Case Report

Rare adult pancreatic hemangioma: review of the literature with a case report

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Abstract: Adult pancreatic hemangioma is an especially rare benign tumor that is hard to diagnose through imaging examinations, meanwhile its histopathological and immunohistochemical studies have rarely been reported. At this time, only 29 cases in 27 publications have been reported. We report a new case as well as review these literatures. A 71-year-old woman came to our hospital with slight pain on left upper abdomen for three days. But the results obtained from the physical or laboratory examination were all negative so that her symptoms could not be explained clearly. The imaging examinations including ultrasonography and computed tomography both showed a mixed mass in the neck of the pancreas. The preoperative diagnosis of cystadenoma or adenocarcinoma was made, with high suspicious of malignancy. The patient underwent a central pancreatectomy with pancreatojejunostomy, but the pathologic diagnosis was pancreatic hemangioma. The immunohistochemical examination found the positive benign vascular markers (CD31, CD34) and negative lymphocyte markers (D2–40). Moreover, Ki-67 negativity also revealed its benign nature. After 36 months of follow-up, the patient has no complaints for abdominal pain. In conclusion, adult pancreatic hemangioma is extremely rare without any specific clinical manifestations. It is usually diagnosed postoperatively by histological examination and immunohistochemical studies. Imaging examinations, including computed tomography and magnetic resonance imaging, can't give definite conclusion. Endoscopic-ultrasound guided fine needle aspiration is conditionally worth doing, which can give some hints and exclude the malignancy of the lesion. If malignancy can be safely ruled out, the surgical decision must be made according to risk-benefit analysist. Maybe close observation and regular follow-up are more beneficial options.

Keywords: Pancreatic; hemangioma; adult; case report

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Introduction

Hemangiomas are benign tumors which comprised a large quantity of different blood vessels and can be found in all organs. Among them, hepatic hemangiomas account for nearly one-third of these internal lesions. Pancreatic hemangiomas are extremely rare, collectively accounting for only 0.1% in all pancreatic tumors (1). They are rarely suspected or clinically diagnosed because of their low morbidity and nonspecific symptoms. As a type of pancreatic tumor, they may also cause clinical symptoms associated with the pancreas. On the other hand, there is no exclusive imaging characteristics of ultrasound, angiography, computed tomography, or magnetic resonance imaging. Therefore, it's often difficult to distinguish them from other pancreatic neoplasms, such as intraductal papillary mucinous neoplasms, solid pseudopapillary neoplasms and mucinous cystic neoplasms. Hence, they are finally definitely diagnosed by histological examination and immunohistochemical studies. To date, only 27 publications for 29 cases of adult pancreatic

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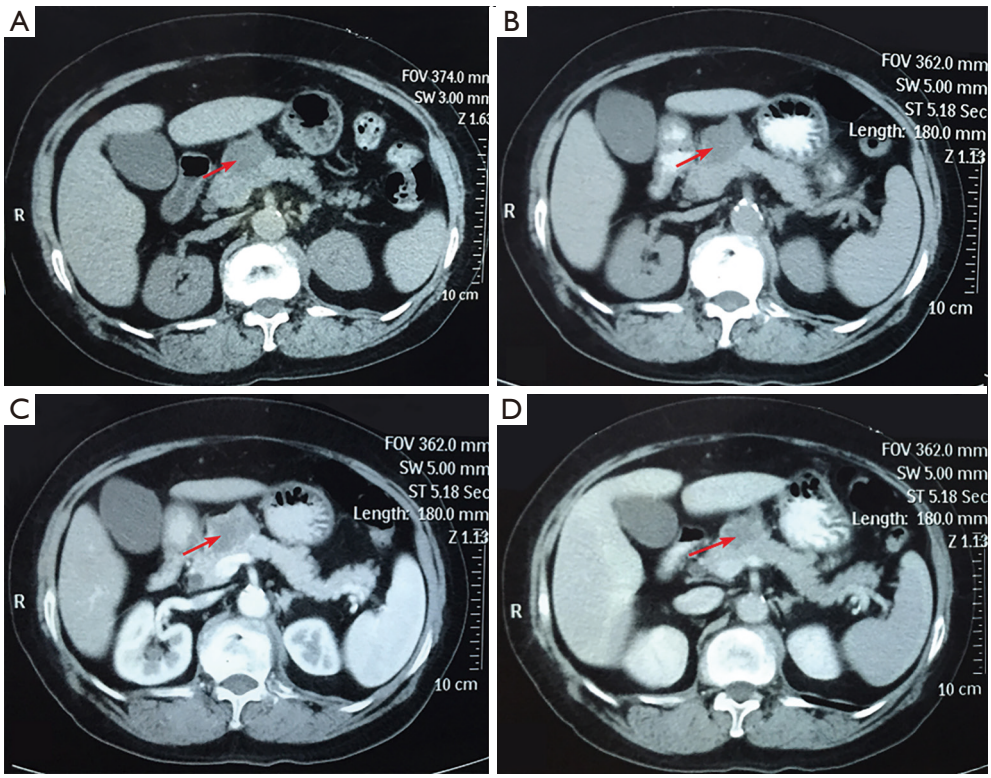

Figure 1 Computed tomography showing a pancreatic mass (red arrows).

hemangiomas have been found in the literature (showed in *Table 1*). Since there are no malignant cases published to date, surgical resection may be avoided if the diagnosis can be firmly made. The aim of the present review on the published case reports of pancreatic hemangioma is to summaries the clinical characteristics of this unusual type of neoplasm. In the present report, we describe a new case of adult hemangiomas located in the neck of the pancreas. We present the following case in accordance with the CARE Reporting Checklist (available at http://dx. doi. org/10. 21037/gs–20–281). Additionally, we reviewed the 29 cases of adult pancreatic cavernous hemangioma reported in the literature in an attempt to identify tumor characteristics.

Case presentation

A 71-year-old woman came to our hospital with slight pain on left upper abdomen for 3 days. She had no past medical histories of diseases or surgeries. The family and psycho-social history including relevant genetic information were not special either. She had no relevant past interventions. Her laboratory test results including blood routine examination, hepatic and renal function tests, were all within normal ranges. The levels of tumor marker including carbohydrate antigen (CA) 19-9, alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA) also reveal no abnormality. A physical examination also failed to reveal any abnormality. No abdominal tenderness or mass was found. An abdominal ultrasonography (US) indicated a mixed pancreatic head mass measuring about 3.2×3 cm, cholecystitis with gallstones, mild dilated common biliary duct measuring about 1 cm, and normal pancreatic duct. An abdominal computed tomography (CT) scan confirmed a well-defined tumor in the neck of the pancreas measuring 3.3×2.5 cm (*Figure 1A*,*B*). It showed a peripheral filling and strong enhancement in the arterial phase (*Figure 1C*). However, it produced heterogeneous enhancement in the venous and late phase without centripetal filling effect (*Figure 1D*). The diagnostic challenge is that there are too many similar diseases. The clinical diagnosis of cystadenoma or adenocarcinoma was made, with high suspicious of malignancy. Other differential diagnoses, such as solid pseudopapillary neoplasms, intraductal papillary mucinous neoplasms and mucinous cystic neoplasms were also

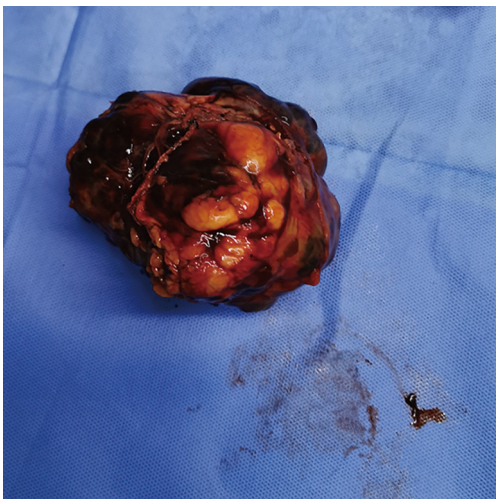

Figure 2 Surgical sample: a reddish tumor comprising multilocular cysts with harder granulation tissue surrounded.

considered, except for pancreatic hemangioma which has a good prognosis. The patient was recommended a surgical resection due to the risk of malignancy. The operation was successfully taken in the fourth day. During the operation, the mass including the adhesive pancreatic parenchyma was found in the pancreatic neck with about 4 cm of diameter (*Figure 2*). It looked like a benign cystic tumor with a complete capsule. Finally, the patient underwent a central pancreatectomy with pancreatojejunostomy. The definite histological examination confirmed a pancreatic hemangioma. Surgical sample revealed a reddish tumor comprising multilocular cysts with harder granulation tissue surrounded. Histology revealed the lesion comprised blood vessels of different size, ranging from glomus-like capillaries to large, cavernous spaces (*Figure 3A*). The CD31 and CD34 immunohistochemical studies were strongly positive,

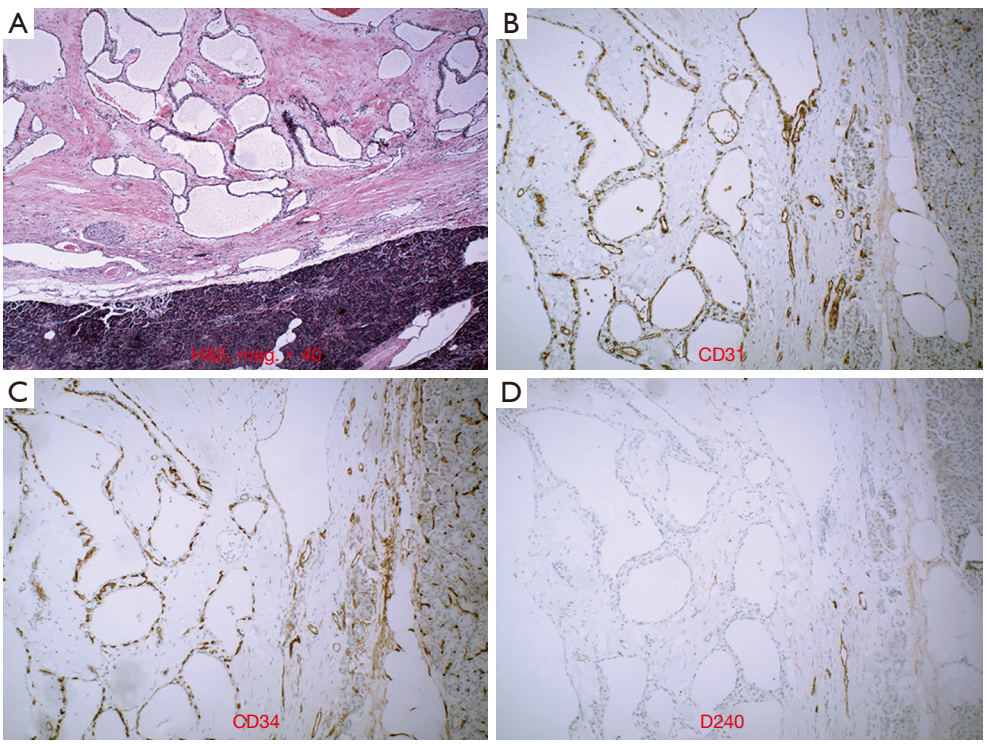

Figure 3 Pancreatic hemangioma: histology and immunohistochemistry (×40). (A) Multiple vascular spaces containing blood in a well-demarcated area and surrounded by fatty tissue (hematoxylin & eosin, ×40). (B,C) Immunohistochemical stain for CD31 and CD 34 showing positive staining of the vascular wall lining and lumen (×40). (D) Immunohistochemical stain for D240 showing negative staining of the vascular wall lining and lumen (×40).

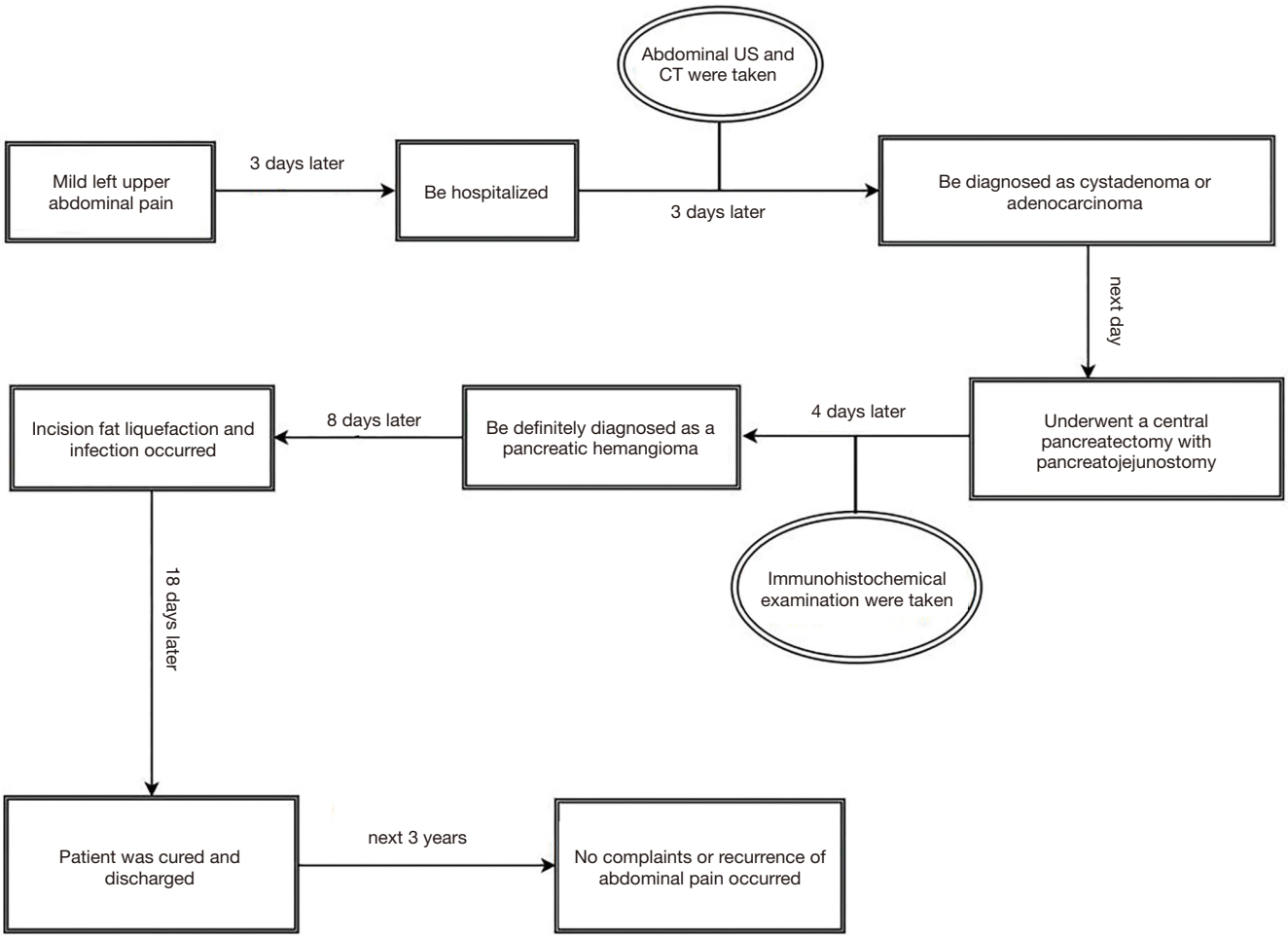

Figure 4 The timeline for the case.

indicating an endothelial origin (*Figure 3B*,*C*). D2-40, a lymphatic endothelium marker, was negative and Ki-67, an antigen assessing malignancy of the tumor, was about 3% (*Figure 3D*). There was no evidence of malignancy. The postoperative course was uneventful except for the incision fat liquefaction and infection. The length of postoperative hospital stay was 26 days. Then the patient was followed up for 36 months without complaints or recurrence of abdominal pain. Regular CT examination failed to find any abnormality either. The patient's compliance is good and there are no adverse or unanticipated events.

Timeline: Mild left upper abdominal pain was felt 3 days ago—The clinical diagnosis of cystadenoma or adenocarcinoma was made after different examinations in the first 3 hospital days—A central pancreatectomy with pancreatojejunostomy was taken in the 4th day—The definite histological examination confirming a pancreatic hemangioma was made in the 8th day—The incision fat liquefaction and infection occurred in the 12th day—Patient was cured and discharged in the 30th day—No complaints or recurrence of abdominal pain occurred in the next 3 years. It is shown in *Figure 4*.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient.

Discussion

Pancreatic hemangioma is an uncommon type of primary cystic neoplasm, which generally arises in childhood.

Hemangiomas have been reported to developed in three phases: the proliferating phase (the capillaries increase rapidly in number and continuously grows up until the child is one year old), the involuting phase (growth declines and reveals inevitable regression until the age of one to five years) and the involuted phase (improvement continues until the child is six to twelve years old, and ultimately a fibro-fatty residuum was produced by adulthood) (29). For this reason, pancreatic hemangioma is hardly to be found in adults. Moreover, pancreatic hemangiomas are especially difficult to give clinical diagnosis. The aim of the present review based on the published case reports of pancreatic hemangioma is to summaries the clinical characteristics of this unusual type of neoplasm. A search of the literature from PubMed, Google Scholar and relevant articles using the keywords "pancreatic hemangioma" was made, and their references were also reviewed. We only find 29 cases from 27 reports have been reported in the literature since 1939 including 3 cases mentioned in a Chinese article by Xu *et al.* (10). Clinical characteristics of all cases are summarized in *Table 1*. According to these cases, just as other hemangiomas, the pancreatic hemangioma is also more commonly found in women (23 in this series, 77%), sometimes during pregnancy (15,23), indicating the importance of excess of female sex hormones in these tumors (30). The average age was 51 years (18–79 years) and most of the cases (20/30, 67%) between 30 and 70 years. The largest diameter ranged from 0.6 to 20 cm, and most of these cases are not less than 5 cm (20/30, 67%). Most patients can't be symptomatic for a long time until the tumor grow large enough to cause relevant symptoms. The most common symptom is still abdominal pain (20/30, 67%), usually in the epigastric region and sometimes irradiating to the back. Other infrequent symptoms such as nausea, vomiting, early satiety, abdominal distension, eating choke and jaundice are caused by occupied tumor. More infrequent symptoms, some of which may be not relevant, such as hematemesis, malaise, thrombocytopenia, dizziness, palpitations, left iliac fossa pain and fever can be also found in different cases. Only 4 cases have no symptoms (2,10,17,25), one found at autopsy (2), while the other three found in incidental imaging examinations. Excluding the one found at autopsy, other asymptomatic cases are all suspicious of malignancy. Maybe these asymptomatic tumors are relatively small and atypical so that the imaging examinations differed more difficultly.

The majority of these cases had been identified by CT (23/30, 77%), followed by ultrasonography or endoscopic ultrasonography (EUS) (21/30, 70%), and magnetic resonance imaging (MRI) that applied in more recent cases (10/30, 33%). Other imaging examinations, such as angiography, gastrointestinal endoscopy, endoscopic retrograde cholangiopancreatography (ERCP), Abdo plain X-ray, cholangiography can be also found in a few cases. Under ultrasound examination, the tumor presents as a hyperechogenic mass with no or low blood flow, in contrast to the adequate blood supply for malignant tumors. By MRI and CT, the tumor usually appears as a well-demarcated, alveolar or multilocular cystic lump, with no expansion of main pancreatic duct. Besides, the pancreatic hemangioma appears as a hypervascular mass and usually shows strong enhancement in the contrast-enhanced arterial phase of CT, as in our case. But this finding was not confirmed in some other cases (6,10,11,13,16,17,21). The reason may be that arteriovenous shunting and neovascularization slow blood flow through cavernous vascular areas of cystic pancreatic tumors and the signal intensity in the arterial phase is impacted by the ratio of cystic to solid tumor tissue, which influences the relative degree of vascularity (21). So, it is still easily misdiagnosed solely based on contrast-enhanced CT. Using enhanced MRI, pancreatic hemangiomas can present hypointense on unenhanced T1w and hyperintense on T2w images, meanwhile they show only moderate gadolinium-enhancement with washout on delayed phase images (9). Thus, it is necessary to undertake both CT and MRI for a more reliable diagnosis. However, it is still difficult to make a definite diagnosis in some cases (11,17,21,22,27) though both CT and MRI were undertaken. Endoscopic-ultrasound guided fine needle aspiration (EUS-FNAB) was undertaken in 3 reports (13,18,22), which can give some hints and exclude the malignancy of the lesion. It is worth doing if conditional.

The therapies to hemangiomas are variable. Unlike recognized observation for pediatric hemangiomas, there are no definitive standards for the treatment of pancreatic hemangiomas in adults. Yet, due to their risk of sudden hemorrhage and the uncertain differential diagnosis with epithelial tumors, surgical resection is often recommended. The surgical method is chosen mostly based on the location of the pancreatic hemangioma, and also influenced by tumor size. Upon reviewing previous literatures, the pancreatic hemangioma is most located in or related to the head of the pancreas (14 in this series, 47%), which may cause clinical symptoms more easily. When the tumor is located at head of the pancreas, pancreaticoduodenectomy is a major option. When the tumor is located at body or

Table 1 Pancreatic hemangiomata previously reported in literature

Reference	Age	Sex	Presentation	Imaging	Clinical diagnosis	Location/size (cm)	Treatment	Histology	Immuno-histochemistry
Ranstrom 1939 (2)	61	F	–	–	At autopsy	Head/7×7	–	–	–
Ringoir 1961 (3)	71	F	Hematemesis, melena, Abdominal pain	Abdo plain X-ray, cholangiography	Not clear	Head/15	Retrocolic- gastroenterostomy, vagotomy	Hemangioma	–
Colardyn 1972 (4)	42	M	Malaise	Abdo plain X-ray, angiography	Not clear	Body, tail/not mentioned	Conservative	-	–
Mangin 1985 (5)	62	F	Malaise, nausea, thrombocytopenia	US, ERCP, native CT	Not clear	Head, body, tail/20×7	Resection of the tumor	Hemangioma	–
Dageforde 1991 (6)	79	F	Abdominal pain	US, ERCP, angiography, enhanced CT	Hemangioma	Body and tail junction/6×3	Observation	–	–
Kobayashi 1991 (7)	30	M	Abdominal pain and distension	US, enhanced CT, angiography, MRI	Possible cavernous hemangioma	Head 20	Pancreatico-duodenectomy	Hemangioma	–
Chang 2003 (8)	70	F	Epigastric pain and tenderness	enhanced CT, angiography	Cystic adenocarcinoma	Body and tail junction/4×3.2	Distal subtotal pancreatectomy	Hemangioma	Factor VIII-related Ag
Plank 2006 (9)	36	M	Abdominal pain and jaundice	enhanced CT, MRI, intraoperative US	Neuroendocrine tumor	Head/3	Laparotomy without resection, observation	–	–
Xu 2008 (10)	60	F	Abdominal pain and fever	US, enhanced CT	Cystic adenoma or adenocarcinoma?	Tail/2×2	Distal spleno-pancreatectomy	Hemangioma	CD31, CD34, Factor VIII-related Ag
	41	F	–	US	Cystic tumor or Islet cell carcinoma?	Body/2.5×2	Distal subtotal pancreatectomy	Hemangioma	CD31, CD34, Factor VIII-related Ag
	30	F	Abdominal pain and Eating choke	US	Cystic or solid tumor?	Head/6×5	Pancreatico-duodenectomy	Hemangioma	CD31, CD34, Factor VIII-related Ag
Mundinger 2009 (11)	45	F	Stabbing epigastric pain radiating through to back	Enhanced CT, MRI	Duplication cyst, cystic GIST, paraganglioma	Head/6.2×5.3	Pylorus preserving pancreatico-duodenectomy	Hemangioma	CD31, CD34
Jarboui 2010 (12)	60	F	nausea, diffuse abdominal pain, and fever	US, enhanced CT, EUS	Pancreatic cystic lesion	Body/2.3×1.8	distal spleno-pancreatectomy	Hemangioma	CD31, CD34
Lee 2011 (13)	49	F	Dizziness, palpitation	US, enhanced CT, EUS-FNAB	Cystic tumor	Body/5	Central pancreatectomy	Hemangioma	CD34
Weidenfeld 2011 (14)	73	F	Pain, nausea	US, enhanced CT	Cystic tumor	Head/5	Whipple's procedure	Hemangioma	CD31, CD34, Factor VIII-related Ag
Franzoni 2012 (15)	19	F	large hematemesis	Gastrointestinal endoscopy, MRI, US	Cystadenoma	Tail/11×9×8	distal pancreatectomy and splenectomy	Hemangioma	-
Malik 2013 (16)	70	F	Abdominal pain	US, enhanced CT, CT angiography, EUS-FNAB	Giant hemangioma	Head/7.9×6.5	Pylorus preserving pancreatico-duodenectomy	Hemangioma	CD31
Lu ZH 2013 (17)	23	F	–	US, enhanced CT, MRI	Not clear	Head/5.4×5×3	Subtotal pancreatectomy	Hemangioma	–
Bursics 2013 (18)	72	M	Pain, jaundice	US, enhanced CT, ERCP	Cystic tumor, possibly IPMN	Head and part of duodenum/8	Pylorus preserving pancreatico-duodenectomy	Hemangioma	CD31, CD34
Naito 2014 (19)	40	F	Abdominal pain	Enhanced CT	Cystic neoplasm	Body and tail/10	Pancreatectomy	Hemangioma	CD31, CD34
Figueroa 2014 (20)	52	F	Abdominal pain and early satiety	US, enhanced CT	Highly suspicious of malignancy	Head/8×6.5×6	pylorus preserving pancreatoduodenectomy	Hemangioma	–
Lu T 2015 (21)	28	F	Epigastric pain	Enhanced CT, MRI	Cystadenoma or pseudocyst with intracystic hemorrhage	Body and tail/10×8	Subtotal pancreatectomy, splenectomy	Hemangioma	–
Mondal 2015 (22)	18	F	Stabbing epigastric pain radiating through to back, Nausea and emesis	Native CT, Contrast MRI, MRCP, EUS-FNAB	Inflammatory benign cyst	Head, uncinate process/6×4×3.5	Pylorus preserving pancreatico-duodenectomy	Hemangioma	CD31, CD34
Kim 2015 (23)	68	F	–	Enhanced CT	Neuroendocrine tumor or metastasis	Tail/0.6×0.5	Nephrectomy, distal pancreatectomy	Hemangioma	CD31, CD34, factor VIII
Soreide 2015 (24)	38	F	Left epigastric pain, nausea, palpable left subcostal mass	US, MRI	Solid pseudopapillary epithelial neoplasm	Tail pancreas and spleen/19.5×10×7	Distal pancreatectomy, splenectomy	Hemangioma	CD31, CD34
Bratu 2016 (25)	64	M	Acute upper abdominal pain, weight loss of 5 kg (in 2 months)	US, endoscopy, enhanced CT	Pancreatic adenocarcinoma	Body/3.2×1.9	Surgical resection of the lesion	Hemangioma	–
Al Warith 2017 (26)	71	F	Left iliac fossa pain	Native CT, MRI, EUS	Mucinous neoplasia	Tail/2.4	Laparoscopic distal pancreatectomy, splenectomy	Hemangioma	–
Raymundo 2018 (27)	36	M	Lumbar pain	Enhanced CT, MRI, ERCP	Neuroendocrine tumour	Body and tail/2.4×2.2	Distal pancreatectomy, splenectomy	Hemangioma	CD31, ERG
Lianyuan 2019 (28)	63	M	Left upper abdominal pain and defecation unformed	Enhanced CT, EUS	Cystic tumor	Head/10×5×5	Pancreatico-duodenectomy	Hemangioma	CD31, CD34, factor VIII, ERG
Present case	71	F	Left upper abdominal pain	Enhanced CT, US	Cystadenoma or adenocarcinoma	Neck/3.5×2.7×2.5	Central pancreatectomy	Hemangioma	CD31, CD34

tail of the pancreas, distal or subtotal pancreatectomy is indicated and combined splenectomy is sometimes necessary. If malignancy can be safely excluded and the mass can be separated fully from pancreas, surgical resection of the lesion with or without surrounded pancreatic tissues is also feasible. Using ultrasound and rapid pathological examination during the operation can also help in choosing the best surgical approaches (denucleation, other more conservative surgical procedures or an extended resection). In our case, the tumor is located in the neck of the pancreas with complete envelope. A central pancreatectomy was undertaken, with head, part of body and tail of pancreas left. Our patient recovered relatively smoothly, though she had a postoperative complication of the incision fat liquefaction and infection, which led to longer hospital stays and higher medical cost. However, the morbidity rate of the patients who underwent pancreaticoduodenectomy was higher than that of the patients who underwent distal pancreatectomy (34.7% *vs.* 27.8%, P<0.05) (31). Therefore, if the tumor is located in the pancreatic head, which is highly suspicious of hemangioma and it cause few manageable symptoms, close observation and regular medical follow-up must be more suitable choices.

After the surgery, as our case, the microscopic specimens usually shows that blood-filled spaces are separated by fibrous connective tissue and this is a typical characteristic of hemangioma (25). For the tumor can be further definitely diagnosed, immunohistochemistry is usually needed. There are some common markers to identify hemangioma. The existence of the factor VIII-related antigen was reported as a vascular endothelium marker by Chang *et al.* (8). After that, Mundinger *et al.* (11) reported that the endothelial markers CD31 and CD34 were also expressed in hemangioma. In our patient, immunohistochemical results were positive for CD31 and CD34. On the other hand, D2-40, a lymphatic endothelium marker, was negative and Ki-67, an antigen assessing malignancy of the tumor, was about 3%. These findings indicated that the tumor mass was a hemangioma. Finally, pancreatic hemangioma is definitely diagnosed by histological examination and immunohistochemical studies with positive markers CD31, CD34 or factor VIII-related antigen.

Conclusions

In conclusion, adult pancreatic hemangioma is especially rare and it have no specific clinical symptoms. It is usually diagnosed postoperatively by histological examination and immunohistochemical studies. Imaging examinations, including CT and MRI, can't give definite conclusion. In contrast to other hemangiomas, the CT signs may not show a typical and strong enhancement in the contrast-enhanced arterial phase. EUS-FNAB is conditionally worth doing, which can give some hints and exclude the malignancy of the lesion. Since the pancreatic surgeries have relatively high rate of morbidity, which can lead to longer hospital stays and higher medical cost, more cautious decision should be made. If malignancy can be safely ruled out, the surgical decision must be made according to risk-benefit analysist. Maybe close observation and regular follow-up are more beneficial options.

Patient perspective

The patient appreciated our surgery because it not only relieved the pain, but also removed her concerns for the tumor. Although she had a postoperative complication of the incision fat liquefaction and infection, which led to longer hospital stays and higher medical cost, she still thought it is worthwhile.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at http://dx.doi.org/10.21037/gs-20-281

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/gs-20-281). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient.

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