Clinical Case Report

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Situs inversus totalis with solid pseudopapillary pancreatic tumor

A case report and review of literature

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Abstract

Rationale: Situs inversus totalis (SIT) is a rare anatomical variation of the internal organs, and solid pseudopapillary tumor of the pancreas (SPTP) is a rare tissue type of pancreatic tumors, classified as benign or low-grade malignancy. However, to our knowledge, a patient with SIT and SPTP is extremely rare and has never been reported.

Patient concerns: We retrospectively analyzed a case of SIT with SPTP in a 45-year-old woman. The main complaints were abdominal pain and sensation of heaviness for 2 weeks. There was tenderness and a mass that could be palpated in the right upper abdomen.

Diagnoses: Heart ultrasonography (USG), chest x-ray, computed tomography (CT), and contrast-enhanced computerized tomography (CECT) revealed a mirror-image dextrocardia and inversion of all abdominal viscera and a space-occupying lesion in the pancreas tail. Abdominal computed tomography angiography (CTA) showed no obvious abnormality of artery. The diagnosis of SPTP was finally made by postoperative pathological examination.

Interventions: The patient underwent resection of the pancreatic body and tail and splenectomy via laparotomy to completely remove the tumor.

Outcomes: The patient was discharged with specific discomfort on postoperative day 7. At the 1.5-year follow-up, she recovered without issue.

Lessons: Surgical resection remains the only effective treatment of SPTP. SIT with SPTP can be accurately diagnosed by heart USG, chest x-ray, CT, and CECT of the upper abdomen. Abdominal aorta CTA before surgery can decrease the injury risk of blood vessels.

Abbreviations: CECT = contrast-enhanced computed tomography, CT = computed tomography, CTA = computed tomography angiography, SIT = situs inversus totalis, SPTP = solid pseudopapillary tumor of the pancreas, USG = ultrasonography.

Keywords: diagnose, pancreatic neoplasms, situs inversus totalis, solid pseudopapillary pancreatic tumor, splenectomy, surgery

1. Introduction

Situs inversus totalis (SIT) is a very rare anatomical variation of the internal organs in the body, termed "mirror man," where all viscera are reversed 180°, including the heart, liver, spleen, stomach, and bowels. The incidence rate is thought to be in the range of 1 in 8000 to 1 in 25,000.[1] Patients always undergo physical examination and are accurately diagnosed using radiography, ultrasonography (USG), computed tomography

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DX, JH, and ZF contributed equally to this work and should be considered co-first authors.

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This study was approved by the ethical review committee of the First Affiliated Hospital of Nanchang University, and written informed consent was obtained from the patient.

The authors have no conflicts of interest to disclose.

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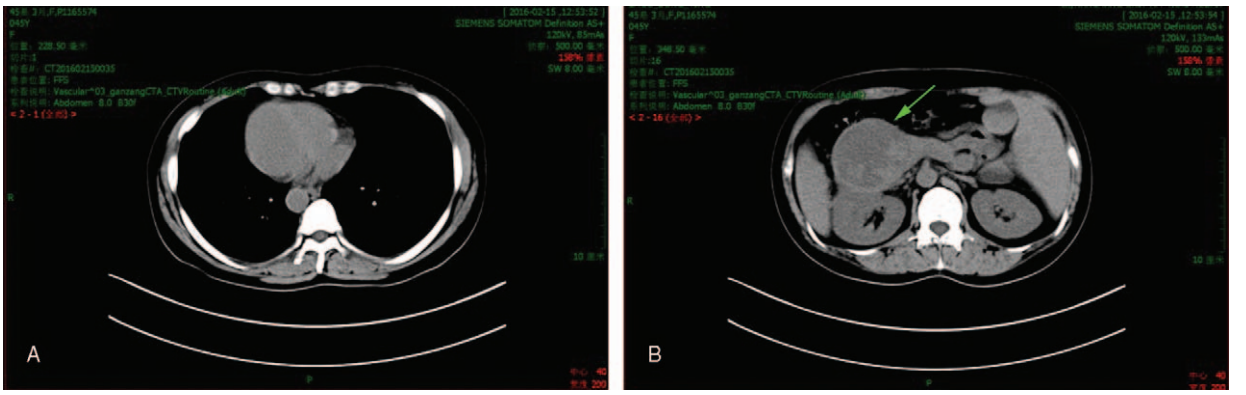

Figure 1. Chest and upper abdomen computed tomography (CT) of the patient. A, Chest CT scan prompted the cardiac reverse position. B, The CT scan of the upper abdomen showed a round mass about 7.5 cm × 6.9 cm in the tail of the pancreas.

(CT), contrast-enhanced computed tomography (CECT), and magnetic resonance imaging.

SIT combined with tumor is rarer. In 1936, Allen[2] first described a patient with SIT and gastric cancer. In addition, in 2009, Sceusi and Wray[3] presented a patient with SIT complicated with moderately differentiated ductal adenocarcinoma of the pancreas who underwent pancreaticoduodenectomy. Solid pseudopapillary tumor of the pancreas (SPTP) is a rare tissue type of pancreatic tumors, and is classified as benign or low-grade malignancy.[4] To the best of our knowledge, SIT with SPTP has not been previously reported.

1.1. Presenting concerns

A 45-year-old woman was presented with a history of abdominal pain for 2 weeks. The pain was a type of epigastralgia distention. In addition, the pain was aggravated with vomiting when she consumed food in excess, which was relieved when she had an empty stomach. A smooth, fixed 5 × 5-cm hard mass could be palpated in the right upper abdomen.

1.2. Clinical findings

The patient had a history of mood disorders for 5 years and was treated with regular oral clozapine. She had no other related past illness, allergy history, and family history. She was physically fit and had normal mental health. Her age of menarche was 12 years. Her normal menstrual cycle was approximately 28 days, and the menstruation was not irregular and usually lasted for approximately 3 days. She gave birth to a son and a daughter with natural labor. There was tenderness in the right upper abdomen, but no rebound pain or fluid thrill. Moreover, physical examination revealed an apical beat situated at the fifth intercostal space of the right midclavicular line.

1.3. Diagnostic focus and assessment

On February 15, 2016, CT (Fig. 1A and B) and CECT (Fig. 2A and B) of the patient's upper abdomen revealed a mirror-image dextrocardia and inversion of all abdominal viscera and a space-occupying lesion in the pancreas tail, which was considered a benign neoplasm and suspected solid pseudopapillary tumor. We assessed cardiac and pulmonary function for surgery which showed a normal electrocardiogram, no obvious abnormality in the lung or diaphragm on chest x-ray, and reversal of all thoracic organs (Fig. 3A). Heart USG revealed mirror-image dextrocardia, and no obvious abnormality of the inner heart stricture and blood current in the quiescent condition (Fig. 3B). Abdominal computed tomography angiography (CTA) showed no obvious abnormality and indicated a low risk of accidental artery injury (Fig. 3C). Coagulation function, liver function, renal function, and blood electrolyte tests were normal. Routine blood examination showed the following: white blood cell count, 3.39×10^9/L (3.69×10^9–9.16×10^9/L); hemoglobin concentra-

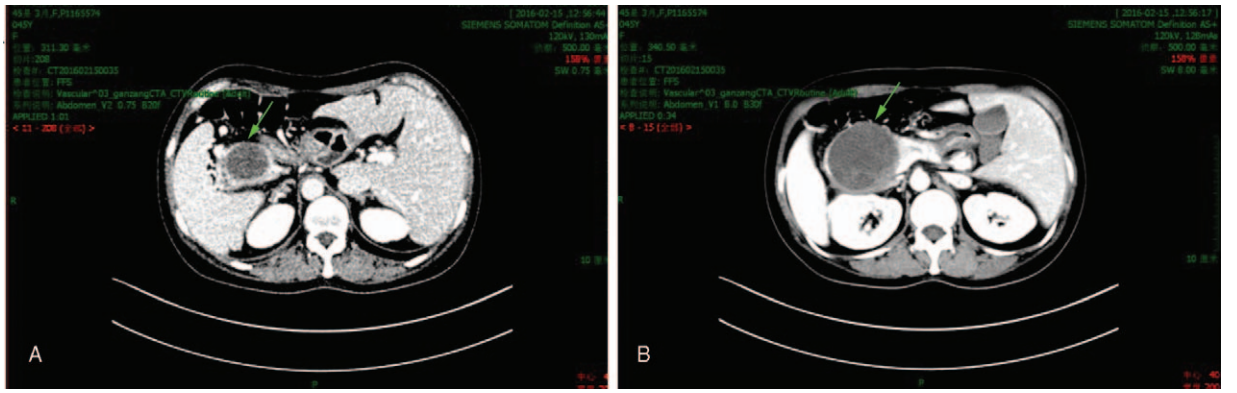

Figure 2. Upper abdomen contrast-enhanced computed tomography (CECT) of the patient. A, Arterial phase. B, Venous phase.

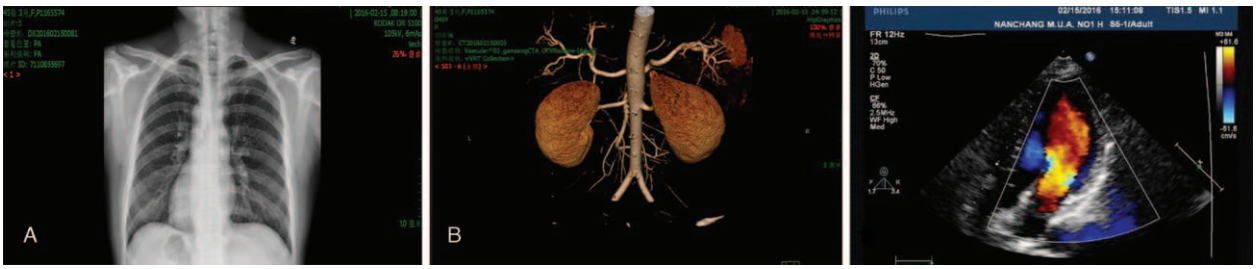

Figure 3. Chest x-ray, heart ultrasonography (USG) and abdominal computed tomography angiography (CTA) of the patient. A, Chest x-ray. B, Heart USG. C, Abdominal CTA.

tion, 102 g/L (113–151 g/L); packed cell volume, 0.313 L/L (0.335–0.45 L/L); lymphocyte count, 0.77×10^9/L (0.80×10^9–4.0×10^9/L).

1.4. Therapeutic focus and assessment

On March 3, 2016, the patient underwent surgery under general anesthesia. When choosing the incision site, traditionally, we make a median vertical incision around the umbilicus in resection of the pancreatic tail tumor and splenectomy (mostly the median straight incision around umbilicus); however, this is not advantageous in patients with SIT. Thereafter, we chose a backward "L" incision on the right side of upper abdomen to sufficiently expose the spleen and blood vessels around the pancreas tail. We observed the mirrored position of all abdominal viscera. We saw no dropsy in the abdominal cavity, and no metastatic mass above the pelvic peritoneum was present on palpation. The surfaces of the liver and spleen were soft. There was no obvious abnormality in the gastric wall. A cystic mass approximately 6×5.5 cm in size with a medium quality and thick wall was visible in the pancreatic tail and downstream of porta lienis, and was tightly adhered to the spleen, colon, mesentery, right kidney, kidney upper pole, and right adrenal gland. There was a space between the spleen and mass, and the splenic artery and vein were pushed back. No enlarged lymph nodes were found around the pancreas. Obvious varicose gastric fundus veins and other veins were noted. We decided to perform a distal pancreatectomy and splenectomy.

Resection of the pancreatic body and tail and splenectomy in this patient was performed. Regarding the pancreatic tail resection procedure, we separated the splenic artery carefully under direct vision. First, we ligated it without mutilation, and then separated it from the other tissues behind the pancreas to the transverse pancreatic artery; finally, we ligated it and mutilated it near the tumor. We also confirmed that there was no arteriopalmus 2 cm from the pancreatic head to the proximal end of the pancreatic tumor; then, we opened the retroperitoneal space to find the splenic vein and separated it. We took care not to damage the inferior mesenteric vein and varicose retroperitoneal venous plexus during surgery. After excising the pancreatic tail and body, the resected ends of the pancreas were sutured multiple times and hemostasis applied; we confirmed no pancreatic fistula and sutured the residual vessels twice.

During surgery, we found the tumor adhered to the right kidney upper pole, which made separation difficult. Thus, we invited an experienced urinary surgeon of 30 years to assist with surgery to avoid kidney injury. Because the thickened envelope was left at the right kidney upper pole and was difficult to excise, we removed a portion of envelope to perform pathologic evaluation of the frozen section for considering whether to perform right nephrectomy. On pathologic evaluation, fibrous and adipose tissue hyperplasia and leukomonocytes infiltration were apparent, so we applied electrocoagulation to the envelope. Before the frozen section report of the tumor envelope was available, tumor-free technique was strictly carried out in the operation. Even with the complex anatomy of all transpositions, it was guaranteed not to squeeze the tumor body, and the margin was negative after tumor resection. Finally, we put a drainage tube under the right diaphragm and another tube at the resected ends of body of pancreas.

After surgery, the patient was treated with anti-inflammatory medication, fluid replacement, acid inhibition, and enzyme inhibition. The patient did not have abdominal pain or distention. There was some subflavous fluid in the drainage tube at the resected pancreatic end. We sampled the fluid for amylase daily, and levels during the first 3 days after surgery were 4711, 811, and 944 U/L (0–100 U/L), respectively; the determination of amylase in the drainage fluid was <100 U/L totally. On postoperative day 3, we removed 1 tube from the right diaphragm. On postoperative day 7, the patient was discharged with the drainage tube in the left upper abdomen.

1.5. Follow-up and outcomes

On postoperative day 9, the patient returned to the hospital and we removed the drainage tube at the resected pancreatic ends after assessing the patient. At the 1.5-year follow-up, the patient recovered without issue. On postoperative histopathological assessment, the mass showed some adrenal gland tissue adhering to the adventitia, and 2 lymph glands around the spleen and 6 lymph glands around the mass exhibited reactive hyperplasia (Fig. 4A). The positive results of hematoxylin-eosin staining enabled a definite diagnosis of SPTP (Fig. 4B); the tumor cells were the same size and lined up in solid nests with necrosis and cystic degeneration, and were separated by tiny blood vessels. The endochylema was plentiful with round or orbicular-ovate nuclei, and the surrounding areas showed hyalinization. Immunohistochemistry (Fig. 4C and D) revealed the following: cytokeratin (+), epithelial membrane antigen (−), vimentin (2+), cluster of differentiation 10 (2+), cluster of differentiation 56 (2+), cluster of differentiation 34 (−), cluster of differentiation 31 (−), neuron-specific enolase (+), chromogranin A (−), synaptophysin (−), S-100 protein (part+), nuclear-associated antigen Ki-67 (<1%+), α-antitrypsin (+), estrogen receptor (−), and progesterone receptor (2+). Table 1 summarizes the timeline of this patient.

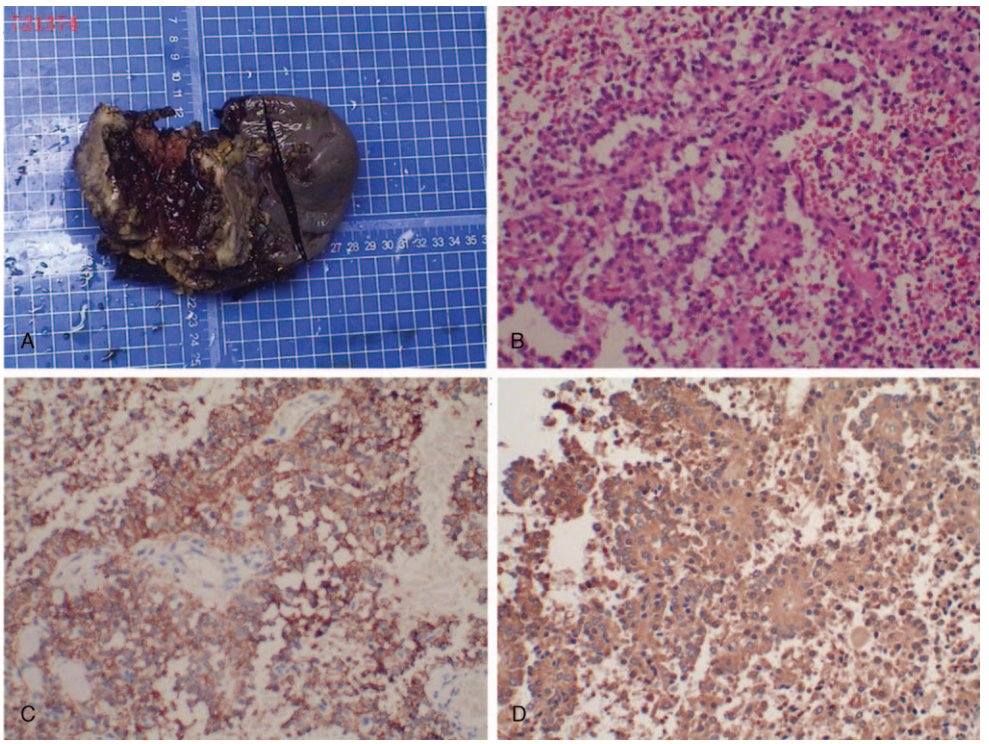

Figure 4. Postoperative histopathology of the resected tissue. A, Pancreatic mass and spleen. B, HE staining of solid pseudopapillary tumors of the pancreas (SPTP). C, CD56 immunohistochemistry of SPTP. D, CD56 immunohistochemistry of SPTP. HE = hematoxylin-eosin.

2. Discussion

SIT is a rare congenital deformity,[5] which was first reported by Fabricius in 1600.[6] The etiology of SIT has not been fully clarified; evidence suggests that it might be correlated with congenital factors.[7] One study showed that simple SIT is mostly related with familial genetic factors, changes in chromosome structure and number, and ciliary dyskinesia in the fetus.[8] However, individuals with SIT can be as high functioning as people with normal viscera orientation; thus, it often does not affect the quality of life or lifespan. However, the risk of heart, spleen, and hepatobiliary malformations increases in patients with SIT.[9] Symptoms and signs of the malformation will present in the location compared to normal individuals. Diagnosis is challenging if not identified. To avoid misdiagnosis, meticulous examination should be performed before surgery is undertaken. CT, chest radiography, and electrocardiogram are important for accurate diagnosis. Spiral CT can reliably diagnose SIT.[10]

For SPTP, Geers et al[11] described that its pathogenesis was related to the expression of galectin-3 and female hormones. By 1995, <300 cases were reported worldwide. In 2000, SPTP accounted for approximately 1% to 2% of pancreatic tumors.[12] Because of increased attention by specialized physicians and radiologists, the number of patients increased to approximately 800 in 2007. Subsequent domestic reports on this disease showed a significant increasing trend. The literature revealed that SPTP represented 1% to 3% of pancreatic tumors after 2010,[13] which was significantly higher than that before 2010.

Currently, the treatment of SIT with malignant tumor is timely surgery, but consideration must be given to conditions such as arterial and venous contacts of tumor, distant metastasis, cardiopulmonary insufficiency, liver and renal dysfunction,

Table 1

Case report timeline.

Complaint/investigations	Details
Presenting symptoms	Abdominal pain for 2 weeks and a mass could be palpated in the right upper abdomen
First investigations	There was tenderness in the right upper abdomen; physical examination revealed an apical beat situated at the fifth intercostal space of the right midclavicular line; coagulation function, liver function, renal function, blood electrolyte tests, and routine blood were detected
CT and CECT of the upper abdomen	A mirror-image dextrocardia and inversion of all abdominal viscera and a space-occupying lesion in the pancreas tail
Chest x-ray	Reversal of all thoracic organs
Heart USG	Mirror-image dextrocardia
Abdominal CTA	No obvious abnormality, which indicated a low risk of accidental artery injury
Surgical intervention	Resection of the pancreatic body and tail and splenectomy; postoperative pathology: SPTP
Postoperative follow-up	1.5-Year follow-up: recovered without issue; consecutive follow-up needed.

CECT = contrast-enhanced computed tomography, CT = computed tomography, CTA = computed tomography angiography, SPTP = solid pseudopapillary tumors of the pancreas, USG = ultrasonography.

infection and other diseases that contraindicate surgery, or general anesthesia. It is difficult to perform surgery for patients with SIT.[14] However, as surgical proficiency improves, the laparoscopic-assisted procedure is gaining in popularity. The reverse laparoscopic-assisted procedure increases surgical difficulty. In this case, because the mass was attached to the splenic hilum, the right kidney upper pole, and other important tissues, compression of the mass caused pancreatic portal hypertension and lead to varices of the splenic vein, resulting in great risks; we thus decided to perform laparotomy. In some abnormal conditions, deformity of the spleen could lead to hemorrhage of short gastric vessels.[15] The surgeons must fully prepare by performing abdominal aorta CTA examination to confirm the absence of arteriovascular deformity that could increase injury risk. In addition, surgeons must have sufficient knowledge of the anatomical complexity and be able to identify reversed structures, especially the morphology of the reactionary arteries and veins by distinguishing and confirming larger organs. These diagnostic and preoperative preparations will result in favorable intraoperative and postoperative outcomes.

The author retrospectively analyzed the patient's clinical information verified through pathological evaluation after surgery, reviewed the literature, and studied the CT imaging features and antidiastoles of this disease, to expand the knowledge on SPTP and reduce the misdiagnosis rate to improve treatment outcomes.

SPTP affects young women aged 20 to 40 years,[16] and is much less common in men and older women. Our patient was outside the typical age range; this led to a difficult diagnosis before surgery. Her clinical symptoms were atypical; some patients may have abdominal pain or no symptoms.[17] The space-occupying masses in the abdominal cavity are found on physical examination; some masses can be palpated from the abdominal surface and can be very large. Laboratory examination shows pancreatic portal normotension or hypertension that can result in hypersplenia, and the blood routine examination may be normal. Imaging may reveal a clearly defined cystic solid pancreatic tumor, and the enhancement of the edge of the arterial phase was obviously enhanced. The solid part of the tumor was slightly enhanced; the cystic part was not enhanced obviously.

In some cases, aspiration cytology of pancreatic tumors is carried out before surgery. Irregular adenoid, solid block, and pseudopapillary structures can be found.

SPTP and pancreatic cystadenocarcinoma can be easily confused on imaging. Pancreatic cystadenocarcinoma affects women aged 40 to 60 years, and the mean age is older than in SPTP.[18] Patients with pancreatic cystadenocarcinoma can have no symptoms, but appear to have jaundice because the bile duct is obstructed by the tumor. Imaging shows a round or lobulated tumor with cystic wall of varying thickness or a wall with shell calcification. In addition, strip separation in the tumor interior can be obviously enhanced using CT. On CECT, some malignancies show a more obvious line division than before. The present case was distinguished from pancreatic cystadenocarcinoma through imaging examination. The patient was a 45-year-old woman, who was within the typical age range for cystadenocarcinoma. However, the tumor mass in this patient was of low density and not enhanced; furthermore, the envelope was considerably enhanced, and the cystic cavity was of moderate density before and after the enhancement.

The size of SPTP varies, with a diameter ranging from 1.5 to 30 cm.[12] The tumor is often brown or red, and slightly soft. Cystic structures are rarely seen in small tumors; large tumors often show a fibrous pseudocapsule with hemorrhage, necrosis, and cystic degeneration. The tumor exhibits a variety of different structures on light microscopy, and is mainly characterized by solid, pseudopapillary, and cystic areas. In solid areas, the tumor cells are arranged in solid nests, separated by thin small vessels, with the surrounding area often hyalinized. The size of the tumor cells is consistent, appearing as triangular epithelial cells; the nuclei are round or oval, and gyriform, and sometimes the nuclear sulcus is visible. The nuclear atypia is very small without pathological division, and the cytoplasm is fragile. It is very rare that true SPTP tumor cells appear necrotic and apoptotic. In solid areas, the tumor cells far from small vessels are gradually degenerated, and the perivascular cells are arranged around the fibrous vascular layers, allowing for easy formation of pseudopapillary processes to become the characteristic pathological changes in SPTP. Although the SPTP envelope is intact, there are small amounts of infiltration to the surrounding pancreatic tissues, which show pancreatic acinar and islet cells trapped in the tumor parenchyma; the tumor nests are also insular and spread into pancreatic tissues. Regarding ultrastructural features, the tumor cell cytoplasm is abundant, with an abundant number of mitochondria and rough endoplasmic reticulum, and annular lamellar substances and lipid droplets are observed without zymogen.

Immunohistochemistry often reveals diffuse vimentin (+), α-antichymotrypsin (+), α-antitrypsin (+), synaptophysin (+) (in some cases), cytokeratin (AE1/AE3) weakly (+), cluster of differentiation 56 (+), cluster of differentiation 10 (+), progesterone receptor (+), and chromograninA omni (−). Immunohistochemistry staining shows diverse expression characteristics, multitissue expression, and no correlation with estrogen; in addition, it does not have specific tumor markers. After analyzing 7 cases of SPTP and in 43 cases collected from the literature, Pettinato et al[19] stated that the preoperative and operative fine-needle aspirate cytological features are highly characteristic and quite distinct from those of other pancreatic tumors, which is reliable for preoperative SPTP diagnosis. However, in clinical scenarios, the tissues obtained by fine-needle aspiration are little, and the process has limitations and risks. Moreover, the pathological cellular morphology shows single cells and lack of differentiation, which is mainly diagnosed by immunohistochemistry. Most specimens cannot meet the requirements for pathological diagnosis.

Because SPTP does not respond to chemotherapy and radiotherapy,[20] surgical resection is the only effective treatment. There are 4 types of surgery: local tumor resection, segmental pancreatic resection, extended tumor resection, and partial tumor resection. Local tumor resection is mainly applied to a tumor that is well circumscribed on the surface or has growth on the outer pancreas, a well-defined capsule, and well-defined surrounding tissue without invasion. Local tumor resection is more appropriate for SPTP located at the pancreas head because of the adjacent anatomical structures, such as the common bile duct, duodenum, and large vessels, to reduce surgical difficulty and reduce postoperative complications (including bleeding and pancreatic leakage). Segmental pancreatic resection is suitable for tumors situated in the pancreatic parenchyma that are small in size and adjacent without invasion to the main pancreatic duct or surrounding vessels. Sealing off the proximal end and caudal pancreaticojejunostomy in the distal end are usually carried out in the pancreatic stump during surgery. Extended tumor resection includes duodenopancreatectomy, and pancreatic body and tail resection with splenectomy. SPTP compression of splenic

vessels causes hypersplenotrophy and hypersplenism, which results in less intraoperative likelihood of preserving the spleen.[21] Extended tumor resection is appropriate for tumors in the pancreas head or tail. In exploratory surgery, if the pancreatic tumors are found to encroach on the peripancreatic tissues or important surrounding vessels, invasion by the pancreas head tumors into the duodenum and superior mesenteric veins is evidenced, and pancreas body and tail tumors and tail encroach on the splenic hilum. Extended tumor resection is appropriate for radical excision, but it increases surgical difficulties and expands the scope, which increase the risk of postoperative complications accordingly. Partial tumor resection is a palliative surgery for tumors invading important vessels around or has been transferred to the abdominal cavity, and some tumor tissues will remain. Some reports also showed the therapeutic value of bone marrow–derived stem cells transplantation.[22]

SPTP is a low-grade malignancy tumor with the possibility of recurrence or metastasis after surgery. Tipton et al[23] followed up 14 patients with SPTP for 20 years, and 1 patient relapsed. Therefore, the tumor should be resected as completely as possible during surgery. After the SPTP is completely removed, the overall prognosis is good and only 5% of patients have local recurrence. The recurrence rate is obviously increased if there are malignant biological indications such as nerve or vascular invasion, obvious nuclear atypia, or splitting.

In this case report, we found that surgical resection remains the only effective treatment of SPTP. Furthermore, SIT with SPTP can be accurately diagnosed by heart USG, chest x-ray, CT, and CECT of the upper abdomen. Abdominal aorta CTA before surgery can decrease the injury risk of blood vessels. A good mastery of the operative skills together with a multidisciplinary approach for treatment can increase the success rate and avoid complications.

2.1. Statement of ethical

This information was approval by the patient and patient consent form has been signed in person. The Ethics Committee of the First Affiliated Hospital of Nanchang University was approval for this case.

Author contributions

Conceptualization: D. Xiang, J. He, F. Xiong, G. Wang, J. Shi.
Data curation: D. Xiang, J. He, Z. Fan, F. Xiong, J. Ai, R. Wan, G. Wang.
Formal analysis: D. Xiang, J. He, J. Li, J. Ai, R. Wan, G. Wang, J. Shi.
Funding acquisition: J. Shi.
Investigation: D. Xiang, J. He, Z. Fan, F. Xiong, G. Liu, S. Chen, W. Wen, J. Li, J. Ai, R. Wan, G. Wang, J. Shi.
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Project administration: J. Shi.
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Validation: S. Chen.
Visualization: J. He, F. Xiong, G. Liu, G. Wang.
Writing – original draft: D. Xiang, S. Chen.
Writing – review & editing: J. He, Z. Fan.

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