Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Pancreatic solid pseudopapillary neoplasm with concomitant left unilateral renal agenesis and bicornuate uterus: a case report

Madhur Bhattarai MBBS[a], Ayush Shrestha, MBBS[a], Suyog Bhandari, MBBS, MS, MCH[b,*], Niravkumar Buha, MBBS, MS[b], Rituraj Baral, MBBS, MD[c], Shreya Shrivastav, MBBS, MD[c], Paleswan Joshi Lakhey, MBBS, MS, MCh[b]

Introduction: A solid pseudopapillary neoplasm (SPN) of the pancreas is a rare tumor of the pancreas. Concomitant SPN with urogenital anomalies is a very rare presentation.

Case Presentation: A 16-year-old female presented with a chief complaint of abdominal pain 30 days back. Solid pseudopapillary neoplasm (SPN) of the pancreas was diagnosed with the aid of ultrasonography and contrast-enhanced computed tomography of the abdomen and pelvis. Incidentally, concomitant left unilateral renal agenesis and bicornuate uterus were also detected in radiological findings. The patient underwent spleen-preserving distal pancreatectomy, and SPN was confirmed with the histopathological report.

Discussion: Symptomatic SPN patients present with an abdominal mass and pain or very rarely jaundice. Most of the SPNs are benign. Complete surgical excision results in more than 95% cure. SPN with concomitant urogenital anomalies is extremely rare, and their concurrent occurrence can be better attributed to Wnt signaling pathway owing to their similar pathogenic mechanism.

Conclusion: The solid pseudopapillary tumor has an excellent prognosis if timely resected. Proper evaluation of the patient with imaging is necessary to suspect and diagnose SPN who has urogenital anomalies and vice versa.

Keywords: bicornuate uterus, solid pseudopapillary neoplasm, unilateral renal agenesis, urogenital anomalies

Introduction

A solid pseudopapillary neoplasm (SPN) of the pancreas is a rare low-grade malignant neoplasm of the pancreas that accounts for 0.13–2.7% of all pancreatic tumors and usually presents with a well-encapsulated mass and predominantly affects young women[1–4]. Very few cases of SPN in association with pancreatic anomalies and urogenital anomalies have been reported. Here we present radiological and histological findings of a case of pancreatic SPN with concomitant urogenital malformations – left renal agenesis and bicornuate uterus. Renal agenesis is a congenital anomaly due to the complete failure of embryonic kidney formation. Unilateral renal agenesis (URA) is one of the mechanisms that result in a solitary kidney[5]. A bicornuate uterus is a rare uterine anomaly that results due to partial fusion of Müllerian ducts forming a heart-shaped uterus instead of a pear-shaped one[6]. In the literature, URA and bicornuate uterus presenting together have been reported many times; however, their presentation with solid pseudopapillary tumor is exceedingly rare. We briefly describe the presentation and try to explore their possible association. This case report has been reported in line with the SCARE (Surgical CAse REport) Criteria[7].

HIGHLIGHTS

- A solid pseudopapillary neoplasm (SPN) of the pancreas is a rare, low-grade malignant tumor of the pancreas that predominantly affects young women.
- A cure rate of greater than 95% can be achieved via complete surgical excision.
- Concomitant SPN and urogenital anomalies are very rare presentations.
- SPN demands proper clinical evaluation in a patient diagnosed with urogenital anomalies and vice versa.

[a]Institute of Medicine, Tribhuvan University, Maharajgunj Medical Campus, [b]Department of Surgical Gastroenterology and [c]Department of Pathology, Institute of Medicine, Tribhuvan University, Maharajgunj, Nepal

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Institute of Medicine, Tribhuvan University, Maharajgunj 44600, Nepal. Tel. +977-9841881823. E-mail address: suyogbhandari1@gmail.com (S. Bhandari).

Annals of Medicine & Surgery (2023) 85:1166–1171

Received 16 November 2022; Accepted 12 February 2023

Published online 27 March 2023

http://dx.doi.org/10.1097/MS9.0000000000000360

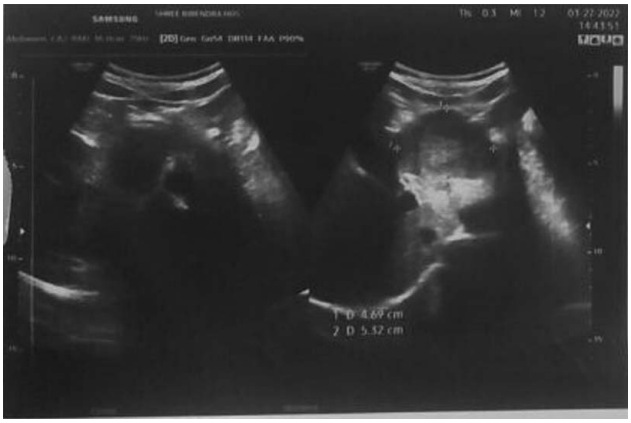

Figure 1. Ultrasonography of the abdomen and pelvis shows a well-defined hyperechoic lesion in the body region of the pancreas.

Case presentation

A 16-year-old female presented to our tertiary care center with a chief complaint of abdominal pain 30 days back. There has been no pain since then. Her vitals were normal. On per abdominal examination, the abdomen was soft, and tenderness was present in the right hypochondriac and epigastric region. There was no abdominal distension. There was no history of fever, diarrhea, black stool, and jaundice. Her liver function test, renal function test, and other hematological parameters were unremarkable. She had a surgical history of deroofing of ureterocele 2 years back. Family history is insignificant.

Ultrasonography (USG) of the abdomen and pelvis showed a well-defined hyperechoic lesion in the body region of the pancreas (Fig. 1). In contrast-enhanced computed tomography (CECT) of the abdomen and pelvis, heterogeneously enhancing hypodense mass lesion in the body of pancreas was depicted (Fig. 2). Accordingly, a working diagnosis of SPN was made. Incidentally, the USG abdomen and pelvis also revealed the absence of the left kidney and the presence of a bicornuate uterus, which is also delineated by CECT (Figs. 3, 4). The result of 99m-Technicium DMSA (dimercaptosuccinic acid) renal scan and DTPA (diethylenetriamine pentaacetate) renogram is also consistent with the absence of the left kidney (Fig. 5).

A spleen-preserving distal pancreatectomy was performed via the Kimura technique, and the specimen was sent for

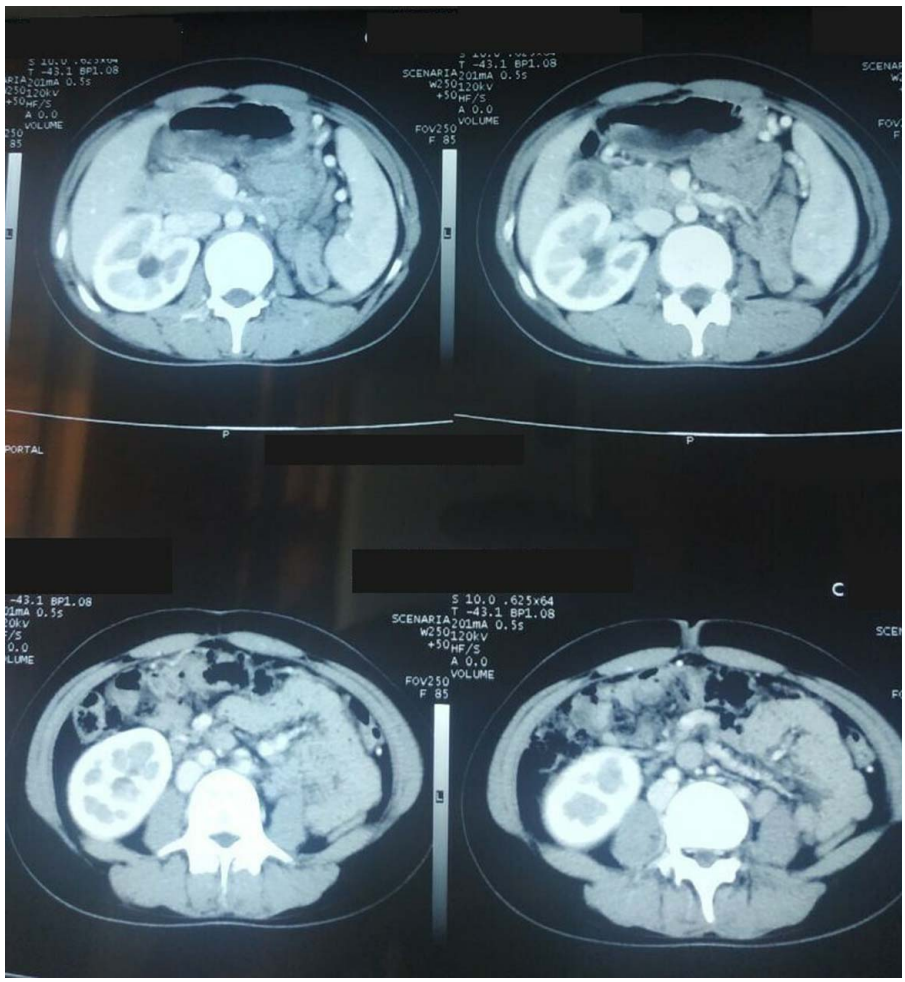

Figure 2. Contrast-enhanced computed tomography of the abdomen and pelvis reveals a heterogeneously enhancing hypodense mass lesion in the body of the pancreas and the absence of the left kidney.

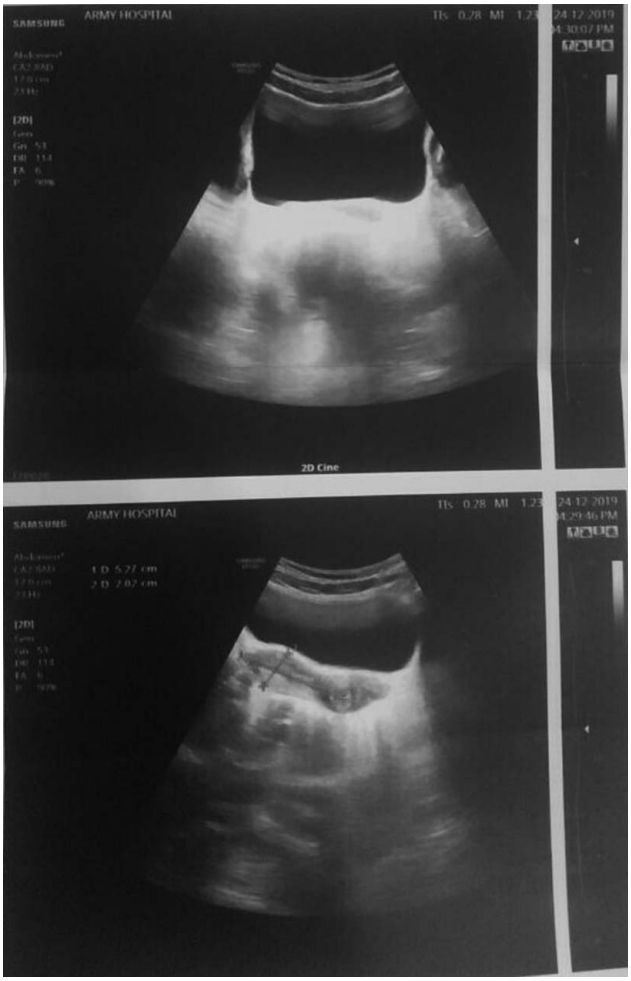

Figure 3. Ultrasonography of the abdomen and pelvis shows a bicornuate uterus.

histopathology. It showed a circumscribed but unencapsulated mass with tumor cells arranged in nests, papillae, trabeculae, and frequent perivascular arrangement. These cells had a scant to moderate amount of cytoplasm, round to ovoid nuclei, granular chromatin, and inconspicuous nucleoli. These cells exhibited a mild degree of nuclear pleomorphism. Atypia and necrosis were not seen. Areas of hemorrhage were seen (Fig. 6). These findings confirmed SPN in the body of the pancreas, which was 7 cm in size and TNM [tumor (T), node (N), and metastases (M)] staging pT3N0. Lymphovascular invasion and perineural invasion were not identified. Resected margin and all pancreatic surfaces were free of tumors.

On the third postoperative day, high D-dimer (8.24 μg/ml), fibrinogen (522 mg/dl), and APTT (activated partial thromboplastin time) (27) were found on investigation for which free frozen plasma was transfused. Then the patient was discharged satisfactorily without any complications.

Discussion

Pancreatic SPNs are defined by the fifth edition of the WHO Classification of Digestive System Tumors as 'a low-grade malignant pancreatic tumor composed of poorly cohesive epithelial cells forming solid and pseudopapillary structures that lack a specific line of pancreatic epithelial differentiation'[3]. Before it was labeled as SPN by WHO in 1996, it was also known as Franz's tumor or Hammoudi tumor[2]. The tumors are more commonly seen in young Asian and African-American women. Females are 10 times more affected than males, and the mean age of presentation is 22 years[2]. It is found that 38.1% of the patients do not present with any signs or symptoms[8]. If symptomatic, SPN patients present with an abdominal mass and pain or jaundice (very rarely). The patient may present with acute abdomen following abdominal trauma due to intratumoral hemorrhage. SPN can involve any portion of the pancreas with a slight preponderance to the tail[9]. Our patient presented with a tumor in the body of pancreas. Most pseudopapillary tumors are diagnosed via ultrasound or computed tomography of the abdomen, as in our case. MRI can also be used. On computed tomography imaging, hypervascular, well-encapsulated, round tumors with cystic and solid components are seen. Cystic areas are centrally situated, whereas enhanced solid areas are primarily situated peripherally. Several peripheral or central stippled calcifications may be present within the tumor[10]. On MRI imaging, a well-defined mass with heterogeneous signal intensity on T1-weighted and T2-weighted images can be spotted. The mass indicates the solid and cystic nature of the tumor[11]. Currently, all the SPNs are classified as low-grade malignant neoplasm because the metastatic or aggressive clinical course cannot be predicted by perineural invasion, angioinvasion, and deep infiltration of surrounding structures[3]. The universally accepted definitive treatment of SPN is surgical excision. A cure rate of greater than 95% can be achieved via complete surgical excision[8,12]. There is usually an excellent long-term prognosis for localized, metastatic, and recurrent disease, with a long disease-free period after complete surgical resection. Among the few patients who die from metastatic SPN are mostly those whose tumors harbor an undifferentiated component that lacks pseudopapillary structures characterized by diffuse sheets of cells with increased nuclear atypia and proliferative index. These foci of high-grade malignant transformation are described as one histological subtype, SPN, with high-grade carcinoma in the latest edition[3,13]. Procedures such as distal pancreatectomy and splenectomy, spleen-preserving distal pancreatectomy, central pancreatectomy, pancreaticoduodenectomy, pylorus-preserving pancreaticoduodenectomy, and total pancreatectomy are the most common surgical procedures[8]. In our case, spleen-preserving distal pancreatectomy was performed via the Kimura technique.

There have been occasional reports of SPN cases with pancreatic anomalies such as pancreatic dorsal agenesis[14–16] and pancreatic divisum[17,18]. There are instances of SPN being reported with familial adenomatous polyposis[19,20]. Similarly, very few cases of SPN with urogenital anomalies[1,21] are reported. Guan *et al.*[1] reported SPN with solitary kidney and uterus didelphys, while Sharma *et al.*[21] reported SPN with left duplex kidney and vaginal septum. Concomitant occurrences of SPN and urogenital anomalies are extremely rare. We incidentally found left renal agenesis and bicornuate uterus in this patient, confirmed by USG and CECT of the abdomen and pelvis.

URA is mostly an incidental radiological diagnosis. The left kidney is more commonly involved in contrast to the right kidney, similar to what was seen in our case. During the fifth week of

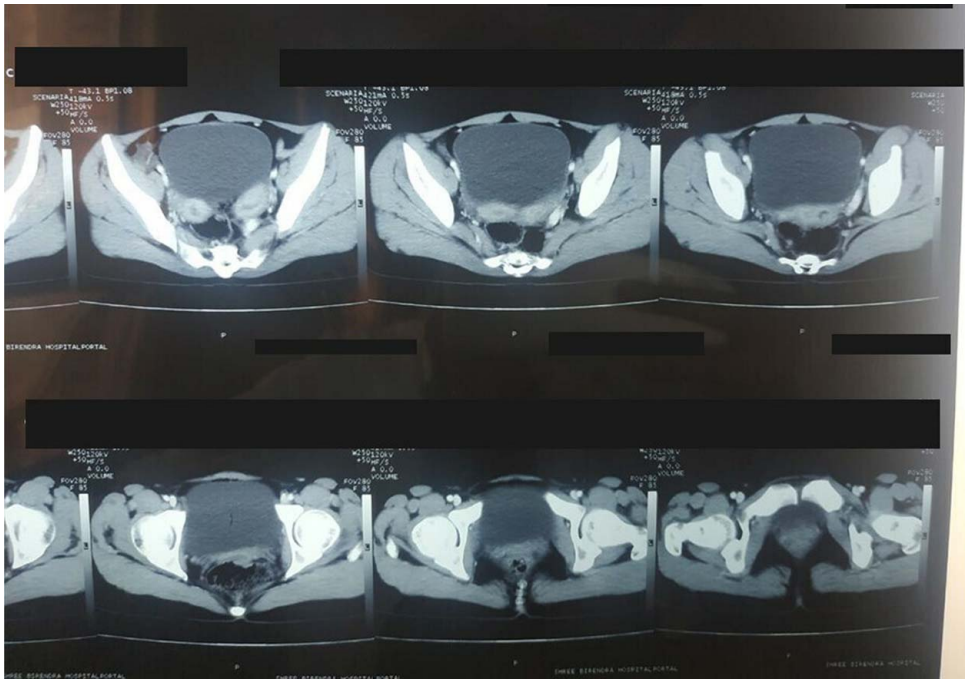

Figure 4. Contrast-enhanced computed tomography of the abdomen and pelvis reveals a bicornuate uterus with two separate cornua which are joining at the cervix.

gestation, a portion of the Wolffian duct swells to form the ureteric bud. The ureteric bud then invades the nearby metanephric mesenchyme forming the metanephric blastema or metanephros, which is a precursor of the adult human kidney. Failure of induction of ureteric bud or absence of metanephric blastema leads to the development of renal agenesis[22]. Bicornuate uterus results due to the incomplete fusion of the Müllerian ducts during the second stage fusion of the ducts. It can be either accompanied by a single cervix (unicollis) or a double cervix (bicollis) based on the extent of duplication[6]. Failure of fusion or anomalous development of the Müllerian ducts gives rise to a myriad of Müllerian duct anomalies. The Müllerian anomalies are classified into seven categories (I–VII) by the American Fertility Society. The bicornuate uterus which is present in our case, belongs to class IV[23]. The development of Müllerian and Wolffian ducts along with the urogenital sinus is interlinked. Thus, renal anomalies are frequently found in association with Müllerian anomalies[24]. In young females, one of every three females with renal agenesis will be associated with a significant anomaly of the uterus, ovary, or vagina. So, on early detection of a solitary congenital kidney on routine imaging or incidental imaging studies, the physician should also look for associated genital anomalies, especially in young females[25].

The SPN of the pancreas has an unclear origin. Several studies hypothesize that SPNs originate from multipotent primordial cells, whereas others suggest extrapancreatic origin from genital ridge angle-related cells[26]. Over 90% of SPN tumors have been reported with *CTNNB1* gene mutations, a gene that encodes β-catenin[27]. A major role in the tumorigenesis of the SPN of the pancreas is played by diffuse cytoplasmic and aberrant nuclear expression of β-catenin and a lack of membranous E-cadherin due to Wnt signaling associated with mutation of β-catenin (*CTNNB1*)[28]. Upregulation of notch, hedgehog, and androgen receptor signaling pathways has also been found in SPN[29]. Liu *et al.*[30] found 6 out of 12 SPN displayed Hedgehog signaling using immunohistochemistry. Recent studies suggest that Wnt5a, which acts through Ror2 for the induction of metanephric mesenchyme and renal morphogenesis via a noncanonical pathway, is critical for early kidney development. Mutation of *Wnt5a* could cause disruption of multiple tissue differentiation and development, leading to urogenital defects of the congenital anomalies of the kidney and urinary tract (CAKUT)[31].

The concomitant occurrence of SPN and urogenital anomalies can be better attributed to Wnt signaling pathway owing to their similar pathogenic mechanism. The possibility of this association requires further molecular studies in the future.

Conclusion

A solid pseudopapillary tumor is a rare low-grade malignant tumor of the pancreas but has an excellent prognosis. SPN may occur concurrently with extrapancreatic abnormalities, especially urogenital abnormalities, which demands focused investigations of these anomalies in a patient diagnosed with SPN and vice versa. The possibility of the occurrence of SPN and urogenital anomalies as a syndromic feature in the future cannot be underestimated, and the role of the β-catenin–Wnt pathway or any alternative explanation is subject to future investigations.

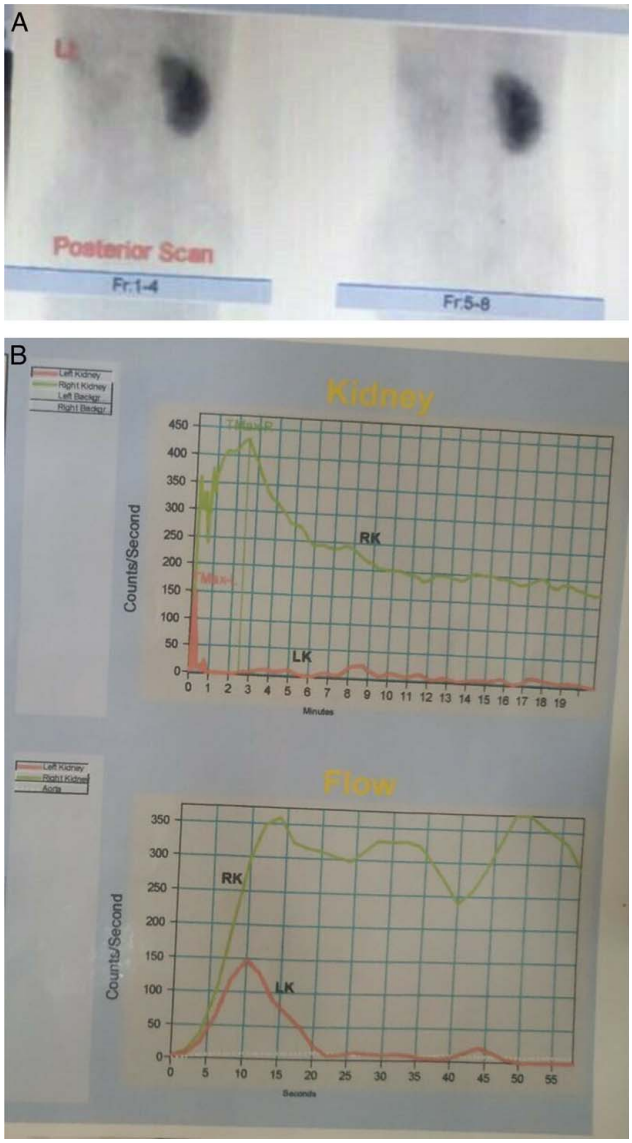

Figure 5. 99m-Technicium dimercaptosuccinic acid renal scan and diethylenetriamine pentaacetate renogram show the absence of left renal uptake.

Ethical approval

None.

Patient consent

Written informed consent was obtained from her patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

No funding was received for the study.

Author contribution

M.B., A.S., and S.B.: wrote the original manuscript and reviewed and edited the original manuscript; M.B., A.S., S.B., N.B., S.P., R.B., S.S., and P.J.L.: reviewed and edited the original manuscript.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: none.
2. Unique identifying number or registration ID: none.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): none.

Guarantor

Dr Suyog Bhandari, Institute of Medicine, Tribhuvan University, Maharajgunj 44600, Nepal,
E-mail: suyogbhandari1@gmail.com

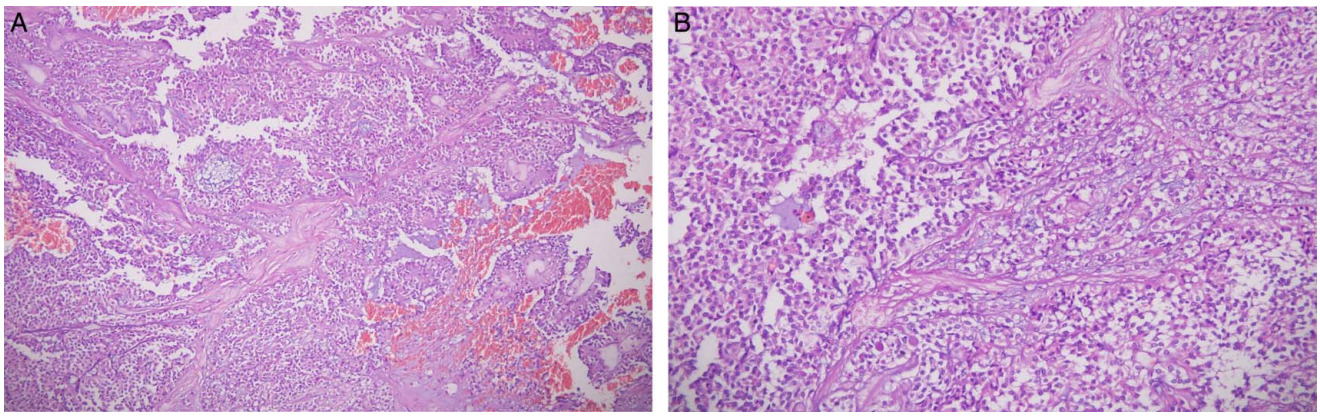

Figure 6. Histopathology: tumor cells are arranged in nests, papillae, trabeculae, and frequent perivascular arrangement. Pseudopapillary structures are seen. These cells have a scant to moderate amount of cytoplasm, round to ovoid nuclei, granular chromatin, and inconspicuous nucleoli. Tumor cells exhibit a mild degree of nuclear pleomorphism. Atypia and necrosis are not seen.

Provenance and peer review

Not commissioned, externally peer-reviewed.

References

[1] Guan ZW, Sun L, Wang YQ, *et al*. Solid pseudopapillary tumor of the pancreas and concomitant urogenital malformations in a young woman. Diagn Pathol 2013;8:35.

[2] Shuja A, Alkimawi KA. Solid pseudopapillary tumor: a rare neoplasm of the pancreas. Gastroenterol Rep 2014;2:145.

[3] G Kloppel, O Basturk , Klimstra DS, *et al*. Solid pseudo-papillary neoplasm of the pancreas. In: Gill AJ, Klimstra DS, Lam AK, editors. WHO Classification of Tumours of the Digestive System, 5th ed. International Agency for Research on Cancer (IARC); 2019:pp. 340–342.

[4] Yadav SK, Bhattarai HB, Rijal A, *et al*. Duodenal gastrointestinal stromal tumor: a case report. Ann Med Surg 2022;82:104574.

[5] Hiraoka M, Tsukahara H, Ohshima Y, *et al*. Renal aplasia is the predominant cause of congenital solitary kidneys. Kidney Int 2002;61: 1840–4.

[6] Zakarin Safier L, Rackow BW, Bicornuate uterus. In: Pfeifer S, editor. Congenital Müllerian Anomalies. Springer; 2022.

[7] Agha RA, Franchi T, Sohrabi C, *et al*. The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg 2020;84:226–30.

[8] Law JK, Ahmed A, Singh VK, *et al*. A systematic review of solid-pseudopapillary neoplasms: are these rare lesions? Pancreas 2014;43:331.

[9] Omiyale AO. Solid pseudopapillary neoplasm of the pancreas. World J Hepatol 2021;13:896.

[10] Kawamoto S, Scudiere J, Hruban RH, *et al*. Solid-pseudopapillary neoplasm of the pancreas: spectrum of findings on multidetector CT. Clin Imaging 2011;35:21–8.

[11] Chung EM, Travis MD, Conran RM. Pancreatic tumors in children: radiologic–pathologic correlation. Radiographics 2006;26:1211–38.

[12] Sandlas G, Tiwari C. Solid pseudopapillary tumor of pancreas: a case report and review of literature. Indian J Med Paediatr Oncol 2017;38: 207.

[13] Tomioka K, Ohike N, Aoki T, *et al*. Solid pseudopapillary neoplasm of the pancreas with high-grade malignant transformation involving p16-RB pathway alterations. Case Rep Surg 2020;2020:5980382.

[14] Ulusan S, Bal N, Kizilkilic O, *et al*. Case report: solid-pseudopapillary tumour of the pancreas associated with dorsal agenesis. Br J Radiol 2005;78:441–3.

[15] Nakamura Y, Egami K, Maeda S, *et al*. Solid and papillary tumor of the pancreas complicating agenesis of the dorsal pancreas. J Hepatobiliary Pancreat Surg 2001;8:485–9.

[16] Santana DP, Abreu DV, Santos EC, *et al*. Solid pseudopapillary tumor associated with agenesis of the dorsal pancreas: a case report. Braz J Oncol 2021;17:1–5.

[17] Watanabe D, Miura K, Goto T, *et al*. Solid pseudopapillary tumor of the pancreas with concomitant pancreas divisum. A case report. JOP 2010;11:45–8.

[18] Nakamura S, Okayama Y, Imai H, *et al*. A solid cystic tumor of the pancreas with ossification and possible malignancy, coexisting nonfusion of the pancreatic ducts. J Clin Gastroenterol 2001;33:333–6.

[19] Naoi D, Koinuma K, Sasanuma H, *et al*. Solid-pseudopapillary neoplasm of the pancreas in a patient with familial adenomatous polyposis: a case report. Surg Case Rep 2021;7:35.

[20] Inoue T, Nishi Y, Okumura F, *et al*. Solid pseudopapillary neoplasm of the pancreas associated with familial adenomatous polyposis. Intern Med 2015;54:1349–55.

[21] Sharma R, Sarin H, Luthra M. Solid pseudopapillary neoplasm of the pancreas in a pediatric patient with associated urogenital anomalies. J Indian Assoc Pediatr Surg 2019;24:129.

[22] Mishra A. Renal agenesis: report of an interesting case. Br J Radiol 2014;80:591–e192.

[23] Lal A, Pavunesan SK, Mahalingam H, *et al*. A triad of complete dorsal pancreatic agenesis, pancake kidney and bicornuate uterus. An association or an incidental finding: first case in literature. JOP J Pancreas 2015;16:189–91.

[24] Hall-Craggs MA, Kirkham A, Creighton SM. Renal and urological abnormalities occurring with Müllerian anomalies. J Pediatr Urol 2013;9:27–32.

[25] Barakat AJ. Association of unilateral renal agenesis and genital anomalies. Case Rep Clin Pract Rev 2002;3:57–60.

[26] Zuriarrain A, Nir I, Bocklage T, *et al*. Pseudopapillary tumor of the pancreas in a 17-year-old girl. J Clin Oncol 2011;29:e395–6.

[27] Rodriguez-Matta E, Hemmerich A, Starr J, *et al*. Molecular genetic changes in solid pseudopapillary neoplasms (SPN) of the pancreas. Acta Oncol 2020;59:1024.

[28] Tanaka Y, Kato K, Ijiri R, *et al*. Frequent β-catenin mutation and cytoplasmic/nuclear accumulation in pancreatic solid-pseudopapillary neoplasm. Cancer Res 2001;61:8401–4.

[29] Park M, Kim M, Hwang D, *et al*. Characterization of gene expression and activated signaling pathways in solid-pseudopapillary neoplasm of pancreas. Mod Pathol 2014;27:580–93.

[30] Liu M-S, Yang P-Y, Yeh T-S, *et al*. Sonic hedgehog signaling pathway in pancreatic cystic neoplasms and ductal adenocarcinoma. Pancreas 2007;34:340–6.

[31] Wang Y, Zhou CJ, Liu Y. Wnt signaling in kidney development and disease. Prog Mol Biol Transl Sci 2018;153:181.