. 2000[11] | M | 85 | Physical findings | CT: abundant blood supply; cystic solid | Head; 6.0 | FS: NET | pNEN | TLR | no | 40m |
| 4 | Ohkawara et al. 2005[12] | F | 72 | Abdominal pain | CT: abundant blood supply; cystic solid | Head; 4.0 | – | pNEN | RPH | no | – |
| 5 | Perrot et al. 2007[13] | F | 41 | Weakness; hyperglycaemia | EUS: low echo; CT: abundant blood supply, inhomogeneous density and necrosis; MRI: T1 low signal and T2 high signal | Tail; 4.3 × 3.2 × 2.5 | – | p-PGL | TLR | yes | 18m |
| 6 | Kim et al. 2008[14] | F | 57 | Lumbar discomfort | US: blood flow signal; EUS: low echo; CT: clear boundary, arteriovenous phase enhancement (low attenuation) | Head; 6.5 × 6.0 × 6.0 | – | non-functional insulinoma | PPPD | no | – |
| 7 | Tsukada et al, 2008[15] | F | 57 | Physical findings | US: low echo; CT: obvious enhancement; MRI: T1 and T2 low signal, obvious enhancement | Uncinate process; 2.5 × 2.0 | – | pNEN | TLR | no | – |
| 8 | Paik. 2009[16] | F | 70 | Physical findings | CT: inhomogeneous enhancement | Tail; 5.5 × 4.4 | – | – | DP + L-ADX | no | 12m |
| 9 | Sangster et al. 2010[17] | M | 50 | Abdominal pain | CT: abundant blood supply; PET: strong uptake | Uncinate process | FNA: poorly differentiated carcinoma | Pancreatic cancer | Surgery; radiotherapy | no | 36m |
| 10 | He et al. 2011[18] | F | 40 | Physical findings | CT: clear boundary; solid; obvious enhancement in arteriovenous phase | Head; 4.5 × 4.2 | – | – | RPH | no | – |
| 11 | Lightfoot et al. 2011[19] | M | 66 | Abdominal pain | CT: cystic solid; PET: mild metabolic elevation | Head and uncinate process; 6.0 | – | – | PD | no | – |

(continued)

**Table 1.** Continued.

| No. | Reference | Sex | Age y | Signs/symptoms | Imaging features | Location*/size, cm | FNA/FS | Preoperative diagnosis | Treatment | Functional | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 12 | Singhi et al. 2011[20] | F | 52 | Abdominal pain | unknown | Body; 14.0 | FNA: PGL | p-PGL | – | – | – |
| 13 | Singhi et al. 2011[20] | F | 61 | Abdominal pain | unknown | Tail; 14.0 | FNA: PPC | PPC | DP: 4 cases; | – | – |
| 14 | Singhi et al. 2011[20] | F | 54 | Abdominal pain | unknown | Head; 6.5 | FNA: PGL | p-PGL | PD: 2 cases; | – | – |
| 15 | Singhi et al. 2011[20] | M | 40 | Physical findings | unknown | Body; 5.1 | FNA: NET | pNEN | TLR: 2 cases | – | – |
| 16 | Singhi et al. 2011[20] | F | 78 | Abdominal pain | unknown | Body; 17.0 | FNA: spindle cell tumour | unknown | | – | – |
| 17 | Singhi et al. 2011[20] | M | 44 | Physical findings | unknown | Head; 5.5 | FNA: PGL | p-PGL | | – | – |
| 18 | Singhi et al. 2011[20] | M | 38 | Abdominal pain | unknown | Body; 15.0 | FS: PGL | unknown | | – | – |
| 19 | Singhi et al. 2011[20] | M | 47 | Abdominal pain | unknown | Body; 7.5 | FS: NET | pNEN | | – | – |
| 20 | Singhi et al. 2011[20] | F | 37 | Abdominal pain | unknown | Tail; 5.7 | FS: NET | pNEN | | – | – |
| 21 | Liu et al. 2011[21] | F | 50 | Physical findings | US: mixed echo; CT: hybrid density; arteriovenous phase enhancement | Tail; 10.0 | – | – | TLR | no | – |
| 22 | Higa and Kapur. 2012[22] | F | 65 | Physical findings | CT: hybrid density; arterial phase enhancement gradually attenuated | Uncinate process; 2.0 | – | – | PD | no | – |
| 23 | Ganc et al. 2012[23] | F | 37 | Physical findings | EUS: low echo | Head; $4.8 \times 3.2 \times 4.3$ | FNA: NET | pNEN | PD | no | – |
| 24 | Al-Jiffry et al. 2013[24] | F | 19 | Abdominal pain | CT: solid; hepatic parenchymal infiltration | Head and neck; $9 \times 5 \times 9.5$ | FNA: NET | p-PGL | PD + hepatic segmentectomy | yes | 36m |
| 25 | Borgohain et al. 2013[25] | F | 55 | Abdominal pain | CT: cystic; pancreatic cancer tendency | Tail; $17 \times 19$ | – | – | TLR | no | 10m |
| 26 | Straka et al. 2014[26] | F | 53 | Abdominal discomfort | CT: abundant blood supply | Head; $8.1 \times 8.5$ | – | – | PPPD | no | 49m |
| 27 | Zhang et al. 2014[27] | F | 50 | Hypertension; headache; palpitations; sweating | CT: solid; abundant blood supply; liver metastasis | Head; 6.0 | FNA: PGL | p-PGL | – | yes | death 4 years later |
| 28 | Zhang et al. 2014[27] | M | 63 | Hypertension | CT: solid; abundant blood supply; 123I-MIBG: abnormal uptake | Head; 4.0 | – | – | TLR | yes | 3m |
| 29 | Meng et al. 2015[28] | F | 54 | Abdominal pain | US: low echo; abundant blood flow signals; CT: unclear boundary; equal density; | Head; $3 \times 2.5$ | – | – | TLR | no | – |

(continued)

**Table 1.** Continued.

| No. | Reference | Sex | Age y | Signs/symptoms | Imaging features | Location*/size, cm | FNA/FS | Preoperative diagnosis | Treatment | Functional | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | inhomogeneous enhancement in arterial phase; homogeneous enhancement in venous phase | | | | | | |
| 30 | Meng et al. 2015[28] | F | 41 | Physical findings | US: clear boundary; low echo; partial blood flow signal; CT: inhomogeneous density; arterial phase enhancement | Head; 6 × 5 | – | – | – | no | – |
| 31 | Misumi et al. 2015[29] | F | 47 | Physical findings | US and EUS: low-density inhomogeneous echo; blood flow signal; CT: arteriovenous phase enhancement (low attenuation); MRI: T1 low signal and T2 high signal | Head; 1.5 × 1.2 | – | pNEN | PD | no | 12m |
| 32 | Ünver et al. 2015[30] | F | 41 | Loss of appetite; tired; weakness | USG: pancreatic tail and splenic hilum mass; MRI: mass invading splenic hilum | Tail; 8 × 7 × 8 | – | – | TLR + splenectomy | no | 6m |
| 33 | Liang and Xu. 2016[31] | M | 41 | Physical findings | CT: arteriovenous phase enhancement (low attenuation); MRI: T1 low signal; T2 slightly high signal; inhomogeneous enhancement | Uncinate process; 4 × 6 | FNA: unidentified | pNEN | PD | no | 1m |
| 34 | Lin et al. 2016[32] | F | 42 | Abdominal pain | CT: solid low density; arterial phase enhancement | Body; 5.2 × 6.3 | – | pNEN | CP | no | 12m |
| 35 | Tumuluru et al. 2016[33] | F | 62 | Physical findings | EUS: solid hypoechoic | Body; 2.8 × 2.8 × 2.7 | FNA: chronic pancreatitis | pNEN | DP + splenectomy | no | 18m |
| 36 | Ginesu et al. 2016[34] | M | 55 | Lumbago | US: solid; CT: arterial phase enhancement (low attenuation) | Uncinate process; 1.3 | – | pNEN | PPPD | no | 24m |
| 37 | Lin et al. 2016[35] | F | 42 | Abdominal pain | CT: solid; clear boundary; arterial phase | Body; 5.2 × 6.3 | – | pNEN | CP | no | 15m |

(continued)

**Table 1.** Continued.

| No. | Reference | Sex | Age y | Signs/symptoms | Imaging features | Location*/size, cm | FNA/FS | Preoperative diagnosis | Treatment | Functional | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | obvious enhancement; delay phase equal density | | | | | | |
| 38 | Furcea et al. 2017[36] | F | 53 | Dyspepsia | US: inhomogeneous low echo; CEUS: arterial phase enhancement | Neck; 3.5 × 2.5 × 2.5 | – | pNEN | CP | no | – |
| 39 | Nonaka et al. 2018[37] | F | 68 | Physical findings | EUS: low echo; CT: arterial phase enhancement; venous inhomogeneous enhancement; PET: high intake; malignant possibility | Body; 2.2× 2.2 × 1.0 | FNA: insufficient material | pNEN | PPPD + DP + L-ADX | no | 12m |
| 40 | Zeng et al. 2017[38] | F | 58 | Abdominal pain | EUS: low echo; clear boundary; MRI: inhomogeneous signal | Body; 6.5 × 6.1 × 4.4 | FNA: NET | pNEN | TLR | no | – |
| 41 | Zeng et al. 2017[38] | F | 53 | Abdominal pain | CT: soft tissue mass | Head; 2.5 × 1.7 × 1.8 | FNA: NET | pNEN | TLR | no | – |
| 42 | Nguyen et al. 2018[39] | F | 70 | Constipation; early satiety | EUS: low echo; CT: cystic solid | Tail; 3.6 × 5 × 4.5 | FNA: NET? | – | TLR | no | – |
| 43 | Fite & Maleki. 2018[40] | M | 40 | Lumbago; haematuria | Image: abundant blood supply with necrosis | Peripancreatic; 5.1 | FNA: NET | pNEN | – | no | – |
| 44 | Fite & Maleki. 2018[40] | F | 23 | Palpitations | Image: heterogeneous mass | Peripancreatic; 7.0 | FNA: NET | pNEN | – | no | – |
| 45 | Liu et al. 2018[41] | F | 73 | Physical findings | Isodensity, central with calcification; arterial phase enhancement; portal vein phase isodensity | Body; 1.2 × 1.4 | – | pNEN | DP | no | 6m |
| 46 | Chattoraj et al. 2019[42] | F | 36 | Abdominal pain | CT: no enhancement | Body and tail; 7 × 4 | – | GIST | TLR | no | – |
| 47 | Zongo et al. 2019[43] | M | 52 | Abdominal pain | CT: inhomogeneous density | Body and tail; 8.6 × 8.3 | – | – | DP | yes | 17m |
| 48 | Wang et al. 2019[44] | M | 59 | Physical findings | MRI: long T1 long T2 signal; DWI high signal; inhomogeneous enhancement | Head; 2.7 × 2.5 × 2.4 | – | pNEN | RPH | no | – |

(continued)

**Table 1.** Continued.

| No. | Reference | Sex | Age y | Signs/symptoms | Imaging features | Location*/size, cm | FNA/FS | Preoperative diagnosis | Treatment | Functional | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 49 | Xu et al. 2019[45] | M | 50 | Abdominal pain | CT: abundant blood supply | Head; 17.0 | – | pNEN | PD | no | 3m |
| 50 | Abbasi et al. 2020[46] | F | 61 | Physical findings | MRI: T2 hyperintense; arterial phase enhancement | Head and uncinate process; 7.2 × 6.5 | FNA: NET | pNEN | PD | yes | 12m |
| 51 | Jiang et al. 2021[4] | M | 41 | Physical findings | EUS: low echo; CT: solid; inhomogeneous | Body; 4.1 × 4.2 | FNA: malignant possibility; FS: pNEN | pNEN | DP | no | 12m |
| 52 | Wang et al. 2021[47] | F | 75 | Abdominal pain | CT: abundant blood supply; arterial phase enhancement; MRI: T1WI low or equal signal; T2WI high signal; obvious enhancement | Neck; 3.1 × 3.8 | – | p-PGL; Castleman; pNEN | TLR | no | – |
| 53 | Lanke et al. 2021[48] | F | 73 | Physical findings | EUS: low echo | Head; 2.0 × 1.1 | FNA: PGL | p-PGL | – | no | 12m |

*Location in the pancreas; – not available or unknown.

Abbreviations: 123I-MIBG: metaiodobenzylguanidine; CT: computed tomography; CEUS: contrast-enhanced ultrasound; CP: central pancreatectomy; DP: distal pancreatectomy; DWI, diffusion weighted imaging; EUS: endoscopic ultrasound; F: female; FNA: fine needle aspiration; FS: frozen section; GIST: gastrointestinal stromal tumour; L-ADX: left adrenalectomy; M: male; MRI: magnetic resonance image; NET: neuroendocrine tumour; PCN: pancreatic cystadenoma; PD: pancreaticoduodenectomy; PET: positron emission tomography; pNEN: pancreatic neuroendocrine neoplasm; PPC: pancreatic pseudocyst; p-PGL: paraganglioma of pancreas; PPPD: pylorus preserving pancreaticoduodenectomy; RPH: resection of the pancreas head; TLR: tumour local resection; US: ultrasound; USG: ultrasonogram diagnosis.

**Table 2.** Summary of the characteristics of several rare pancreatic tumours.[49–51]

| Feature \ Disease | PPGL | p-PGL | pNEN | SCN | MCN | IPMN |
|---|---|---|---|---|---|---|
| Sex ratio, (male: female) | 1: 1 | 1: 2 | 1: 1 | 3: 7 | 1: 10 | 1: 1 |
| Age, y | 30–50 | 40–70 | 40–70 | 60–70 | 40–50 | 60–70 |
| Predilection site | Adrenal gland and adrenal sympathetic crest | Pancreatic head | No preference | Head, body and tail of pancreas | Body and tail of pancreas | Head and uncinate process of pancreas |
| Clinical signs and symptoms | Hypertension; cephalalgia; palpitations; hyperhidrosis; postural hypotension | Abdominal pain/ asymptomatic (non-functional); hypertension, palpitations and fatigue (functional) | Mostly asymptomatic; 66% non-functional; 33% functional; mainly insulinoma | Mostly asymptomatic; nonspecific nausea due to mass occupying effect | Mostly asymptomatic; abdominal pain (large mass) | Mostly asymptomatic; acute pancreatitis; more prone to clinical symptoms (malignant transformation) |
| Tumour markers | CgA↑;NSE↑ (possible) | CgA↑ (possible) | CgA↑; NSE↑; FAP, CEA, CA125 and CA19-9↑ | CA19-9↑; CEA↑; (malignant tumour) | CA19-9↑; CEA↑ (malignant tumour) | CA19-9↑; CEA↑ (malignant tumour) |
| US features | Clear boundary; round or quasi round; high, low, equal echo; blood flow signal (solid part) | Low or inhomogeneous echo, with blood flow signal | Smooth edges; heterogeneous, with cystic degeneration or necrosis (large mass) | High echo; lobulate; clear boundary | Clear boundary; multilocular cystic, surrounded by walls | Echo (mucin rich); low echo (BD-IPMN); difficult to distinguish from pancreatic tissue |
| CT features | Round or quasi round; inhomogeneous density; mostly necrosis, bleeding and calcification; enhanced by contrast agent | Clear boundary; Abundant blood supply; enhancement (arterial phase) and slightly reduced (venous phase) | Large and inhomogeneous density (non-functional); small and uniform density (functional); obvious enhancement | Clear boundary; marginal lobulated; central fibrous scar; stellate calcification; vesicles (number $\geq$6, size $\leq$2 cm); septum and capsule wall enhanced (portal vein stage); fibrous | Multilocular large vesicles (number $<$ 6, size $>$ 2 cm); single room (minority) | Diffuse or staged expansion of main pancreatic duct (MD-IPMN); cystic lesions communicating with pancreatic duct and "grape cluster" appearance (BD-IPMN) |

(continued)

**Table 2.** Continued.

| Feature \ Disease | PPGL | p-PGL | pNEN | SCN | MCN | IPMN |
|---|---|---|---|---|---|---|
| | | | | scar enhanced (delayed period) | | |
| MRI features | T1 low signal; T2 high signal | T1 low signal; T2 high signal | T1 low signal; T2 high signal | T1 low signal; T2 high signal; scattered high signal cysts | T1 slightly high or low signal; T2 high signal | T1 low or high signa; T2 high signal; mural nodule enhancement |
| Pathology | "Zellballen" solid small cell nest with beam cord structure; round, oval or spindle shaped tumour cell surrounded by supporting cells and vascular spaces; rich cytoplasm | "Zellballen" solid small cell nest with beam cord structure; round, oval or spindle shaped tumour cell surrounded by supporting cells and vascular spaces; rich cytoplasm | Nuclei of uniform size; transparent cytoplasm with granules; NSE (+); CGA (+) | Composed of monolayer cubic epithelial cells or flat epithelial cells; rich glycogen | Cyst wall containing ovarian like stroma | Viscous mucin and pancreatic duct dilation (MD-IPMA); single cyst or multiple grape clusters communicating cyst, containing liquid, albumin and tumour cells (BD-IPMN) |
| Malignant risk | Metastatic rate: 10–17%. | Metastatic rate: 13% | (Malignant rate); insulinoma 5–10%; gastrinoma 50–60%; glucagon tumour 50–80%; somatostatin tumour 50–60%; neuroendocrine tumours producing ACTH >90%; vasoactive intestinal peptidoma 40–80%; non-functional tumour 60–90% | Benign and grow slowly | Potential malignancy; 5-year survival rate: 38% | Malignant rate: 57–92%; 5-year survival rate: 80%; (MD-IPMA) malignant rate: 6–46% (BD-IPMN, <3 cm) |

Abbreviations: BD-IPMN: Branch duct intraductal papillary mucinous tumour; CEA, carcinoembryonic antigen; CgA: Chromogranin A; CT: computed tomography; FAP, Fibroblast-activation protein; IPMN: intraductal papillary mucinous tumour; MCN: mucinous cystadenomas; MD-IPMN: Main duct intraductal papillary mucinous tumour; MRI: magnetic resonance image; NSE: neuron specific enolase; pNEN: pancreatic neuroendocrine neoplasm; p-PGL: paraganglioma of pancreas; PPGL: pheochromocytoma and paraganglioma; SCN: serous cystadenoma.

regarding treatment of PGL. However, surgery is the principal treatment modality, supplemented by chemotherapy and radiotherapy for patients with malignant tendencies, but, as demonstrated by our present case study, the choice of surgical procedure should be determined according to the close relationship between the tumour and the pancreatic parenchyma and vessels. Definitive diagnosis of this rare pancreatic tumour depends on postoperative histopathological and immunohistochemical examinations.

In summary, pancreatic PGL is a rare entity and so preoperative diagnosis is challenging. The tumour tends to be nonfunctional and found either incidentally on imaging, or in a patient with abdominal pain. The main treatment is surgical resection and postoperative histopathological and immunohistochemical diagnosis is essential. This present case highlights the importance of a multidisciplinary team approach in the diagnosis of PGL involving radiologists, endocrinologists, pathologists, oncologists, and surgeons.

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## References

1. Granberg D, Juhlin CC and Falhammar H. Metastatic Pheochromocytomas and Abdominal Paragangliomas. *J Clin Endocrinol Metab* 2021; 106: e1937–e1952.
2. Ebbehoj A, Stochholm K, Jacobsen SF, et al. Incidence and Clinical Presentation of Pheochromocytoma and Sympathetic Paraganglioma: A Population-based Study. *J Clin Endocrinol Metab* 2021; 106: e2251–e2261.
3. Calissendorff J, Juhlin CC, Bancos I, et al. Pheochromocytomas and Abdominal Paragangliomas: A Practical Guidance. *Cancers (Basel)* 2022; 14: 917.
4. Jiang CN, Cheng X, Shan J, et al. Primary pancreatic paraganglioma harboring lymph node metastasis: A case report. *World J Clin Cases* 2021; 9: 8071–8081.
5. Lin S, Peng L, Huang S, et al. Primary pancreatic paraganglioma: a case report and literature review. *World J Surg Oncol* 2016;14:19.
6. Sobocki BK, Perdyan A, Szot O, et al. Management of Pheochromocytomas and Paragangliomas: A Case-Based Review of Clinical Aspects and Perspectives. *J Clin Med* 2022; 11: 2591.
7. Kimura N, Takekoshi K and Naruse M. Risk Stratification on Pheochromocytoma and Paraganglioma from Laboratory and Clinical Medicine. *J Clin Med* 2018; 7: 242.
8. Gagnier JJ, Kienle G, Altman DG, et al; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. *Headache* 2013; 53: 1541–1547.
9. Cope C, Greenberg SH, Vidal JJ, et al. Nonfunctioning nonchromaffin paraganglioma of the pancreas. *Arch Surg* 1974; 109: 440–442.
10. Fujino Y, Nagata Y, Ogino K, et al. Nonfunctional paraganglioma of the pancreas: report of a case. *Surg Today* 1998; 28: 209–212.
11. Parithivel VS, Niazi M, Malhotra AK, et al. Paraganglioma of the pancreas: literature review and case report. *Dig Dis Sci* 2000; 45: 438–441.
12. Ohkawara T, Naruse H, Takeda H, et al. Primary paraganglioma of the head of

pancreas: contribution of combinatorial image analyses to the diagnosis of disease. *Intern Med* 2005; 44: 1195–1196.
13. Perrot G, Pavic M, Milou F, et al. Difficult diagnosis of a pancreatic paraganglioma. *Rev Med Interne* 2007; 28: 701–704.
14. Kim SY, Byun JH, Choi G, et al A case of primary paraganglioma that arose in the pancreas: the Color Doppler ultrasonography and dynamic CT features. *Korean J Radiol* 2008; 9: 18–21.
15. Tsukada A, Ishizaki Y, Nobukawa B, et al. Paraganglioma of the pancreas: a case report and review of the literature. *Pancreas* 2008; 36: 214–216.
16. Paik KY. Paraganglioma of the pancreas metastasized to the adrenal gland: a case report. *Korean J Gastroenterol* 2009; 54: 409–412.
17. Sangster G, Do D, Previgliano C, et al. Primary retroperitoneal paraganglioma simulating a pancreatic mass: a case report and review of the literature. *HPB Surg* 2010; 2010: 645728.
18. He J, Zhao F, Li H, et al. Pancreatic paraganglioma: A case report of CT manifestations and literature review. *Quant Imaging Med Surg* 2011; 1: 41–43.
19. Lightfoot N, Santos P and Nikfarjam M. Paraganglioma mimicking a pancreatic neoplasm. *JOP* 2011; 12: 259–261.
20. Singhi AD, Hruban RH, Fabre M, et al. Peripancreatic paraganglioma: a potential diagnostic challenge in cytopathology and surgical pathology. *Am J Surg Pathol* 2011; 35: 1498–1504.
21. Liu D, Liu JH and Han XL. Paraganglioma of pancreas: a case report. *Chin J Diffic and Compl Cas* 2011; 10: 946–947.
22. Higa B and Kapur U. Malignant paraganglioma of the pancreas. *Pathology* 2012; 44: 53–55.
23. Ganc RL, Castro AC, Colaiacovo R, et al. Endoscopic ultrasound-guided fine needle aspiration for the diagnosis of nonfunctional paragangliomas: a case report and review of the literature. *Endosc Ultrasound* 2012; 1: 108–109.
24. Al-Jiffry BO, Alnemary Y, Khayat SH, et al. Malignant extra-adrenal pancreatic paraganglioma: case report and literature review. *BMC Cancer* 2013; 13: 486.
25. Borgohain M, Gogoi G, Das D, et al. Pancreatic paraganglioma: An extremely rare entity and crucial role of immunohistochemistry for diagnosis. *Indian J Endocrinol Metab* 2013; 17: 917–919.
26. Straka M, Soumarova R, Migrova M, et al. Pancreatic paraganglioma - a rare and dangerous entity. Vascular anatomy and impact on management. *J Surg Case Rep* 2014; 2014: rju074.
27. Zhang L, Liao Q, Hu Y, et al. Paraganglioma of the pancreas: a potentially functional and malignant tumor. *World J Surg Oncol* 2014; 12: 218.
28. Meng L, Wang J and Fang SH. Primary pancreatic paraganglioma: a report of two cases and literature review. *World J Gastroenterol* 2015; 21: 1036–1039.
29. Misumi Y, Fujisawa T, Hashimoto H, et al. Pancreatic paraganglioma with draining vessels. *World J Gastroenterol* 2015; 21: 9442–9447.
30. Ünver M, Öztürk Ş, Erol V, et al. Retroperitoneal paraganglioma presenting with pancytopenia: A rare case with rare manifestation. *Int J Surg Case Rep* 2015; 14: 77–79.
31. Liang W and Xu S. CT and MR Imaging Findings of Pancreatic Paragangliomas: A Case Report. *Medicine (Baltimore)* 2016; 95: e2959.
32. Lin S, Peng L, Huang S, et al. Primary pancreatic paraganglioma: a case report and literature review. *World J Surg Oncol* 2016; 14: 19.
33. Tumuluru S, Mellnick V, Doyle M, et al. Pancreatic Paraganglioma: A Case Report. *Case Rep Pancreat Cancer* 2016; 2: 79–83.
34. Ginesu GC, Barmina M, Paliogiannis P, et al. Nonfunctional paraganglioma of the head of the pancreas: A rare case report. *Int J Surg Case Rep* 2016; 28: 81–84.
35. Lin SR, Xiao WD, Huang S, et al. Paraganglioma of pancreas: a case report. *Chinese Journal of Practical Surgery* 2016; 36: 585–586.
36. Furcea L, Mois E, Al Hajjar N, et al. Pancreatic gangliocytic paraganglioma – CEUS appearance. *J Gastrointestin Liver Dis* 2017; 26: 336.

37. Nonaka K, Matsuda Y, Okaniwa A, et al. Pancreatic gangliocytic paraganglioma harboring lymph node metastasis: a case report and literature review. *Diagn Pathol* 2017; 12: 57.
38. Zeng J, Simsir A, Oweity T, et al. Peripancreatic paraganglioma mimics pancreatic/gastrointestinal neuroendocrine tumor on fine needle aspiration: Report of two cases and review of the literature. *Diagn Cytopathol* 2017; 45: 947–952.
39. Nguyen E, Nakasaki M, Lee TK, et al. Diagnosis of paraganglioma as a pancreatic mass: A case report. *Diagn Cytopathol* 2018; 46: 804–806.
40. Fite JJ and Maleki Z. Paraganglioma: Cytomorphologic features, radiologic and clinical findings in 12 cases. *Diagn Cytopathol* 2018; 46: 473–481.
41. Liu M, Tu YY, He JQ, et al. Paraganglioma of body and tail of pancreas (1 case report). *J Surg Concepts Pract* 2018; 23: 379–380
42. Chattoraj AK, Rao UM, Sarkar N, et al. Non-functional retroperitoneal paraganglioma: A case report. *J Family Med Prim Care* 2019; 8: 1497–1499.
43. Zongo N, Koama A, Kambou/Tiemtoré BMA, et al. Ectopic pheochromocytoma or paraganglioma of the ZUCKERKANDL organ: A case report and review of the literature. *Int J Surg Case Rep* 2019; 60: 120–122.
44. Wang YY, Yang FL and Guo L. Pancreatic paraganglioma: Case report. *Chin J Med Imaging Technol* 2019; 35: 1408–1409.
45. Xu HJ, Li XX and Liu K. A case of giant paraganglioma of the pancreas. *J Chin Hepatol* 2019; 35: 2300–2301.
46. Abbasi A, Wakeman KM and Pillarisetty VG. Pancreatic paraganglioma mimicking pancreatic neuroendocrine tumor. *Rare Tumors* 2020; 12: 2036361320982799.
47. Wang W, Qin Y, Zhang H, et al. A rare case of retroperitoneal paraganglioma located in the neck of the pancreas: a case report and literature review. *Gland Surg* 2021; 10: 1523–1531.
48. Lanke G, Stewart JM and Lee JH. Pancreatic paraganglioma diagnosed by endoscopic ultrasound-guided fine needle aspiration: A case report and review of literature. *World J Gastroenterol* 2021; 27: 6322–6331.
49. Fan JH, Zhang YQ, Shi SS, et al. A nationwide retrospective epidemiological study of gastroenteropancreatic neuroendocrine neoplasms in china. *Oncotarget* 2017; 8: 71699–71708.
50. Wu W, Jin G, Li H, et al. The current surgical treatment of pancreatic neuroendocrine neoplasms in China: a national wide cross-sectional study. *J Pancreatol* 2019; 2: 35–42.
51. Cheung VKY, Gill AJ and Chou A. Old, new and emerging immunohistochemical markers in pheochromocytoma and paraganglioma. *Endocr Pathol* 2018; 29: 169–175.