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CASE REPORT

Pancreatic granular cell tumor diagnosed by endoscopic ultrasound-guided fine needle aspiration biopsy

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Abstract
Pancreatic granular cell tumors (GCTs) are rare and making an imaging diagnosis of pancreatic GCT is difficult because it has no definite characteristics on contrast-enhanced computed tomography (CE-CT) or magnetic resonance imaging (MRI) owing to varying findings. We report about a 32-year-old woman who presented with an incidental finding of a pancreatic tumor with a past history of excision of a right forearm GCT nodule 12 years ago. CE-CT revealed a 23-mm-sized homogeneous low enhancement tumor in the arterial phase in the pancreatic body. Abdominal MRI revealed a lobulated hypointense mass in T1WI and high signal in DWI. Endoscopic ultrasonography (EUS) revealed that the tumor was oval, hypoechoic with posterior echo enhancement, and had a well-defined border. Although EUS-guided fine needle aspiration revealed benign granular cells of the pancreas, she underwent laparoscopic surgery because the metastatic tumor from the past lesion was not excluded. The pathological finding was benign GCT of the pancreas and it was considered as an original lesion. In the previous reports, most of the resected cases were considered to be pancreatic cancer or neuroendocrine tumor preoperatively. Compared to CE-CT and MRI, EUS imaging and EUS-FNA are more reliable diagnosis tools for pancreatic GCT. Although malignant GCT accounts for approximately 1–2% of all cases, surgical resection or strict follow-up should be considered because it is difficult to predict its biological behavior.

Keywords Granular cell tumors (GCT) · Pancreatic GCT · Endoscopic ultrasound-guided fine needle aspiration biopsy

Introduction

Granular cell tumors (GCTs) are rare tumors originating from Schwann-like mesenchymalcells. Abrikossoff first described a skeleton muscle GCT of the tongue in 1926 [1]. GCT can occur in any body part, although it is most commonly located in the skin and tongue. Gastrointestinal tract GCT is found in only 5–9% of cases, with its common presentation in the esophagus, large intestine, stomach, biliary tract, and duodenum [2]. Furthermore, < 1% of GCTs are found in the biliary tract, with most being found in the common bile duct and gallbladder (GB); however, pancreatic GCT is less commonly found [3].

Pancreatic GCT, a very rare tumor, is difficult to detect because it is mostly asymptomatic. GCT has a unique characteristic of being positive for S-100 protein on immunohistochemistry (IHC), but negative for desmin and vimentin [4]. However, making an imaging diagnosis is difficult because pancreatic GCT has no definite characteristic on contrast-enhanced computed tomography (CE-CT) or magnetic resonance imaging (MRI). Nowadays, endoscopic ultrasonography (EUS) and endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) have an important role in defining tumor characteristics and obtain quality tissue for histopathologic diagnosis of cancer. Here, we report a case of a pancreatic GCT that was diagnosed using EUS-FNA preoperatively and summarize the EUS findings that may be helpful for diagnosing future cases.

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Case report

A 32-year-old woman had an incidental finding of a pancreatic mass by MRI follow-up of asymptomatic GB polyps. The patient underwent right transverse rectus abdominis myocutaneous flap surgery for ductal carcinoma in situ of the right breast and excision of a granular cell tumor (GCT) of the right forearm nodule 12 years ago. An abdominal CE-CT scan showed a well-defined, round tumor in the pancreatic body, which had a homogenous hypoenhancement in the arterial phase and isoenhancement in the delayed phase (Fig. 1). Abdominal MRI revealed a 20-mm-sized non-uniform tumor in the pancreatic body that was a hypointense septate lobular mass on T1WI, hyperintense on T2WI, and had high signal on diffusion-weighted image (DWI) with no pancreatic duct dilatation (Fig. 2). Endoscopic ultrasound (EUS) findings

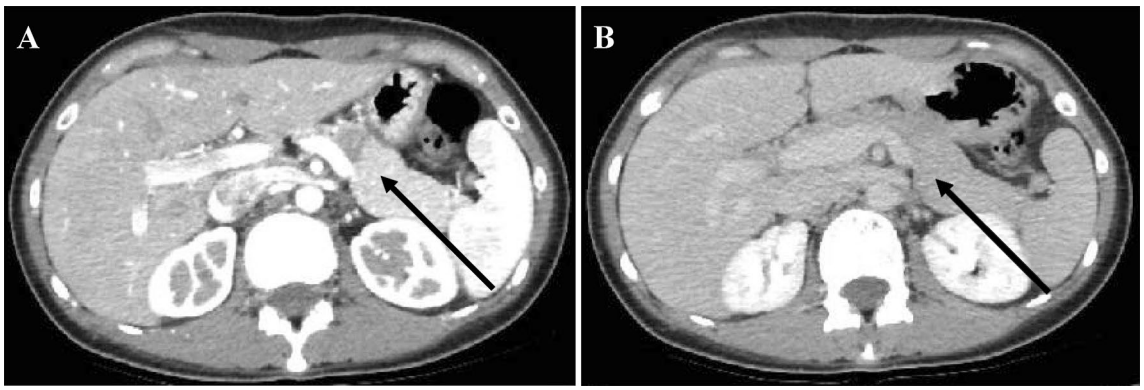

Fig. 1 Contrast-enhanced computed tomography. **a** Homogenous hypovascular tumor in the arterial phase in the pancreatic body (arrow). **b** Isovascular tumor in the delayed phase (arrow)

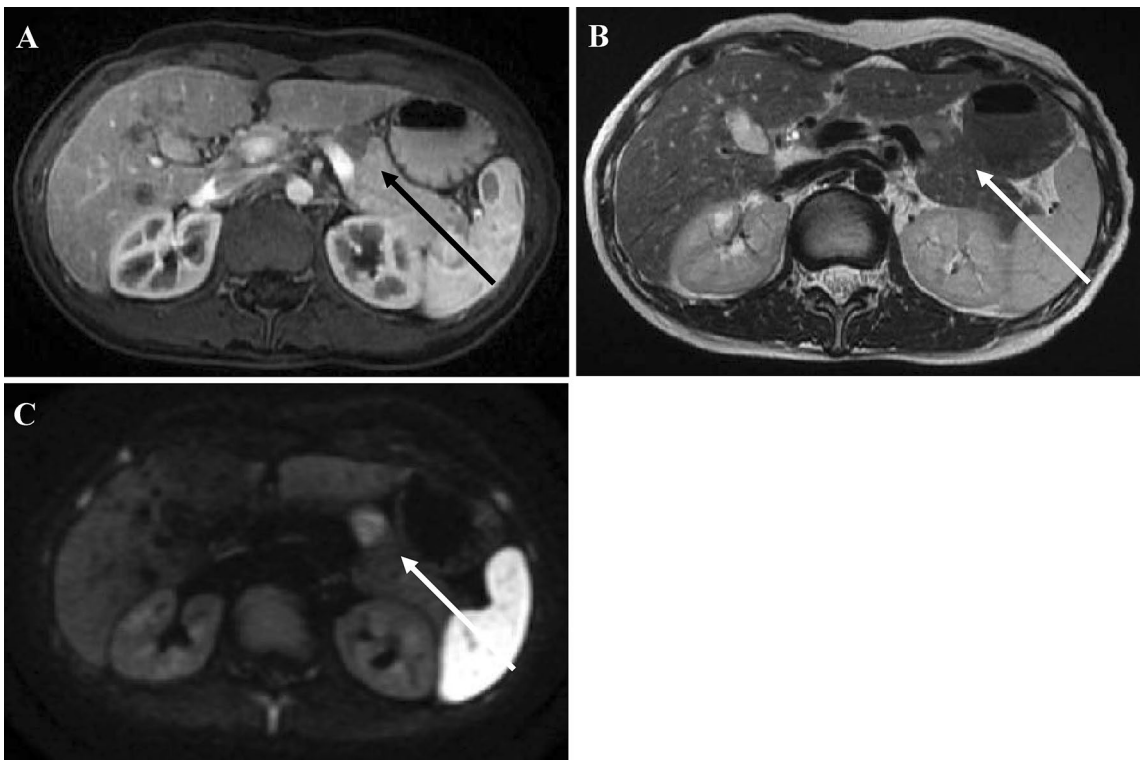

Fig. 2 Magnetic resonance imaging. **a** The tumor shows a well-defined, hypointense mass on T1-weighted image (T1WI) in the pancreatic body without pancreatic duct dilatation (black arrow). **b** Hyperintense mass on T2-weighted image (T2WI) (white arrow). **c** High signal of tumor on diffuse weighted image (DWI) (white arrow)

revealed an oval-shaped tumor, measuring 16 × 10 mm in size with a well-defined border, as a homogenous hypoechoic mass with posterior echo enhancement and vessel thickening. Based on the hyperechoic posterior enhancement noted, pancreatic neuroendocrine tumor (NET) and microcystic-type serous cystic neoplasm were suspected. EUS elastography showed a slightly elastic, but harder than normal pancreatic parenchyma (Fig. 3). Contrast-enhanced EUS with Sonazoid showed hypoenhancement of the tumor in arterial phase (15 s after contrast was injected) with the vessel inside, and the contrast was washed out after 1 min (Fig. 4).

As malignant tumors, NET or pancreatic cancer was not excluded, EUS-FNA was performed using a 22-gauge EZ shot 3 plus needle (Olympus, Tokyo, Japan) with a 20-ml syringe suction; the tumor was punctured thrice from the stomach. The cytological result revealed a benign granular cell tumor that was positive for S-100 and neutron-specific enolase (NSE) on IHC (Fig. 5). A definitive diagnosis of pancreatic GCT preoperatively was obtained, but whether the lesion had a pancreatic origin or had metastasized from the right forearm nodule resected 12 years ago was not confirmed.

The patient underwent laparoscopic distal pancreatectomy with splenectomy without any complication. An intraoperative frozen section was obtained to confirm R0 resection. The macroscopic finding of the resected tumor was a yellowish-white lobular mass measuring 20 × 15 mm in size. The histological results revealed granular cells located in the pancreatic acinar cells with increasing circular to ellipsoidal nuclei, and different sizes and polymorphism of nuclei were observed. The tumor had central fibrosis, clear boundary, and heterogeneous granular cells in packed and loose areas. The tumor was positive for S-100 and neuron-specific enolase (NSE) on IHC (Fig. 6). The proliferative Ki-67 activity was very low. The final diagnosis was GCT of pancreatic origin. Abdominal CE-CT 6 months after the operation showed no local recurrence and metastasis.

Discussion

The present case describes a pancreatic GCT after the excision of a right forearm GCT nodule 12 years ago. The tumor was diagnosed as a benign GCT by EUS-FNA preoperatively; however, whether the tumor was of pancreatic origin

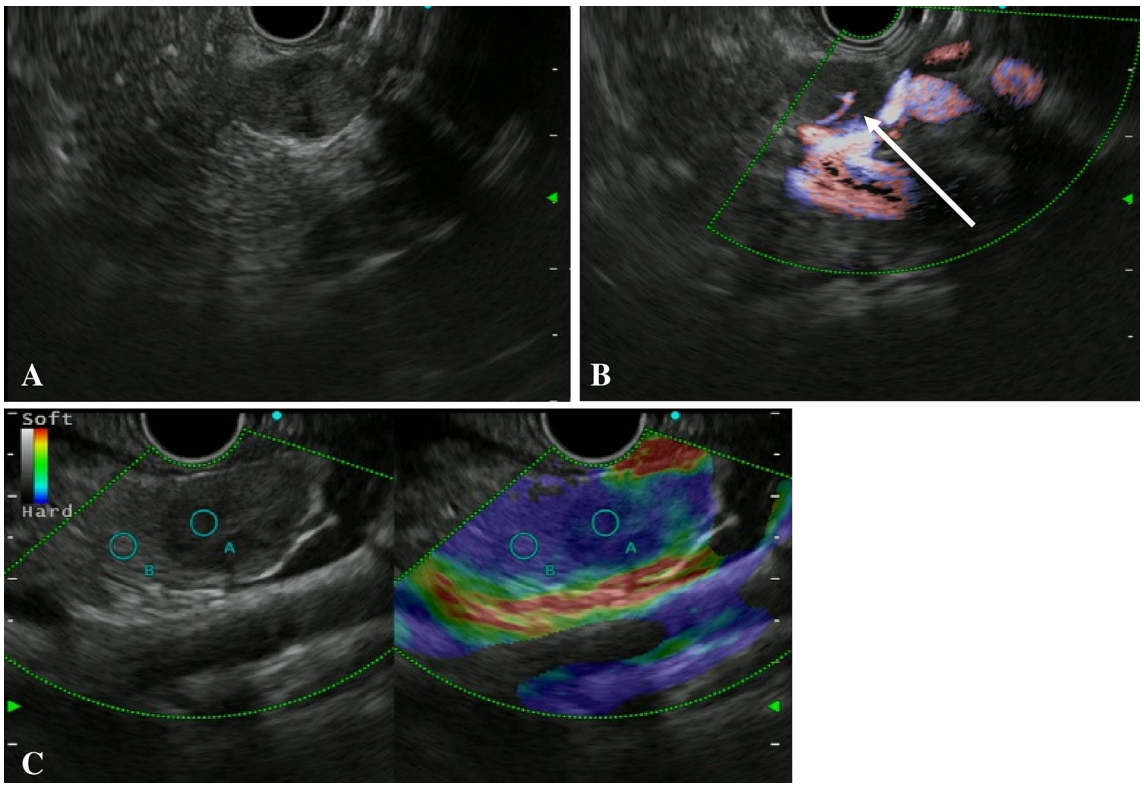

Fig. 3 Endoscopic ultrasonography of the tumor. **a** The tumor shows a homogenous, well-defined hypoechoic mass measuring 16 × 10 mm in size in the pancreatic body with posterior hyperechoic shadow. **b** Thick vessel inside the tumor (arrow). **c** Elastography of the tumor shows elastic harder parenchyma than in normal pancreas

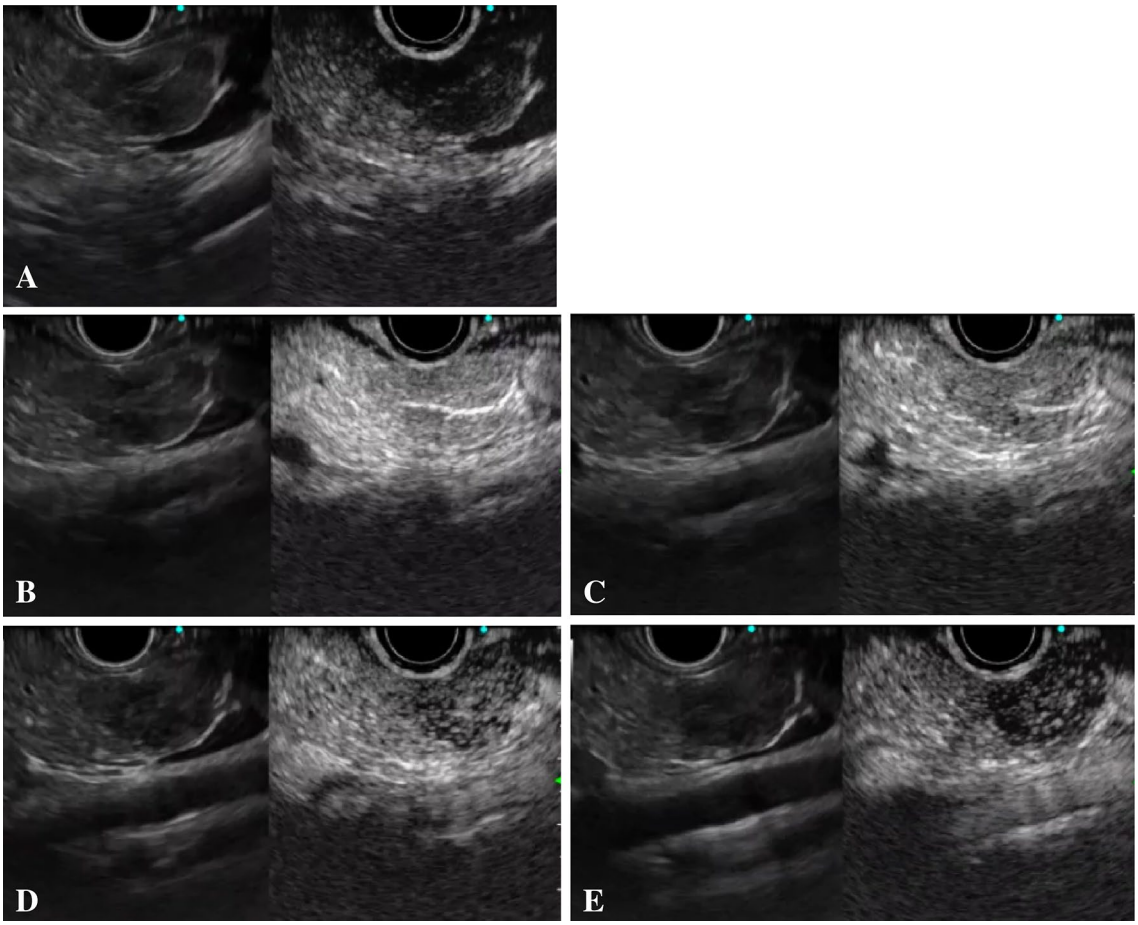

Fig. 4 Contrast-enhanced endoscopic ultrasound after Sonazoid contrast injection. **a** Tumor before Sonazoid contrast injection. **b** The arterial phase, 15 s after contrast injection, shows hypoenhancement of the tumor and a single vessel inside the tumor. **c** The perfusion phase, 30 s, shows more hypoenhancement of the tumor. **d** The contrast washed out at 1 min after injection. **e** The contrast washed out clearly 2 min after injection

or a metastatic lesion from the right forearm nodule was not confirmed.

To our knowledge, this is the tenth case of pancreatic GCT. A summary of the English literature on pancreatic GCT is mentioned in Table 1. Pancreatic GCT occurs more commonly in women (70%) than in men, the average age is 43.8 years, the average widest size of the tumor is 10.6 mm (5–22 mm), and the tumors are commonly found in the pancreatic body (60%), head (30%), and tail (10%), respectively [2, 5–13]. From the EUS imaging, GCT of the pancreas is round to oval in shape, hypoechoic, and shows a well-defined border with a hyperechoic posterior shadow. In elastography, the pancreatic mass is harder than the normal pancreatic parenchyma and CE-EUS shows hypoenhancement in early phase and washed out in delayed phase. As Table 1 shows, there have been no reports about EUS elastography and CE-EUS of pancreatic GCT in previous articles. Table 2 shows a comparison of CE-EUS for differentiation of pancreatic tumors. Differentiation between GCT and pancreatic adenocarcinoma is of great concern for management stratergies. GCT has a homogenous distribution; on the other hand, pancreatic adenocarcinoma has a heterogeneous distribution in general, whereas both GCT and pancreatic adenocarcinoma show a similar hypoenhancement pattern after contrast injection in the early phase and late phase [14]. In the present case, CE-EUS revealed a thick artery in the tumor unlike pancreatic adenocarcinoma, but still definite differentiation of these tumors seemed to be difficult only by CE-EUS.

Abdominal CE-CT and MRI findings cannot define the specific characteristics of GCT. For example, a pancreatic duct dilatation has been found in six out of nine cases and tumor shows hypo-iso enhancement in CE-CT and MRI. Hence, in the previous reports, it was considered pancreatic cancer in seven cases and pancreatic NET in one among the nine cases. Bean et al. reported a mediastinal GCT that was successfully diagnosed using EUS-FNA [13]. Takahashi et al. [11] reported a case of pancreatic

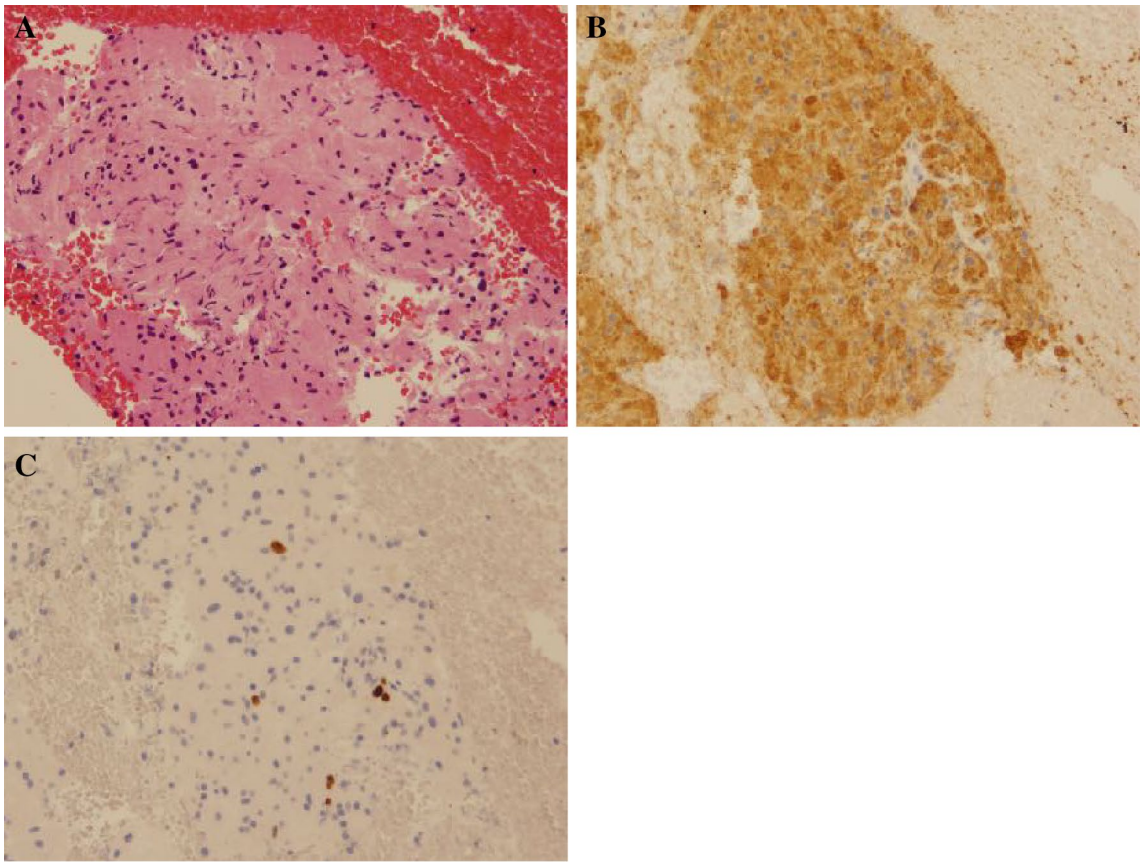

Fig. 5 The histological findings of fine needle aspiration specimen. **a** Hematoxylin and eosin (H&E) stain findings of granular cells. **b** S-100 staining is positive. **c** Neuron-specific enolase (NSE) staining is positive

GCT that was diagnosed using EUS-FNA because of which surgery was avoided. This is the second case of pancreatic GCT successfully diagnosed using EUS-FNA. The images of each examination are similar to those of pancreatic NET and small pancreatic cancer; thus, EUS-FNA should be performed for definitive diagnosis of this kind of round and low echoic mass [15].

Although most GCTs are benign, malignancy has been reported in 1–2% of cases, in the subcutaneous leg tissue and esophagus [16, 17]. Sonobe et al. [18] reported a metastasis of GCT from the left radial nerve to the skull 5 years after resection without any local recurrence. Some reports show recurrence or metastasis in spite of having a benign histological appearance. Although the morphology cannot reliably predict the biological behavior of GCT, local recurrence, rapid growth, and infiltrative growth have the possibility of malignancy and the potential of metastasis. Chen et al. [19] reported a single case of malignant GCT of the abdominal wall and right groin with breast metastasis which is not typical and reviewed the common sites for distant metastases including bone, peripheral nerve, peritoneal cavity, and lung.

In the present case, as the patient had a past history of GCT in the right forearm, one of the differential diagnoses was metastasis to the pancreas. Therefore, we recommended a surgical resection of the tumor. For differentiation between metastasis and original lesion, Sercan Aksoy et al. [17] summarized that most of the metastasis developed within 2 years after the first diagnosis. Fanburg-Smith et al. [20] reported histological criteria predicting malignant behavior, which comprise of spindling cells tumor, presence of vesicular nuclei with large nuclei, increased mitotic rate (2/10 high power fields), high nuclear to cytoplasmic ratio, pleomorphism, and necrosis. The tumor that meets > 3 criteria is classified as malignant GCT and has 50% risk of metastasis. The histology of the tumor of the right forearm did not meet any criteria and 12 years might be too long to metastasize. Therefore both lesions of the right forearm and the pancreas should be considered as original lesions. However, the fact that Ki-67 of proliferative activity was

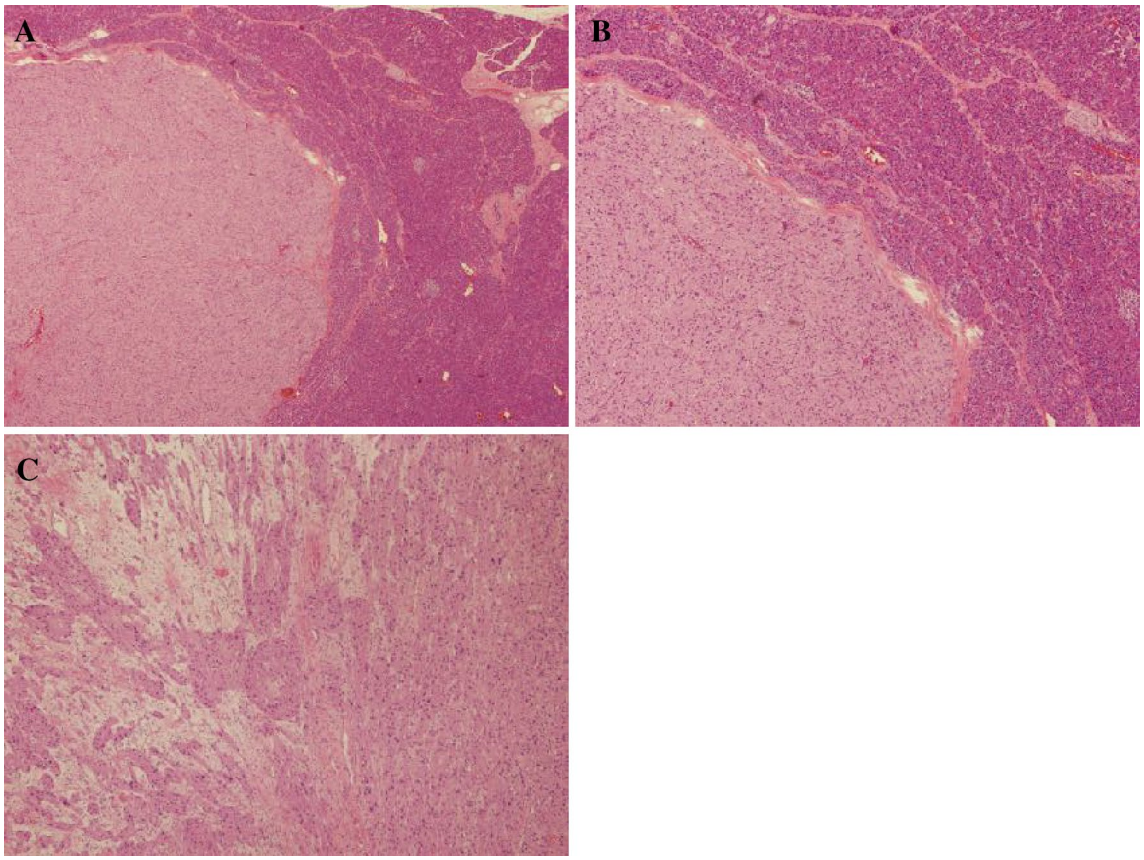

Fig. 6 The histological findings of the resected specimen. **a** Hematoxylin and eosin (H&E) stain in low power field. **b** Granular cells in a high power field. **c** Heterogeneity of granular cells between packed and loose areas

just 1% and there were heterogeneous and loose areas of granular cells with central fibrosis are compatible with the metastatic lesion of a slow-growing tumor. It is difficult to conclude whether this is a metastatic tumor or not, so long-term follow-up is necessary to confirm the clinical history and monitor prognosis.

Conclusion

We summarized about 10 cases of pancreatic GCT, including the present case. Pancreatic GCT should be considered in the differential diagnosis when EUS shows round-to-oval shape, hypoechoic, well-defined border tumors with posterior echo enhancement. Although EUS-FNA is a reliable modality for getting a definite diagnosis, surgical resection or strict follow-up should be considered because pancreatic GCT is rarely reported and its clinical course remains unknown.

Table 1 Summary of previous reports of pancreatic granular cell tumor

Sex	Age	Location	Tumor size (mm)	MPD	Diagnosis imaging					Pre-treatment diagnosis	Treatment	Pathological result
					EUS	CE-EUS	Contrast CT	MRI	ERCP			
M [5]	29	Head	6	NA	NA	NA	NA	NA	NA	Post-mortem diagnosis	NA	Benign
F [6]	62	Tail	7	Normal	NA	NA	NA	NA	MPD dilated in the tail	Pancreatic carcinoma	Distal pancreatectomy	NA
F [7]	31	Head	5	Dilated	NA	NA	NA	NA	MPD stenosis in the body	Pancreatic carcinoma	Pancreaticojejunostomy	Benign
F [8]	50	Body and tail	NA	Dilated	NA	NA	NA	NA	MPD stenosis at mid-distal	Malignant MPD stricture	Distal pancreatectomy and splenectomy	NA
M [2]	58	Head	13	Dilated	MPD dilated	NA	Hypovascular mass	NA	MPD dilated	Pancreatic cancer	Pyloric-preserving pancreaticoduodenectomy	Benign GCT combine with carcinoma in situ
F [9]	26	Body and tail	5	Dilated	NA	NA	No mass	No mass	NA	Pancreatic cancer	Distal pancreatectomy	NA
M [12]	43	Body	16	Dilated	Hypoechoic nodule, well-define border	NA	Slightly hyper vascular mass	Small fat suppressed area in T1WI	NA	Pancreatic endocrine tumor (combined with right side colonic cancer)	Distal pancreatectomy and splenectomy and right hemicolectomy	M [12]
F [present case]	32	Body	20	Normal	Hypoechoic mass with posterior echo enhancement, well-defined border	Hypoenhancement in early phase, washout after 1 min	Hypoenhancement in the arterial phase, isoenhancement in the delayed phase, well-defined border	Hypointense in T1WI, hyperintense on T2W, high signal on DWI	NA	Granular cells tumor (by EUS-FNA) (combined with right forearm granular cell tumor)	Distal pancreatectomy with splenectomy	F [present case]

M Male, *F* female, *MPD* main pancreatic duct, *EUS* endoscopic ultrasonography, *CE-EUS* contrast-enhanced endoscopic ultrasonography, *CT* computed tomography, *MRI* magnetic resonance imaging, *T1WI* T1-weighted image, *T2WI* T2-weighted image, *DWI* diffusion weighted image, *ERCP* endoscopic retrograde cholangiopancreatography, *NA* not available

Table 2 Comparison of contrast-enhanced EUS

Imaging pattern	Enhancement pattern		Distribution type	Enhancement speed	Washout pattern
Disease	Early phase	Late phase			
Granular cell tumor (GCT)	Hypoenhancement	Hypoenhancement	Homogenous	Slow	Fast
Pancreatic adenocarcinoma	Hypoenhancement	Hypoenhancement	Heterogenous	Slow	Fast
Neuroendocrine tumor (NET)	Hyperenhancement	Isoenhancement	Homogenous	Fast	Slow

EUS Endoscopic ultrasonography, *GCT* granular cell tumor, *NET* neuroendocrine tumor

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Human and animal rights This study does not include any data about human specimen. All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent This is a case report and does not involve human subjects and does not apply to giving informed consent.

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