

Primary solid pseudopapillary neoplasm of the ovary: Report of a case and review of the literature

Primary solid pseudopapillary neoplasm of the ovary

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Abstract

Solid pseudopapillary neoplasm (SPN) is an uncommon neoplasm of the pancreas. Extrapancreatic cases of SPN are exceedingly rare. To the best of our knowledge, the primary SPN of the ovary was reported in only 13 cases. We report a case located in the right ovary in a 30-year-old woman, morphologically and immunophenotypically identical to pancreatic SPN. The tumor is presented because of its rarity, and our case is the second case with the longest follow-up period, treated with cystectomy, and the second case who gave birth after treatment.

Keywords

Solid Pseudopapillary Neoplasm, Ovary, Pancreas

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Introduction

Solid pseudopapillary neoplasm (SPN) is a rare neoplasm of the pancreas that occurs in 1-3% of all pancreatic tumors, with a low malignant potential, occurring predominantly in young women (about 90%). It was first recognized by Frantz in 1959 [1]. In general, the prognosis is good. Complete resection is curative in over 95% of patients [1].

On the other hand, extrapancreatic cases of SPN are exceedingly rare. Extrapancreatic SPN can be seen in the ovary, omentum, mesocolon, peritoneum, gastroduodenal area and liver. In these cases, the tumor mostly arises from ectopic pancreatic tissue [1]. There are only 13 previous cases of primary ovarian SPN in the English literature [2-12]. We report here, an additional case of ovarian SPN, which is morphologically and immunophenotypically similar to that of the pancreas, in the right ovary of a 30-year-old woman, with a review of the literature on extrapancreatic SPN.

Case Report

A 30-year-old female with abdominal discomfort was found to have a right ovarian cyst. No menstrual abnormalities were reported. Ultrasonographic evaluation showed a recent increase in the size of the

cyst. Laboratory tests, CA125, CA19-9, AFP and CEA were within the normal range. Radiologically, our patient demonstrated no pancreatic lesion. MRI examination revealed that the uterus and left ovary were normal size and anatomy. A cyst of 51x41mm, which has a solid component of 4 mm was detected in the right ovary. Laparoscopic unilateral right cystectomy was performed. The left ovary was grossly normal. There was no evidence of intraabdominal disease. During a cesarean section which was performed 15 months after the laparoscopy, both ovaries were normal in size and shape.

The cystectomy material measured 4.5x3x1 cm. The external surface was smooth. Cut surface and histologic evaluation were predominantly multilocular cystic with a minor solid component. The solid component was yellowish-white. There were no papillary areas grossly. Solid cellular nests, sheets and pseudopapillary architecture were identified histologically. The pseudopapillae were composed of central fibrovascular cores. Nests were surrounded by thick fibrous septae. The neoplastic cells were cuboidal with abundant pale eosinophilic cytoplasm with uniform, round to oval nuclei with fine chromatin and single, small eccentrically placed nucleoli. Few intracellular and extracellular PAS-positive eosinophilic globules were seen focally

Table 1. Clinicopathologic features of reported cases of ovarian solid pseudopapillary neoplasm.

| Case No | Author & References No | Age (yr) | Menopause | Location | Diameter (cm) | Presentation | Pancreas | Procedure | Gross features | Microscopic features | Follow-up (months) | Recurrence / Metastasis | Outcome |
|---------|------------------------|----------|-----------|----------|---------------|---|----------|----------------------------|--------------------------------------|--|--------------------|-------------------------|---------|
| 1 | Deshpande [2] | 17 | No | LO | 25.5 | Large abdominal mass | NED | USO | Solid & cystic | Nuclear groove + Infarct+ Mitosis - Atypia- | 72 | - | NED |
| 2 | Deshpande [2] | 57 | Yes | RO | 3 | Asymptomatic | NED | BSO | Solid & cystic | Nuclear groove + Mitosis - Atypia- | NA | - | NA |
| 3 | Deshpande [2] | 21 | No | LO | 14 | Abdominal swelling | NED | USO | Solid & cystic | Nuclear groove + Mitosis - Atypia- | NA | - | NA |
| 4 | Cheuk [3] | 25 | No | RO | 16.5 | Abdominal fullness & Menorrhagia | NED | UO | Predominantly solid & focally cystic | Nuclear groove + Mitosis - Atypia- | 144 | - | NED |
| 5 | Syriac [4] | 45 | Pre M. | RO | 8 | Weight loss, abdominal pain, bloating, Adnexal mass, Ascite. 2 metastatic mass in right hepatic lob | NED | USO, Oment, LN, Debulk, CT | Solid 80% & cystic 20% | Mild pleomorphism + Mild atypia + Mitosis 62/50 HPF, Necrosis intensive + LVI and capsule invasion + | 8 | M: Om, Li, FT | DOD |
| 6 | Stoll [5] | 48 | No | LO | 8,9 | Left lower abdominal and back pain | NED | SO | Multilocular cystic, focal solid | | 9 | - | NED |
| 7 | Kominami [6] | 18 | No | RO | 10 | Abdominal fullness | NED | UO | Multilocular, cystic & solid | | NA | NA | NA |
| 8 | Chen [7] | 47 | Pre M. | LO | 6 | Large left pelvic mass | NED | USO | Solid & cystic | Mitosis- Atypia <%, Necrosis- | 18 | - | NED |
| 9 | He [8] | 39 | No | RO | 6 | Abdominal pain | NED | Partial O | Cystic | Nuclear grooves + Mitosis <1/10HPF Atypia- | 36 | R: (Po- 3 mo) | NED |
| 10 | Gahlot [9] | 25 | No | RO | 12 | Abdominal pain | NED | USO, Oment, LND, Debulk | Solid & cystic | Mitosis- Atypia -Necrosis- | 18 | M: Om, LN | NED |
| 11 | Singh [10] | 49 | Post M | RO | 4,5 | Abdominal pain Postmenopausal bleeding | NED | TAH, BSO | Solid & cystic | Necrosis- LVI - | 12 | - | NED |
| 12 | Komorti [11] | 18 | No | LO | 17,5 | Left ovarian mass | NED | USO | Solid & cystic | Nuclear grooves +Necrosis + Mitosis- Atypia- | 3 | - | NED |
| 13 | Nguyen [12] | 24 | No | RO | 5,2 cm | Abdominal pain | NED | USO | Solid & cystic | | 18 | No | NED |
| 14 | Present case | 30 | No | RO | 4,5 cm | Abdominal pain | NED | Cystectomy | Multilocular cystic focal solid | Nuclear grooves + Mitosis- Atypia - Necrosis- | 105 | - | NED |

NED: No evidence of disease, NA: Not Available; Pre M: Premenopausal; Post M: Postmenopausal; LVI: lymphovascular invasion; LO: Left Ovary, RO: Right Ovary; O: oophorectomy, USO: Unilateral Salpingo-oophorectomy, BSO: Bilateral Salpingo-oophorectomy, TAH: Total Abdominal Hysterectomy, Oment: Omentectomy, LND: Lymph Node Dissection, Debulk: Debulking, CT: Chemotherapy, DOD: Died of disease; M: Metastasis, Om: Omentum, Li: Liver FT: Fallopian tube, LN: Lymph nodes, R: Recurrence, Po: Postop.

Table 2. Immunohistochemical features of reported cases of ovarian solid pseudopapillary neoplasm.

| Case | Author & References No | β-catenin | PCK | Vim. | CD56 | CD10 | PR (Nuc) | Inhib | WT-1 | Ó1-AT | Ki67 | CTNNB1 Mutation |
|------|------------------------|-------------|-------|-------|--------|------------|----------|-------|--------|--------|----------|-----------------|
| 1 | Deshpande[2] | Nuc & cyt + | - | Diff+ | Diff + | Foc+ | Diff + | - | NA | NA | NA | - |
| 2 | Deshpande[2] | Nuc & cyt + | - | NA | Diff + | NA | - | - | NA | NA | NA | - |
| 3 | Deshpande[2] | Nuc+ | - | NA | NA | NA | - | - | NA | NA | NA | - |
| 4 | Cheuk [3] | Nuc & cyt + | - | NA | Diff + | Golgi + | - | - | NA | NA | NA | - |
| 5 | Syriac [4] | Nuc & cyt + | Foc+ | NA | - | - | - | - | - | NA | 20-30% + | - |
| 6 | Stoll [5] | Nuc & cyt + | Foc+ | Diff+ | Diff + | 10%+ | Foc+ | - | NA | HG + | 5-10% + | - |
| 7 | Kominami [6] | Nuc & cyt + | - | Diff+ | Diff+ | dot-like + | NA | NA | Diff + | Diff + | NA | S37Y |
| 8 | Chen [7] | Nuc+ | Foc+ | Diff+ | Foc+ | Diff+ | Diff+ | - | Diff+ | NA | 5% | - |
| 9 | He [8] | Nuc & cyt + | - | Diff+ | Diff+ | NA | Foc+ | - | NA | NA | 5% | - |
| 10 | Gahlot [9] | Nuc & cyt + | NA | NA | Diff + | Diff+ | - | - | NA | NA | NA | - |
| 11 | Singh [10] | Nuc & cyt + | Diff+ | Diff+ | Diff+ | Diff+ | - | - | Diff+ | NA | 1-5% | S33C |
| 12 | Komorti [11] | Nuc & cyt + | - | Foc+ | Diff+ | dot-like + | Diff+ | - | - | NA | 1-2% | - |
| 13 | Nguyen [12] | Nuc + | - | NA | NA | NA | NA | - | NA | NA | NA | NA |
| 14 | Present case | Nuc + | Foc+ | Diff+ | Diff + | Diff + | Foc+ | - | - | Diff + | NA | - |

Nuc: Nuclear, Cyt: Cytoplasmic, Diff: Diffuse, Foc: Focal, NA: Not Available, PR: Progesterone Receptor, PCK: Pancytokeratine, Ó1-AT:Alpha 1-antitrypsin, Vim: Vimentine, Inhib: Inhibine, HG: Hyaline globular

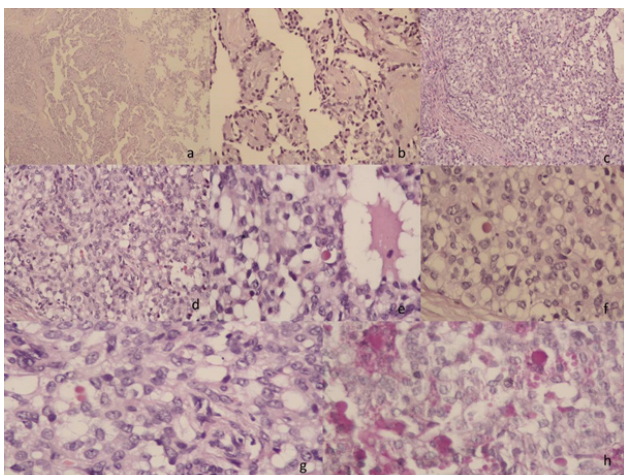


Figure 1. Low-power view shows a solid and pseudopapillary pattern HE x4 (a); pseudopapillary pattern HE x20(b); nests of tumor cells surrounded by thick fibrous septa HE x10 (c); scattered eosinophilic globules in solid area HE x20 (d); microcysts filled with colloid-like material HE x40 (e); uniform tumor cells and scattered eosinophilic globules HE x40 (f,g) and PAS-positive eosinophilic globules x40 (h)

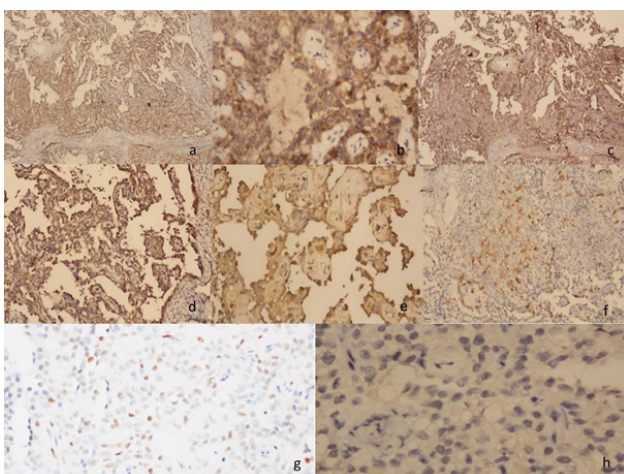


Figure 2. Abnormal nuclear b-catenin immunostaining x20 (a); diffuse cytoplasmic expression of CD10 x20 (b), CD56x4 (c), vimentin x10 (d) and trypsin x20 (e); focal cytoplasmic expression of pancytokeratin x10 (f) and progesterone x40 (g); negativity of inhibin x40 (h).

(Figure1a-h). No nuclear grooves were identified. Mitoses, nuclear atypia, vascular and capsular invasion were not seen. No pancreatic tissue was seen within or adjacent to the tumor.

Immunohistochemistry (IHC) revealed diffuse nuclear positivity for β-catenin and diffuse cytoplasmic positivity for CD10, CD56, vimentin and Alpha 1-antitrypsin (Figure 2a-d). Pancytokeratin and progesterone receptor (PR) were focally positive (Figure 2e-f). Inhibin and WT-1 stains were negative (Figure 2h). Pancreatic and abdominal screening by CT scan / after the diagnosis of aSPN revealed no pancreatic and other intraabdominal lesions. With this finding, the case was confirmed to be a primary ovarian SPN.

Clinicopathologic and immunohistochemical features of ovarian SPN cases, including ours are summarized in Tables 1 2.

The patient gave birth to a healthy child 15 months after her initial diagnosis and had no recurrence in her follow-up of 105 months.

Informed consent was obtained from the patient.

Discussion

Solid pseudopapillary neoplasm (SPN) of the pancreas is an uncommon, usually benign neoplasm that constitutes approximately 1-3% of all exocrine pancreatic malignancies. It occurs predominantly in young women. SPN occurring as primary tumors outside the pancreas are exceedingly rare, constituting up to 1.01% to 1.8% of cases [1]. Extrapaneatic SPN has been documented in other areas such as retroperitoneum, omentum, mesocolon, gastroduodenal area, colon and liver, which occur in ectopic pancreatic tissue [1]. The most common extrapancreatic site is the ovary (totally 14 cases, including the present case) [2-12]. Deshpande et al first reported 3 cases located in the ovary in 2010 [2]. All cases of ovarian SPN have been reported to occur in the absence of ectopic pancreatic tissue [2-12]. In the present case also, despite the whole sampling of the specimen, we did not find any ectopic pancreatic tissue within or adjacent to the tumor.

The age of the patients ranged from 17 to 57, with a mean age of 35.5 years, and the median age of 25 in primary ovarian SPNs. Ovarian SPNs are located in the right ovary in 63.6% of the cases [2-12]. The diameter of tumors ranged from 3 to 25.5 cm, in our case it was 4.5 cm.

SPNs are often asymptomatic or are associated with uncharacteristic abdominal symptoms. Three patients presented with an abdominal mass [2,7,11,12] and dysmenorrhea [12]. Totally nine cases, including

ours, had abdominal pain or discomfort [2,3,5,6,8,10,12]. One patient presented with weight loss, abdominal pain, bloating, adnexal mass, ascites and metastatic 2 masses in the right hepatic lobe, and this case had a malignant course [4].

Three of the 12 cases underwent oophorectomy [3,6,8], salpingo-oophorectomy was performed in six cases [2,5,7,11,12], bilateral salpingo-oophorectomy was performed in one of them [2], total abdominal hysterectomy was performed in one of them [10], two of them underwent salpingo-oophorectomy, omentectomy, lymph node dissection and debulking [4,9]. Our case underwent only cystectomy. Similar to the pancreatic SPN, extrapancreatic SPN can vary from entirely cystic with a small mural nodule to solid but most tumors are solid and cystic. Histologically, the tumor contains a mixture of solid, cystic, and pseudopapillary patterns in varying proportions. Characteristic morphologic features of these neoplasms include solid and pseudopapillary patterns, hyaline globules, clusters of uniform cells, and variable longitudinal nuclear grooves [1].

SPN of the pancreas is a mysterious tumor, the cell of origin of which has not been fully elucidated yet. Immunohistochemically, SPN variably expresses epithelial, mesenchymal and endocrine markers. Neoplastic cells express nonspecific markers such as vimentin and CD10 diffusely. Epithelial differentiation of this tumor is incomplete with focal or weak expression of pancytokeratin (PCK). Its neuroendocrine differentiation is also unclear with the frequent expression of CD56 and neuron-specific ('non-specific') enolase (NSE), however, with the typical absence of chromogranin, the most specific endocrine marker. Alpha-1-antitrypsin (AAT) stains the PAS-positive globules [1].

Including ovarian cases such as ours, extrapancreatic SPNs, demonstrate similar IHC profiles (except PCK) as their pancreatic counterparts. Most of the ovarian SPNs (7 cases) have been reported to be negative for PCK [2,3,6,8,11,12] however, our case with its focal positivity for PCK, was similar to the remaining three cases [4,5,7,10,11] and pancreatic SPNs [1].

Several authors suggest that SPN may be related to hormonally sensitive tissue from the gonads. Firstly, this neoplasm usually occurs in young females and in addition, the neoplastic cells consistently express progesterone receptor (PR), suggesting a role for hormones in the evolution of these neoplasms [1]. There is a close proximity of the genital ridges to the pancreas during embryogenesis, raising the possibility that cells from the primitive ovary may be incorporated into the embryonic pancreas. The diagnosis of SPN in the ovary may provide evidence to support this hypothesis in the pathogenesis of this neoplasm [2-8]. Nearly all pancreatic SPNs have been reported to be positive for PR. In contrast, most cases of ovarian SPN are negative for PR [2-4,9,10], except three cases reported as diffusely positive [2,7,11]. Stole and He et al. reported focal PR positivity similar to our case [5,8]. Immunohistochemically, aberrant nuclear localization of β -catenin is the result of mutations in exon 3 of this β -catenin gene (CTNNB1), and this finding is observed in nearly all cases (90-100%) of pancreatic SPN and can provide strong support for the diagnosis of SPN. This mutation cancels glycogen synthase kinase 3-mediated degradation of this protein. Some studies showed the role of Wnt signaling, mostly associated with β -catenin mutations in the tumorigenesis of SPN [1,6,10]. Nuclear and cytoplasmic β -catenin positivity has been reported in nine primary ovarian SPN [2, 6,8-11]. Nuclear β -catenin positivity has been reported in four cases [2-7,12]. Additionally, Kominami and Singh et al. have identified nuclear immunoreactivity for β -catenin and mutations in exon 3 of CTNNB1 [6,10]. These results suggest that activated Wnt signaling, which was primarily due to mutations in exon 3 of CTNNB1, plays an important role in the tumorigenesis of both ovarian and pancreatic SPN [6,10].

Although uniform cells and common positivity for CD56 and NSE in SPN may mimic a neuroendocrine tumor (NET) (but without "salt and pepper type" chromatin and insular and trabecular patterns), unlike NET, chromogranin is typically negative in SPN. Furthermore, in contrast to NET, SPN uniformly lack cytoplasmic membrane staining for E-cadherin [1,12].

The presence of solid growth patterns and tumor cells exhibiting grooves and nuclear membrane irregularity can mimic the diffuse pattern of adult granulosa cell tumors (GCT). GCT and Sertoli cell tumors (SCT) can rarely exhibit a pseudopapillary pattern. On the other hand, the predominance of solid growth and cells along with vacuolated pale and eosinophilic cytoplasm are features that SCT of the ovary. However, ovarian SPN lacked the typical architectural patterns, such as microfollicular, insular, and gyriform, that are seen in GCT. Lack of immunoreactivity for calretinin and inhibin also distinguishes these neoplasms from GCT and SCT of the ovary [2,3,5,12].

SPNs of the pancreas are usually benign or indolent tumors with less than 5% displaying aggressive behavior [1]. Complete surgical excision is curative also in extrapancreatic cases. In extrapancreatic SPNs, metastasis has been reported only in two cases located in the ovary [4,9]. One of the presented cases with malignant morphological features and metastasis had a fatal behavior [4]. Another case has been reported with metastasis in the omentum, parametria, and pelvic lymph nodes, who lived for 1.5 years of follow-up [9].

The histopathology and immunohistochemistry of all primary ovarian SPNs in all the cases including ours, closely resembled their pancreatic counterparts. Radiological studies showed an unremarkable pancreas in all ovarian SPNs, including our case [2,11].

He et al. reported that 3 months postoperatively, a cystic shadow in the right ovary was detected by ultrasonography, but no evidence of any recurrence was found during a follow-up of 3 years [8]. Three of the reported cases have no prognostic information [2,6]. There was no evidence of disease in these seven cases, which were followed from 3 months to 12 years [2,3,5,7-11,12].

In our case, there were no morphologic signs of malignant behavior such as mitosis, atypia, or vascular and capsular invasion. After the pathological diagnosis, meticulous abdominopelvic evaluation of the patient (with special regard to the pancreatic region) revealed no evidence of any other tumor, and the tumor in our case was diagnosed as primary ovarian SPN. Our case is the second case with the longest follow-up period, after the 144-month follow-up case reported by Cheuk et al. [8]. In her follow-up of 105 months, she gave birth (like the patient in the literature 12 (Nguyen MT et al.)) to a healthy child 15 months after her initial diagnosis and did not have any recurrence.

Conclusion

We report the 14th case of primary SPN of the ovary with follow-up. These neoplasms are histologically and immunohistochemically similar to their pancreatic counterparts. This rare ovarian neoplasm with a solid and pseudopapillary appearance should be considered in the differential diagnosis of ovarian masses, and immunohistological staining should be performed for accurate diagnosis. Positive nuclear staining with β -catenin supports the diagnosis of an SPN. It should be kept in mind that metastases of the pancreatic SPNs to the ovaries can also occur. The presence of a primary pancreatic SPN should be excluded with radiological studies, before the diagnosis of a primary ovarian SPN.

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Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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