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Solid pseudopapillary neoplasm of the pancreas during pregnancy presenting as gastrointestinal stromal tumor: A case report and review of literature

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Abstract:

Solid pseudopapillary neoplasm (SPN) is a rare tumor that can complicate pregnancy. More than its rarity, SPNs are unique neoplasms because of their obscure histogenesis, cytology, immunohistochemical profile, and imaging characteristics. This report describes the case of a 32-year-old gravida 2 para 1 (1001) seen at 24 weeks with an intra-abdominal mass. The patient presented with a long-standing history of abdominal mass with the working impression of gastrointestinal stromal tumor. We employed a multidisciplinary approach to closely monitor tumor growth, ensure maternal and fetal well-being, avert complications, and avoid unnecessary clinical interventions. Histopathological evaluation and immunohistochemistry studies of representative specimens taken at the time of delivery revealed the diagnosis of SPN of the pancreas. Based on a review of local search engine databases, this is the first documented case of SPN complicating pregnancy in the Philippines.

Keywords:

Intra-abdominal mass, pregnancy, solid pseudopapillary neoplasm

Introduction

Pregnancy-associated pancreatic cystic lesions are the rare cystic neoplasms of the pancreas, the most common of which are mucinous cystic neoplasms followed by solid pseudopapillary neoplasms (SPNs).[1] SPNs are rare low-grade malignant pancreatic tumors that represent 1%–2% of all pancreatic tumors, and it is even rare during pregnancy, with only 17 cases reported in the literature to date.[2] More than its rarity, SPNs are unique neoplasms by their obscure histogenesis, cytology, immunohistochemical profile, and imaging characteristics. More importantly, SPNs pose a particular challenge because of the associated accelerated growth during pregnancy that may be life-threatening.[3] Occasionally, the diagnosis of SPN is made by pathological examination postoperatively following a provisional diagnosis of gastrointestinal stromal tumor (GIST).[4]

We report the case of SPN during pregnancy presenting as a giant GIST and highlight the multidisciplinary approach in diagnosis, antenatal surveillance, and surgical management. In addition, we present a literature review of published reports of SPN during pregnancy.

Case Report

A 32-year-old woman gravida 2 para 1 (1001), with an unremarkable medical history, presented to our high-risk pregnancy clinic at 24 weeks and 6 days age of gestation. She has a 4-year history of

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increasing abdominal girth associated with early satiety and unintentional weight loss, for which an abdominal ultrasound was done, revealing a solid mass of unknown etiology located on the right upper quadrant measuring 11.0 cm × 6.4 cm × 5.4 cm. Computed tomography (CT) scan of the abdomen at that time revealed a heterogeneously enhancing complex predominantly solid mass at the right hemiabdomen seen inferior to the gallbladder measuring 6.1 cm × 5.7 cm × 8.3 cm. A GIST was suspected, and the patient was advised to undergo surgery. However, the patient was lost to follow-up until she presented at 7 weeks of amenorrhea. Physical examination revealed a palpable right abdominal mass necessitating additional diagnostic evaluation. Abdominal magnetic resonance imaging (MRI) done at 13 weeks gestational age showed a large lobulated complex mass in the right upper abdomen measuring up to 12.7 cm × 10.9 cm × 8.7 cm [Figure 1]. The mass was predominantly cystic with interspersed solid components appearing as T1/T2 hypointense, with patchy areas of restricted water diffusion and magnetic susceptibility artifacts. The pancreatic head and duodenum appeared splayed and compressed, along with the gallbladder, hepatic flexure, and proximal transverse colon. The superior mesenteric vessels were displaced to the left, while the inferior vena cava was slightly compressed. There was a distinct fat plane between the mass and the gravid uterus. The impression then was a GIST.

The patient was first seen by the maternal-fetal medicine (MFM) service at 24 weeks age of gestation for a congenital anomaly scan which showed no gross fetal structural anomalies. Ultrasound of the maternal abdominal organs at that time revealed an ovoid, heterogeneous mass measuring approximately 12.46 cm × 13.36 cm × 12.16 cm in the right hemiabdomen showing septations and small cystic components and minimal peripheral and intralesional vascularity was detected on color Doppler interrogation [Figure 2]. Superiorly, the liver and gallbladder were indented. The gallbladder was not compressed. Posteriorly, no hydronephrosis was seen in the right kidney. Inferiorly, there was no gross extension to the uterus. The MFM service planned to monitor maternal symptoms and tumor size with ultrasound, along with antenatal fetal surveillance starting at 28 weeks. Moreover, the MFM service convened a multidisciplinary team of experts consisting of a MFM specialist, hepato-biliary surgeon, medical oncologist, neonatologist, and bioethicist at 28 weeks. The working impression of the team was a GIST. Because of the paucity of established treatment protocols for GIST in pregnancy and the absence of symptoms in our patient, the multidisciplinary team agreed to manage the patient conservatively and delay the resection of the tumor after delivery. The goal was to carry the pregnancy as close to term as possible while monitoring maternal symptoms, tumor progression, and fetal status and to attempt a trial of vaginal delivery at term. The risk of unexpected tumor rupture and the potential of the tumor to externally compress the uterus, which could consequently lead to preterm labor, were discussed with the patient.

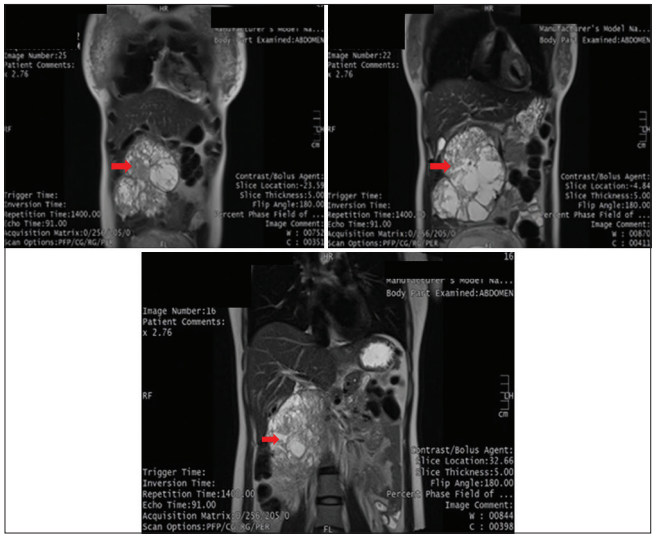

Figure 1: Whole abdominal Magnetic Resonance IMaging (MRI) at 13 weeks age of gestation. A large lobulated complex mass (red arrow) is seen in the right upper abdomen measuring up to 12.7 cm × 10.9 cm × 8.7 cm. It appears mostly cystic with interspersed solid components appearing T1/T2 hypointense, with patchy areas of restricted water diffusion and magnetic susceptibility artifacts

At 29 weeks and 4 days age of gestation, the patient experienced a tolerable, gnawing pain in the right upper abdominal area accompanied by shortness of breath and weakness in both upper and lower extremities. She was given oral analgesics, which provided relief of the abdominal pain and managed as a case of preterm labor, receiving a course of antenatal corticosteroids. A laboratory work-up revealed hypokalemia which was subsequently corrected. A follow-up abdominal ultrasound showed no significant increase in size or any sonologic signs of tumor complications [Figure 3]. Antenatal fetal surveillance was also reassuring. The patient showed improvement and was discharged after 3 days of hospitalization. The rest of the antenatal course was unremarkable, with reassuring antenatal fetal

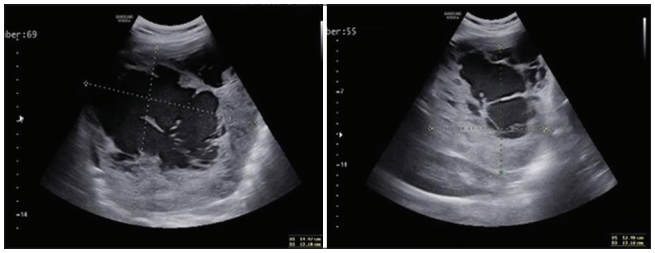

Figure 2: Ultrasound image of the intra-abdominal mass at 24 weeks age of gestation showing an ovoid, mixed, solid and cystic mass measuring approximately 12.46 cm x 13.36 cm x 12.16 cm on the right hemiabdomen

surveillance results. She was admitted at 38 2/7 weeks age of gestation for a trial of vaginal delivery. On admission, the fundal height was 35 cm, and there was a palpable 13 cm × 10 cm cystic, nonmovable, nontender mass at the right upper quadrant. The patient underwent low segment cesarean section for arrest of cervical dilatation secondary to fetopelvic disproportion and delivered a live baby boy, 3835 g, 38 weeks large for gestational age.

Intraoperatively, the mass occupied the upper abdominal quadrants, superior to the uterus. The mass had a smooth outer surface with both cystic and solid components [Figure 4]. After delivery, the surgical team proceeded to resect a representative section of the abdominal mass for histopathological investigation. This revealed round-cell proliferation favoring a neoplastic process [Figure 5]. The preliminary morphological considerations were quite diverse, with the likelihood of an origin in the pancreas being the most significant. Immunohistochemistry studies for CD10, vimentin, beta-catenin, chromogranin, synaptophysin, cytokeratin, and Ki-67 support the diagnosis of SPN of the pancreas showing positivity to CD10 and vimentin, nuclear expression of beta-catenin, and low positivity to Ki-67 (1%) [Figure 6]. Furthermore, histopathological examination of the placenta was unremarkable, with no signs of tumor metastasis.

At the time of writing, the patient is monitored by medical oncology and the surgery outpatient department. The goal is to provide the patient with neo-adjuvant chemotherapy by giving gemcitabine and to perform surgery for the definitive resection of the tumor 3 months postdelivery.

Discussion

The exact incidence of SPN during pregnancy is unknown. In 2020, Santos *et al*. summarized 13 case reports of SPN during pregnancy described in the literature.[5] We conducted a literature review and added four more cases of SPN during pregnancy to this list. Table 1 summarizes these cases.

The clinical presentation of SPN in pregnancy may differ from asymptomatic to severe symptoms, such as abdominal pain and vomiting, which may be

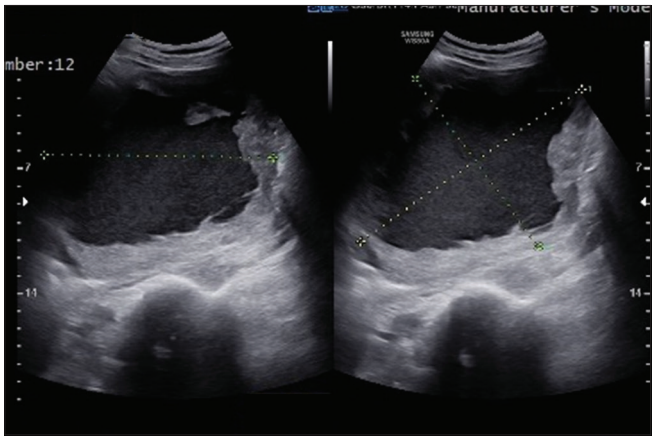

Figure 3: Antenatal ultrasound monitoring of the intra-abdominal mass showed no significant interval change in size from previous scans and no sonologic evidence of tumor complication

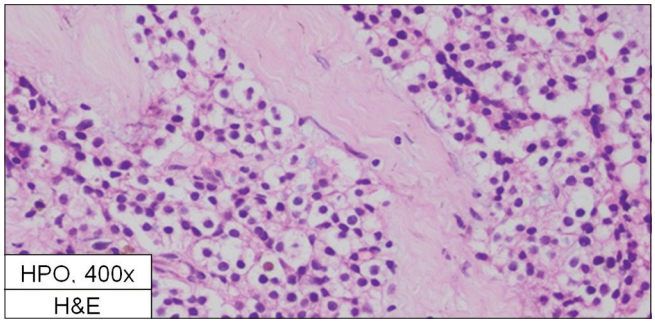

Figure 5: Histopathologic examination of representative sections showed round-cell proliferation favoring a neoplastic process. The cells are monomorphic and have small nuclei and clear cytoplasm

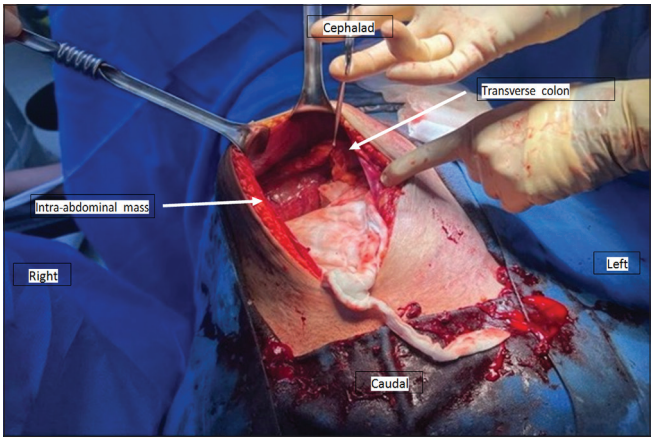

Figure 4: Intraoperative picture showing the intra-abdominal mass, which occupied the upper abdominal area superior to the uterus

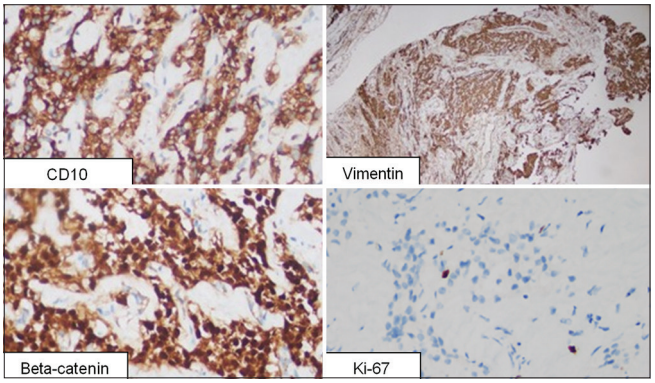

Figure 6: Immunohistochemical studies showing tumor cells positive to C10, vimentin, beta-catenin, and low positivity for Ki-67 (1%)

Table 1: Summary of previously published solid pseudopapillary neoplasms during pregnancy

Authors	Year	Patient age	AOG at diagnosis (weeks)	Surgical timing	Tumor location	Tumor size (cm)	Surgical procedure	Pregnancy outcome
Duff and Greene	1985	35	13	14 weeks AOG	Head	N/A	Needle biopsy, embolectomy, and Whipple	Spontaneous abortion after embolectomy
Bondenson *et al*.	1990	19	4	4–5 weeks AOG	Head	8	EL, biopsy, and Whipple	Postoperative pregnancy termination
Morales *et al*.	1998	21	4	6 weeks AOG	Head	8.2	EL, Whipple	SVD at 39 weeks
Ganepola *et al*.	1999	37	4	23 weeks AOG	Tail	12	DP, spleenectomy and cholecystectomy	SVD at term
Levy *et al*.	2004	27	12	16 weeks AOG	Head	6	Whipple	Labor induction at 34 weeks, SVD
Hajdu *et al*.	2009	29	13	13 weeks AOG	Tail	16	DP	C-section at 38 weeks
Feng *et al*.	2011	26	14	14 weeks AOG	Head	9.5	EL tumor enucleation	Labor at 38 weeks, C-section
Huang *et al*.	2013	29	19	19 weeks AOG	Body and tail	17	Emergent exploratory reverse-T laparotomy; subtotal pancreatectomy and splenectomy	SVD at 29 weeks
MacDonald *et al*.	2014	23	14	18 weeks AOG	Body and tail	16.3	Exploratory laparotomy and distal pancreatectomy, splenectomy, and cholecystectomy	SVD at term
Sharanappa *et al*.	2015	22	16	16 weeks AOG	Head	12	Pylorus preserving Whipple's pancreaticoduodenectomy	Medical termination of pregnancy
Yee *et al*.	2015	39	18	3 months postpartum	Head	10.6	Pylorus preserving Whipple's pancreaticoduodenectomy	SVD at 40 weeks; uncomplicated postoperative course
Tanacan *et al*.	2018	26	35	4 months postpartum	Head	9.5	Subpartial pancreatectomy, partial gastrectomy, duodenectomy, cholecystectomy and omentectomy	C-section at 36 weeks
Huang *et al*.[3]	2018	26	21	22 weeks AOG	Tail	13	Tumor enucleation	SVD at 39 weeks
Al-Umairi *et al*.[11]	2015	34	28	3 months postpartum	Body and tail	13	EL tumor resection	C-section at 38 weeks
Santos *et al*.[5]	2020	23	24	2 months postpartum	Tail	14	Subpartial pancreatectomy, partial gastrectomy, cholecystectomy, total splenectomy, and partial hepatectomy	C-section at 36 weeks
Motsepe *et al*.[6]	2020	28	20	Immediate postpartum	Body	17	Postdelivery tumor resection	C-section at 35 weeks
Ganzoui *et al*.[7]	2021	26	11	11 weeks AOG	Body	5.5	EL left pancreatectomy	Medical termination of pregnancy

The first 12 cases listed on Table 1 have been enumerated and cited in the study of Santos *et al*.[5] N/A: Not available, EL: Exploratory laparotomy, SVD: Spontaneous vaginal delivery, DP: Distal pancreatectomy, C section: Cesarian section, AOG: Age of gestation

accompanied by premature labor.[3] Case reports have demonstrated that abdominal pain or findings of an incidental mass during routine imaging as part of antenatal care are the most common clinical signs or symptoms. Nonspecific symptoms secondary to the tumor compressing the otherwise normal pancreas include nausea, fever, vomiting, weight loss, and jaundice.[3] Despite having an average size of 8–10 cm and being a relatively indolent tumor, it can grow as large as 25 cm.[8] From the reported cases, we calculated the mean tumor size to be 11.87 cm, which could make one infer that these tumors are more likely to present with symptoms, as seen in our patient, who had increasing abdominal girth, early satiety, and weight loss.

Table 1 shows that SPN tends to be diagnosed during the second trimester of pregnancy, with the average age of diagnosis at 15.88 weeks of gestation. Diagnosing pancreatic SPN in pregnant women can be challenging as there are no consistent specific tumor markers associated with these tumors, and imaging features can overlap with other pancreatic tumors, such as GISTs, as seen in our patient.[6] Ultrasonography is often the initial imaging modality used to diagnose SPN during pregnancy. SPN generally appears as a well-defined, solid, hypoechoic mass with peripheral cystic components on ultrasound.[9] On the other hand, GIST can also have hypoechoic areas and is difficult to distinguish from SPN solely based on ultrasound.[10] CT can help differentiate SPN from GIST, as it can provide information about the tumor's size,

contour, and internal structure. SPN typically appears as a well-circumscribed and encapsulated mass with a heterogeneous internal structure featuring solid and cystic areas secondary to hemorrhagic degeneration.[11] On the other hand, GIST tends to be more heterogeneous in density and intensely enhanced with contrast, which can aid in distinguishing them from SPN.[12] MRI is preferred over CT for imaging pregnant women because of the lack of ionizing radiation. SPN typically appears as well-circumscribed masses with cystic components, low-signal intensity on T1-weighted images, and high-signal intensity on T2-weighted images.[13] GIST can also appear as a solid, well-demarcated mass with cystic areas containing a more heterogeneous internal structure than SPN.[14] In our index case, a provisional diagnosis of GIST before pregnancy was made based on the CT scan findings of a heterogeneously enhancing complex, predominantly solid mass in the right hemiabdomen inferior to the gallbladder. The frequent occurrence of GIST as the most prevalent mesenchymal tumor and the resemblances observed in MRI between GIST and SPNs could explain why GIST was the impression on the MRI of our index patient. Misdiagnosis of SPN as GIST can significantly impact the therapeutic decision-making process as the latter is considered to have a poor prognosis while the former has a favorable prognosis.[15]

SPN presents as a round, solitary, and well-circumscribed lesion. Of the 17 cases reported during pregnancy, 9 (53%) were in the pancreatic head, 4 (23%) in the pancreatic tail, 2 (12%) in the body, and the rest occupied the body and tail. Histology and immunohistochemistry, which also aid in separating SPN from other pancreatic neoplasms with equivalent radiologic features, are employed to confirm the diagnosis of SPN during pregnancy. Histologically, the tumor cells are organized as nests, tubules, and pseudopapillae with centrally or eccentrically located nuclei with pale eosinophilic cytoplasm and positive immunohistochemical staining with CD10, vimentin, synaptophysin, progesterone receptors, and nuclear expression of beta-catenin.[7] Rarely seen are mitotic figures (0-6/20 HPF) with no atypical forms and low positivity on Ki-67 immunohistochemical stain.[16] In our case, the diagnosis of SPN was confirmed by histologic examination and immunohistochemistry of the excised specimen with positivity to CD10 and vimentin, nuclear expression of beta-catenin, and low positivity to Ki-67 (1%).

One of the challenges in managing patients with SPN is predicting tumor behavior during presentation. Although pathogenesis and cell origin remain unclear, they are considered low malignant potential tumors.[17] Up to 5%–15% of patients demonstrate gross, malignant features, such as distant metastases or invasion of adjacent organs at the time of diagnosis or during the long-term follow-up after surgery.[18] Although the WHO criteria of malignancy for SPN mainly considers microscopic features, they may not always accurately predict the clinical prognosis of malignancy. Furthermore, the favorable prognosis and long-term survival of SPNs may be due to a lack of reliable clinical parameters and histologic features for predicting malignant behavior.[19]

SPN is more challenging to manage in pregnancy because it poses a risk to maternal and fetal well-being.[18] Maternal and fetal complications of SPN during pregnancy include preterm labor, fetal distress, maternal bleeding, and maternal hypovolemia. SPN during pregnancy can lead to maternal complications due to an increase in the size of the tumor, leading to compression of adjacent organs, disruption of pancreatic ducts, and invasion of adjacent vessels leading to hemorrhage. Often, the complication arises during the second trimester of pregnancy, and surgical intervention becomes imperative.[11] It has been suggested that an elevated level of progesterone during pregnancy may be associated with the growth or rupture of SPNs of the pancreas. As a result, rapid tumor growth may occur during pregnancy.[6] This is likely related to the expression of progesterone-sensitive receptors during pregnancy.[20] However, further research is required to determine the causal relationship between pregnancy and tumor growth.

To date, few case reports have described SPN's clinical and therapeutic management in pregnant patients. Because of its rarity, data gaps and a lack of clinical guidelines exist in the medical literature on managing SPN in pregnancy. The definitive treatment modality for SPN is surgical resection, with organ preservation encouraged if feasible.[20] Surgical intervention becomes mandatory if the tumor is large, causing compression of adjacent structures or gastrointestinal bleeding. The current debate is whether to perform surgery during pregnancy or delay the surgery to postpartum. If surgery is contemplated, it should generally be considered in the second or early third trimester to avoid the risk of preterm labor due to early delivery. Moreover, given the low malignant potential of SPNs, postpartum management could be considered, and surgery should be reserved in case of maternal instability, such as in cases of tumor rupture.[3] Of the 17 cases we found in the literature, 11 (65%) underwent surgery during the second trimester of pregnancy, 1 (6%) underwent surgery during the first trimester, and 5 (29%) underwent surgery postpartum. The timing of surgery postpartum ranged from immediately after delivery to up to 4 months postpartum. In our case, definitive surgery is contemplated 3 months postpartum.

No evidence-based recommendations are available regarding the timing and mode of delivery when SPN complicates pregnancy. It is generally recommended

to schedule delivery after 37 weeks of gestation to avoid prematurity-related neonatal complications and long-term harm if possible.[21] Of the 17 cases in the literature, 9 (53%) were delivered at term, 4 (23%) were delivered preterm, 3 (18%) underwent termination of pregnancy, and 1 had a spontaneous abortion following embolectomy. Cesarean section was notably the most common mode of delivery in reported cases.

Bioethical Considerations

With our patient's initial diagnosis of GIST, we employed a multidisciplinary approach involving a MFM specialist, hepato-biliary surgeon, medical oncologist, neonatologist, and bioethicist. In the case of our patient, there are several bioethical considerations. It is crucial to balance medical indications, patient preferences, quality of life considerations, and contextual factors to provide the best care for the patient and her unborn child.

The medical indications suggest that surgery is the recommended treatment for patients with a provisional diagnosis of GIST, as it can lead to potential complications if left untreated. However, performing surgery at 28 weeks age of gestation can pose risks to both the mother and the fetus, leading to ethical dilemmas. The decision to forego a tissue biopsy and initiate surgical intervention based on imaging findings can be considered reasonable, given the indolent nature of the tumor. However, without a tissue diagnosis, there is always a risk of misdiagnosis and potentially inappropriate treatment decisions. In this scenario, it is essential to weigh the risks and benefits of intervention versus conservative management.

Patient preferences play a significant role in the decision-making process, particularly in a vulnerable population such as pregnant women. In this case, the patient's decision was heavily influenced by economic limitations, as indicated by the parents' hesitation to pursue further diagnostic testing. This highlights the importance of considering the social determinants of health and financial barriers that may impact a patient's ability to access appropriate healthcare.

Quality of life considerations are also crucial in this case, as the patient's well-being and that of her unborn child must be prioritized. Balancing the potential risks of surgical intervention during pregnancy with the need for a definitive diagnosis and appropriate treatment is paramount in ensuring the best possible outcome for both the patient and her child.

Contextual factors, such as access to health-care resources and support systems, must be considered when formulating a treatment plan. Collaborative decision-making between the patient, health-care providers, and other stakeholders is essential to ensure that all relevant factors are considered and that the patient's values and preferences are respected.

Ultimately, the multidisciplinary team reached a consensus to closely monitor tumor progression through serial ultrasound screenings, prioritize the health of both the mother and fetus, prevent potential complications, and refrain from unnecessary clinical interventions.

Summary

SPN is rare in pregnancy, with only 17 cases reported in the literature. This case report highlighted the diagnostic challenge of SPN as its clinical presentation is nonspecific, and its imaging features may be similar to GISTs. Our report delineated the management challenges of SPN during pregnancy, emphasizing the importance of a multidisciplinary and patient-centered approach in ensuring the best maternal and fetal outcomes without subjecting them to unwarranted clinical interventions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Authorship contributions

Stephanie Causin, MD, FPOGS - involved in the conceptualization, methodology, data curation, writing of the original draft, review and editing.

Zarinah G. Gonzaga, MD, MBA, MHM, FPOGS, FPSMFM, FPSUOG - involved in conceptualization, methodology, review and editing of the draft.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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