Solid Pseudopapillary Tumour of Pancreas in Pregnancy: Case Report

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Abstract: Solid-pseudopapillary neoplasms (SPNs) of the exocrine pancreas are rare, accounting for only 2% of pancreatic tumours. These tumours predominantly affect females during the second and third decades of life. Of uncertain histogenesis, it has a low-grade malignant potential with excellent post-surgical curative rates and rare metastasis. Despite advances in imaging, pseudocysts and other cystic neoplasms feature in the differential diagnosis. Pathological and/or cytological evaluation remains the gold standard in reaching a definitive diagnosis. We report a case of asymptomatic SPN in a 22-year-old woman diagnosed at 16 weeks of gestation on routine prenatal ultrasound. Pylorus preserving Whipple’s pancreaticoduodenectomy was performed following medical termination of pregnancy.

Keywords: Solid pseudopapillary tumour, Pancreas, Pregnancy

INTRODUCTION

Solid pseudopapillary tumor of the pancreas (SPT) is a rare neoplasm occurring almost exclusively in young women (91.3% of the cases) [1, 2]. It is also known as solid and papillary epithelial neoplasm, papillary-cystic neoplasm, and cystic-solid papillary carcinoma of the pancreas, Hamoudi or Franz tumour. The tumour has been given several different names according to its macroscopic and microscopic character; until this name, solid pseudopapillary tumour of the pancreas, was defined by the World Health Organization (WHO) as unique tumor in 1996 [3]. First described by Franz in 1959, solid pseudopapillary tumor of the pancreas (SPT) is a rare, low grade malignant tumor of unknown etiology accounting for 0.2-0.7% of all primary pancreatic tumours [1, 4, 5].

Abdominal pain is the most common presenting symptom, with dyspepsia, early satiety, nausea, or vomiting being less common presenting symptoms. Up to 20% of patients are asymptomatic with tumors identified either incidentally on imaging or at operation for unrelated pathology [2, 4, 6, 7-9].

Although it can grow very large, it is mostly locally invasive and metastasizes rarely; the prognosis is therefore favorable, especially after complete resection. Most tumors are surgically resectable; furthermore, SPT is sensitive to radiotherapy, which can be used in the few inoperable cases.

Pancreatic neoplasms, both benign and malignant, are uncommon during pregnancy. There have been only eight reported cases of pancreatic adenocarcinoma [10-17], thirteen cases of cystic pancreatic lesions diagnosed during pregnancy [18-30] and three reported cases of pancreatic neuroendocrine tumors [31, 32]. Their occurrence during pregnancy leads to dilemmas in diagnosis, management, and timing of surgical treatment. In all cases the goal is to minimize both maternal and fetal risk. The timing of surgical resection for pancreatic neoplasms during pregnancy must take into account the risk of maternal disease progression and safety of the developing fetus.

CASE REPORT

A 22 year old G2P1 female undergoing routine prenatal ultrasound at 16 weeks of gestation was found to have large heterogenous space occupying lesion with solid cystic components in the right side of retroperitoneum, in view of the para duodenal / hepato-pancreatic recess location of the mass, possibilities of GIST/ retroperitoneal sarcoma was considered.

The patient has been experiencing epigastric discomfort occasionally, nausea and vomiting which were attributed to pregnancy. There was no constitutional symptoms, weight loss, hematemesis or alteration in genitourinary or bowel habits. On physical examination patient had discomfort in epigastric region on deep palpation, but mass was not palpable.

Following ultrasound, MRI with gadolinium contrast was performed which showed a well defined encapsulated, heterogenous, solid-cystic lesion noted in right upper quadrant in subhepatic region (Fig. 1). The solid components are showing isointensity on T1WI and intermediate signal on T2WI. Superiorly, the lesion is abutting the inferior surface of liver. Posteriorly it is...
abutting the right anterior renal fascia and causing mass effect and pushing the right kidney posteriorly. Medially it is abutting the second part of duodenum, causing medial displacement of common bile duct and inferior vena cava. These features were suggestive of soft tissue tumour of mesenchymal origin/GIST. Other haematological investigations were normal, tumour markers CEA and CA19-9 were normal.

The prognostic benefits of resection and possibility of causing harm to the developing fetus were discussed with the patient. The patient did not wish to continue pregnancy; subsequently medical termination of pregnancy was performed at 16 weeks of gestation. Patient underwent exploratory laparotomy, tumour was found to be arising from head of the pancreas, pylorus preserving Whipples pancretico-oduodenectomy was performed (Fig. 2).

Histopathological assessment of the surgical specimen revealed a well encapsulated grey white soft tumour with duodenum stretched and compressed on its surface measuring together 12X10X8 (Fig. 3). The encapsulated tumour appears to be separate from the intestinal wall attached to serosa. Microscopic sections reveal an encapsulated, cellular tumour consisting of sheets of cells with pseudopapillary structures, haemorrhages and focal necrosis, with occasional mitosis (Fig. 4). These histological features are those of solid pseudopapillary tumour of the pancreas. IHC revealed expression of beta catenin in the nuclei and absence of e-cadherin staining. In addition, the tumor expressed progesterone receptor, vimentin, CD10 and CD56. Focal synaptophysin and chromogranin positivity was seen, Alpha-1 antitrypsin was focally expressed (Fig. 5).
DISCUSSION

Cystic pancreatic neoplasms were first classified by Robson and Moynihan in 1903. Incidental pancreatic cystic lesions have an incidence of 0.2% to 0.7%. Solid pseudopapillary neoplasm (SPN) or Frantz tumor of the pancreas is a rare pancreatic tumor of uncertain lineage seen in young, predominantly Asian females, first reported by Frantz in 1959 [1]. Santini et al. [39] indicate that it probably arises from pluripotent pancreatic cells, as there is no definitive evidence of its pancreatic origin, whether endocrine or exocrine. Kosmahl et al. [37] suggest that the tumor originates from the incorporation of primitive ovarian cells within the pancreatic parenchyma during the seventh week of embryogenesis, though this does not justify the presence of malignancy in males. Earlier detection and increased awareness of these neoplasms has led to their increased prevalence in recent years [34].

SPT has a particularly high prevalence in females younger than 35 years of age. In the largest retrospective review conducted to date including 718 patients with SPT, more than 90% of patients were female with an average age of 22 years [6, 36, 37].
Several hypotheses have been proposed to explain this distribution. The hormonal factor has been mostly implicated, due to the presence of progesterone receptors in the tumor and lesion progression during pregnancy [38]. Kosmahl et al. [37] identified the presence of progesterone receptors in more than 90% of 59 SPTPs through immunohistochemistry.

Many patients present with irrelevant signs and symptoms. When symptomatic, they may have recurrent episodes of pancreatitis, chronic abdominal pain and a palpable mass. Large tumors can compress the stomach, duodenum and bile ducts, resulting in early satiety, vomiting or jaundice. In a study that evaluated 37 patients, it was found that abdominal pain was the most common symptom, affecting 84% of subjects [40].

The most common location of SPTP in the literature is the tail, and the second most common site is the head [41]. The primary tumor is almost invariably ovoid and with large dimensions at diagnosis (usually greater than 6 cm, reaching up to 30 cm), probably due to its indolent growth.

Macroscopically, the mass appears with complex texture, with solid and cystic components and hemorrhagic and/or necrotic content, with internal debris [37, 39]. Microscopically, Frantz tumor presents as an encapsulated lesion with cystic and solid areas. The solid component shows a pseudopapillary structure. Eosinophilic cytoplasm is often observed in the tumor’s cells and cytoplasmic vacuoles may also be evident. The nucleus is round to oval, with a uniform appearance. The stroma can be hyaline or myxoid [37, 39].

The cystic appearance on gross examination may present a diagnostic dilemma with cystic neoplasm of the pancreas. Immunophenotyping has been used to differentiate these tumours from other pancreatic neoplasms. Traditionally, immunohistochemistry shows negative neuroendocrine markers, particularly chromogranin, which has been considered the key in differentiating SPTPs from neuroendocrine tumors. Nguyen et al. [42] showed positivity for synaptophysin in 36%, chromogranin in 15%, and beta-catenin in 100%, the latter being considered the most sensitive and specific marker for Frantz tumor.

CD10 positivity is characteristic of SPTPs and is less useful in the differential diagnosis, as it is positive in about 10% of invasive ductal adenocarcinomas and neuroendocrine tumors.

Alpha-1-antitrypsin and alpha-1-antichymotrypsin indicate exocrine pancreatic origin, while neuron-specific enolase and synaptophysin are characteristic of neuroendocrine tumors [43].

The presence of progesterone receptors is another feature of Frantz tumor [44]. In addition to negative chromogranin, synaptophysin and enolase, which virtually rule out pancreatic islets malignancy, the absence of cytokeratin excludes acinar carcinoma [43, 44].

The imaging features of SPT reflect the pathologic findings of cystic and solid components, intratumoral haemorrhage, a fibrous capsule and, less commonly, calcification. When present, the fibrous capsule and internal haemorrhage are the features that distinguish SPT from other pancreatic tumours [45, 46].

USG and CT show a large well-circumscribed mass with quite variable appearance depending on its composition. Tumours compress adjacent structures rather than invading them. CT shows solid portions of the mass to be iso to hypoattenuating to the pancreas and that of cystic components slightly hyperattenuating than gallbladder due to the presence of blood products and debris. Calcification is seen in one-third of the cases with only minimal enhancement [45, 46].

MRI shows hypointense fibrous capsule and internal haemorrhage (seen as high-signal intensity on T1W images) and is very characteristic of SPT. Solid portions of the tumour are iso to hypointense to pancreas on T1-weighted images and slightly hyperintense to pancreas on T2-weighted images. Early peripheral, heterogeneous enhancement greater than that of the adjacent pancreas and sometimes progressive fill-in on dynamic-enhanced images are seen [46, 47].

SPT was classified according to the WHO criteria as either an SPT with an uncertain potential for malignancy or as a solid pseudopapillary carcinoma (SPC) [48]. Criteria that could distinguish potentially malignant tumors, classified as SPC, included the following: 1) perineural invasion, 2) angioinvasion, 3) deep invasion into the surrounding tissue, and 4) distant metastases. Postoperatively, patients were further classified using the American Joint Committee on Cancer (AJCC)/International Union Against Cancer (UICC) tumor node metastasis (TNM) classification system: R0 (no residual tumor), R1 (microscopic residual tumor), or R2 (macroscopic residual tumor) [49].

The malignant potential of SPT is reported to be 10%-15% [36]. The most common sites of metastases are the liver, regional lymph nodes, mesentery, omentum, and peritoneum [35]. Local invasion may involve adjacent organs, including the duodenum, spleen, portal vein, superior mesenteric
vein, and bile duct; lymph node metastasis also has been reported [50, 51].

The mainstay of treatment for SPNs confined to the pancreas is complete surgical excision. 95% of patients are completely cured when R0 resection is achieved [53, 54]. The most commonly employed surgical procedures include local resection, distal pancreatectomy, and pancreaticoduodenectomy [52].


ganepola et al. [20] reported a 5.5 cm SPN discovered on US during the fourth week of pregnancy. The mass was followed by serial US and was found to grow to greater than 12 cm within four months. In other cases of patients with SPNs outside of pregnancy, the tumors have been slow growing [38, 55]. It might be expected that more cases of SPNs would be observed in young pregnant women due to the effect of progesterone. However, to our knowledge there exist only nine reports of SPN discovered and resected during pregnancy [20, 54, 55, 57-60]. 5 cases presented with pain abdomen, 3 cases presented with mass abdomen, 1 with weight loss. All patients underwent surgery as treatment for SPNs without affecting fetal development except Duff et al. [59].

There are no treatment guidelines for pregnant women with SPNs and decisions around the optimal time for the surgical management can be challenging [44, 56]. The prognostic benefits of resection must be weighed together with patient values, and the possibility of causing harm to the developing fetus and termination of pregnancy was based on patient wishes. Considering that SPNs have low malignant potential, it has been suggested that a small SPN is not an absolute indication for resection during pregnancy [54]. However, there is the possibility for malignant transformation, rapid tumor growth, and tumor rupture, all of which have the potential for harm to the mother and developing fetus [20, 52].

**CONCLUSION**

SPNs of the pancreas are a tumour known to occur in young females in the second to third decade of life. Rapid tumor growth due to elevated levels of progesterone in patients who are pregnant has the potential to offer devastating effects on both mother and the developing fetus. It is well known that the prognosis of patients with SPNs that have been completely resected is very good. Although there are only rare reports of patients with SPNs during pregnancy, those that have been identified demonstrate the relative safety of surgical resection up to the second trimester as fetal organogenesis is complete and size of the fetus allow easier surgical procedure when compared to third trimester operations. Termination of pregnancy before resection of SPNs is based on patients wishes.

**REFERENCES**

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