CASE REPORT

Surgical therapy of a large pancreatic solid-pseudopapillary neoplasm during pregnancy

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SUMMARY

Solid-pseudopapillary neoplasms (SPNs) of the exocrine pancreas are rare, accounting for only 2% of pancreatic tumours. These tumours predominantly affect women during the second and third decades of life. They frequently present with vague symptoms and can pose a diagnostic challenge. Surgical resection remains the treatment of choice that can cure up to 95% of patients when negative resection margins are obtained. SPNs diagnosed during pregnancy are exceptional and with profound implications on the mother and fetus. The authors present a case of an asymptomatic SPN in a 24-year-old woman diagnosed at 14 weeks of gestation on a routine prenatal ultrasound. Distal pancreatectomy, splenectomy and cholecystectomy were successfully performed at 18 weeks of gestation. A healthy full-term male child was born 5 months following surgery without complications.

BACKGROUND

Solid-pseudopapillary neoplasms (SPNs) of the exocrine pancreas^{1–5} account for about 2% of all exocrine pancreatic malignancies.^{1 3 4} SPNs affect predominantly women (>90% female dominance) during their second and third decades of life.^{4–8} SPNs have a typical appearance consisting of a fibrotic capsule surrounding a mass composed of solid and cystic regions with pseudopapillary projections.^{3–7 9} Areas of degeneration, necrosis and haemorrhage are also commonly seen in the central parts of SPNs.^{3 5}

The majority of patients with SPNs present with vague symptoms and the rest are discovered incidentally.^{1 3 7 8 10} Symptoms often develop late when the tumour is large enough to cause compression of adjacent viscera.⁵ Abdominal pain or a non-tender, palpable, upper abdominal mass constitute the most frequent symptom and finding.¹⁰ Other symptoms include early satiety, nausea, vomiting and diarrhoea.^{2 4 7 10}

Various imaging modalities can be used for the diagnosis of SPNs. The most frequent test is an abdominal ultrasound (US) that can reveal a well-circumscribed, heterogeneous pancreatic mass with cystic and solid components.^{7 10} Contrast-enhanced CT scans and MRI are more accurate and have better resolution for some of the typical radiological characteristics of SPNs such as the presence of a well-formed capsule, intratumoural haemorrhages and cystic degenerations.^{7 10}

SPNs are particularly rare during pregnancy and can become quite threatening given the potential for accelerated growth during this time.^{4–6 11} Here,

we report a case of an asymptomatic SPN in a 24-year-old woman diagnosed at 14 weeks of gestation on routine prenatal US. Distal pancreatectomy, splenectomy and cholecystectomy at 18 weeks of gestation were successfully performed. A healthy full-term male child was born 5 months following surgery without complication.

CASE PRESENTATION

A 23-year-old G1P0 woman undergoing routine prenatal examination by her family physician was discovered to have an epigastric mass at 14 weeks of gestation. The patient had been experiencing mild nausea, vomiting and intermittent epigastric discomfort, which were attributed to the pregnancy. There was no weight loss, constitutional symptoms, haematemesis or changes in genitourinary or bowel habits. There were no flushing, palpitations or any other symptoms that may accompany a neuroendocrine tumour.

The patient's medical history was unremarkable. She was a lifelong non-smoker and was not consuming any alcohol. There was no surgical history other than extraction of wisdom teeth. She had no allergies and her only medications were Diclectin and a multivitamin. There was a history of breast cancer and pancreatic adenocarcinoma in second-degree relatives.

Physical examination revealed a well-nourished woman in no apparent distress and with no evidence of jaundice. There was no cervical, supraclavicular or axillary lymphadenopathy. There was a palpable mass in the left epigastrium close to the lowest rib. Mild discomfort was present on deep palpation. The mass was distinguishable from the liver edge. Cardiopulmonary and peripheral vascular examinations were within normal limits.

INVESTIGATIONS

Haematological investigations were normal with the exception of lymphocytes ($1.2 \times 10^9/L$; normal value = $1.5–4.0 \times 10^9/L$) and monocytes ($1.4 \times 10^9/L$; normal value = $0.1–0.9 \times 10^9/L$). Electrolyte panel and liver function tests were within normal limits. Abnormal laboratory values included urea (2 mmol/L; normal value = 2.9–9.3 mmol/L) and lipase (16 U/L; normal value = 22–51 U/L). Carbohydrate antigen (CA) 19–9 was normal (5.6 U/mL; normal value ≤ 35 U/mL) as was carcinoembryonic antigen (1.2 µg/L; normal value < 5 µg/L for non-smokers). α Fetoprotein (20 ng/mL; normal value ≤ 10 ng/mL) and β -human chorionic gonadotrophin (37 414 IU/L; normal value > 9 IU/L after 4 weeks of gestation) were consistent with the patient's pregnancy status.

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US revealed a large heterogeneous soft tissue mass in the mid-abdomen measuring 16.3 cm in the greatest dimension (figure 1). The origin of the lesion was not well appreciated on US imaging. The mass did, however, appear distinct from the liver and the spleen.

Following the abdominal US, a non-gadolinium-enhanced MRI was obtained (figure 2). The MRI revealed a heterogeneous mass arising from the body and the tail of the pancreas. The mass demonstrated a background of intermediate T2 signal with multiple small areas of bright T2 signal, suggestive of fluid. There were also areas of bright T1 signal, indicative of blood within the mass. There was splenomegaly. No biliary ductal dilation was present and there were no hepatic lesions identified. The stomach was displaced anteriorly and to the right. The adrenal glands and kidneys were normal and there was no ascites. The appearance was consistent with an SPN of the pancreas.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of SPN of the pancreas includes:

- ▶ Serous cystadenoma
- ▶ Serous cystadenocarcinoma
- ▶ Mucinous cystadenoma
- ▶ Mucinous cystadenocarcinoma
- ▶ Intraductal, papillary, mucinous, neoplasm (IPMN)
- ▶ Endocrine pancreatic tumours with cystic transformation
- ▶ Pancreatic pseudocyst

Figure 1 Ultrasound image demonstrating a large heterogenous soft tissue mass (14.5×9×16.3 cm) in the mid-abdomen.

TREATMENT

The patient was referred to anaesthesiology as well as to pre-natal specialists to assess for any preoperative abnormalities that would alter the clinical decision-making. A fetal US was performed, which revealed normal growth with no concerning features. The patient received Pneumovax 3 weeks prior to surgery as well as Menactra and a vaccination against *Haemophilus influenzae* type B.

At 18 weeks of gestation, the patient underwent exploratory laparotomy and distal pancreatectomy, splenectomy and cholecystectomy. Pathology assessment of the surgical specimen revealed a mass measuring 15×14×9 cm (figure 3). The mass was well circumscribed with a definite capsule of 0.5–1.0 mm thickness. The distal end of the lesion was attached to the spleen by thin fibrous adhesions but the spleen was not invaded by tumour. Microscopic evaluation showed an encapsulated tumour composed of sheets of neoplastic cells with cystic degeneration. There was a dual population of neoplastic cells. One set had eosinophilic cytoplasm and the other had clear vacuolated cytoplasm as represented in figure 4A,B.

OUTCOME AND FOLLOW-UP

There were no intraoperative complications. The patient had ongoing nausea postoperatively which required insertion of a nasogastric tube with intermittent suction. The fetus was assessed on postoperative days 1 and 3 by ultrasonography, which demonstrated reassuring fetal status. Fetal US on postoperative day 7 revealed a normal fetus in the cephalic position with normal anatomy and an estimated fetal weight of 334 g. The patient was discharged on postoperative day 8 in stable condition.

A healthy full-term male child was born with vaginal delivery 5 months following surgery without complication.

The case was reviewed by a team of medical oncologists to assess the role of adjuvant chemotherapy following delivery. The team concluded that evidence was lacking from the three adjuvant chemotherapy trials available at the time to recommend any further treatment. Moreover, the low potential for metastatic spread with SPNs further deterred the provision of adjuvant chemotherapy.

Follow-up MRI and CT scans at 6 and 8 months postsurgery, respectively, revealed areas of enhancement around the surgical resection bed. This was believed to represent postsurgical change; however, residual or recurrent disease was not definitively excluded. A subsequent CT scan at postoperative 1 year demonstrated no evidence of residual or recurrent disease, with resolution of the focus of soft tissue enhancement previously seen.

DISCUSSION

SPNs of the pancreas are known to occur predominantly in young females. However, they do remain a rare neoplasm and owing to the fact that they typically present with vague, non-specific symptoms, they can pose as a diagnostic challenge.^{3–6} SPNs have a low malignant potential and as a result they are associated with good prognosis.^{1–3, 6–8} Even in the setting of metastatic disease, long-term survival following resection remains high.¹² The mainstay of treatment for SPNs confined to the pancreas is complete surgical excision.^{1–10} Ninety-five per cent of patients are completely cured when R0 resection is achieved.^{3–10} The most commonly employed surgical procedures include local resection, distal pancreatectomy and pancreaticoduodenectomy.¹ Malignant behaviour is typically predicted

Figure 2 Non-gadolinium-enhanced abdominal MRI (coronal and sagittal images) demonstrating a heterogeneous mass arising from the body and tail of the pancreas. Areas of increased T2 signal intensity suggest the presence of fluid-filled regions. Similarly, regions of increased T1-weighted signal intensity are indicative of blood.

based on the existence of vascular and neural invasion, invasion to surrounding tissue or the presence of distant metastases.¹ Most common sites of metastatic disease include the liver, lymph nodes and peritoneum.³ Approximately 10–20% of SPNs have malignant behaviour.^{3–10} Recurrence following R0 resection is rare and has only been reported in 3.5–6.6% of cases, all of which demonstrated malignant behaviour.¹ β -Catenin and E-cadherin proteins are expressed in all SPNs⁹ and the mutation in the β -catenin gene can be used as a distinguishing feature between SPN and pancreatic ductal adenocarcinoma.⁹ On the other hand, immunohistochemical stainings for α -antitrypsin and α -antichymotrypsin are common, but they vary.^{4–9}

Mutation in the β -catenin gene is thought to play a role in the pathogenesis of SPNs,^{8–9} while progesterone receptors (that are overexpressed in 80–100% of SPNs) seem to be responsible for the regulation of the rate of replication of tumour cells. This might

be one of the explanations for the high prevalence of SPNs among young women, and for the increased speed of growth observed when serum progesterone levels are elevated such as in pregnant women.^{4–5–7–9–11} Ganepola *et al*¹¹ reported a 5.5 cm SPN discovered on US during the fourth week of pregnancy. The mass was

Figure 3 Gross appearance of the resected spleen and solid-pseudopapillary neoplasm specimen (15×14×9 cm on cut section).

Figure 4 Sections showing characteristic pseudopapillae composed of aggregates of poorly cohesive monomorphic neoplastic cells between the fibrovascular stalks (A). Tumour cells admixed with abundant foamy histiocytes (B).

followed by serial US and was found to grow greater than 12 cm within 4 months. In other cases of patients with SPNs outside of pregnancy, the tumours have been slow growing.^{4 5} Considering the significant effect played by serum progesterone levels, it might be expected that more cases of SPNs would be observed in young pregnant women. However, to the best of our knowledge, there exist only eight reports of SPN discovered and resected during pregnancy (table 1).

There are no treatment guidelines for pregnant women with SPNs, and therefore decisions around the optimal time for surgical management can be challenging.^{9 13} The prognostic benefits of resection must be weighed together with patient values, wishes and the possibility of causing harm to the developing fetus. Considering that SPNs have low malignant potential, it has been suggested that a small SPN is not an absolute indication for resection during pregnancy.⁷ However, there is a possibility for malignant transformation, rapid tumour growth and tumour rupture, all of which have the potential to harm the mother and the developing fetus.^{1 6 11}

Although reports remain limited, the examples presented in table 1 together with our case provide support for the surgical treatment of SPNs discovered during pregnancy. In all of the examples, with the exception of that by Duff and Greene,¹⁴ fetal development was not impacted by surgery. In the case of Bondeson *et al*,¹⁵ postoperative fetal assessment was normal and termination of the pregnancy was based on patient's wishes. It is suggested that surgical treatment of patients with SPN of the pancreas during pregnancy is relatively safe up to, and including, the second trimester.^{2 6 7} Fortunately, these neoplasms are frequently discovered between gestational weeks 4 and 14, allowing time for accurate diagnosis and operative planning.

Our patient, like many of the other examples, presented with relatively vague symptoms of abdominal discomfort, nausea and vomiting. These may be falsely associated with pregnancy in patients presenting for routine prenatal care. In the absence of a focused physical examination and appropriate diagnostic

workup, SPNs during pregnancy may go undetected for some time. The propensity of these tumours to become rather large could result in spontaneous abortion, intrauterine growth restriction or premature delivery if they are overlooked.⁷

In conclusion, SPNs of the pancreas are a tumour known to occur in young women in the second to third decade of life. Increased growth rates have been observed in the setting of elevated levels of progesterone. As such, rapid tumour growth in patients who are pregnant has the potential to offer devastating effects on the mother and the developing fetus. The prognosis of patients with SPNs that have been completely resected is good. However there are only rare reports of patients with SPNs during pregnancy. Those that have been identified demonstrate the relative safety of surgical resection in the second trimester.

Learning points

- ▶ Solid-pseudopapillary neoplasms (SPNs) of the pancreas are a rare tumour typically affecting women between ages 20 and 30 years.
- ▶ Clinical presentation is often vague and requires careful physical examination and diagnostic evaluation for accurate detection.
- ▶ Increased SPN growth rates have been observed in the setting of excess progesterone.
- ▶ SPNs of the pancreas during pregnancy are rarely reported in the literature but can have profound impacts on the mother and the developing fetus if left undetected.
- ▶ Aggressive, complete surgical resection is the mainstay of treatment for these neoplastic processes and offers patients a very good long-term prognosis.
- ▶ Surgical resection of SPNs performed up to, and including, the second trimester of pregnancy appears to be a safe and effective treatment.

Table 1 Literature examples of SPN during pregnancy

Authors	Patient age (years)	Presentation; gestational age at diagnosis (week)	Gestational age at surgery (week)	Tumour location; size (maximum diameter) in cm	Surgical procedure	Pregnancy outcome
Feng <i>et al</i> ²	26	Palpable abdominal mass; 14	14	Head; 9.5	EL; tumour enucleation	Labour at 38 weeks, C-section
Levy <i>et al</i> ⁴	27	N/V, weight loss; 12	16	Head; 6	Whipple	Labour induction at 34 weeks, SVD
Morales <i>et al</i> ⁵	21	Abdominal pain, N/V; 4	6	Head; 8.2	EL; Whipple	SVD at 39 weeks
Huang <i>et al</i> ⁶	29	Abdominal pain and tenderness, N/V; 19	19	Body and tail; 17	Emergent exploratory reverse-T laparotomy; subtotal pancreatectomy and splenectomy	SVD at 29 weeks
Hajdu <i>et al</i> ⁷	29	Palpable abdominal mass; 13	13	Tail; 16	DP	C-section at 38 weeks
Ganepola <i>et al</i> ¹¹	37	Abdominal pain; 4	23	Tail; 12	DP, splenectomy and cholecystectomy	SVD at term
Duff and Greene ¹⁴	35	Palpable abdominal mass; 13	14	Head; N/A	Needle biopsy, embolectomy and Whipple	Spontaneous abortion after embolectomy
Bondeson <i>et al</i> ¹⁵	19	Abdominal pain; 4	4–5	Head; 8	EL, biopsy and Whipple	Postoperative pregnancy termination
Current	23	Abdominal pain; 14	18	Body and tail; 14×15	Distal splenopancreatectomy and cholecystectomy	SVD at 41 weeks

C-section, caesarian section; DP, distal pancreatectomy; EL, exploratory laparotomy; N/A, not available; N/V, nausea and vomiting; SPN, solid-pseudopapillary neoplasm; SVD, spontaneous vaginal delivery.

Contributors FM wrote the case report and reviewed the literature. VK revised the manuscript and interpreted the radiological findings. MM revised the manuscript, reviewed the literature and performed the surgical resection.

Competing interests None.

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