DR CÉSAR VIVIAN LOPES (Orcid ID : 0000-0003-1820-7192)

Article type : Original article

Diagnosis of pancreatic solid pseudopapillary neoplasms using cell blocks and immunohistochemical evaluation of endoscopic ultrasound-guided fine-needle aspiration biopsy specimens

Running title: Cell blocks for the diagnosis of SPN

Word count: 2118 words

Tables: 2

Figures: 2

Authors:

José Celso Ardengh [1,2] (jcelso@uol.com.br) https://orcid.org/0000-0002-5932-2499 *****

César Vivian Lopes[3] (drcvlopes@gmail.com) https://orcid.org/0000-0003-1820-7192 *****

Filadélfio Euclides Venco[4] (filapath@gmail.com) https://orcid.org/0000.0002.2986.1053

Marcel Autran Machado[5] (dr@drmarcel.com.br) https://orcid.org/0000-0002-4981-7607

*** José Celso Ardengh and César Vivian Lopes contributed equally to this study and should be regarded as joint first authors**.

Authors' departments:

1. Division of Surgery and Anatomy, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil.

2. Endoscopy Unit, Hospital 9 de Julho, São Paulo, Brazil
3. Department of Gastroenterology and Digestive Endoscopy, Santa Casa Hospital, Porto Alegre, Brazil.
4. Diagnostika Pathology Laboratory, São Paulo, Brazil.
5. Department of Surgery, Hospital 9 de Julho, São Paulo, Brazil.

Corresponding author:
César Vivian Lopes, MD, PhD.
Rua Prof. Cristiano Fischer 668 / 1001, C.E.P.: 91.410-000
Porto Alegre-RS, Brazil
E-mail: drcvlopes@gmail.com

Conflicts of Interest: **Authors do not have any conflict of interest.**
Financial Disclosures: **None.**
Data availability statement: **Research data are not shared.**

Abstract

Background and Aims: Preoperative diagnostic imaging of pancreatic solid pseudopapillary neoplasms (SPN) is challenging. A few studies have investigated the role of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) for the diagnosis of SPN. We investigated the diagnostic yield of cell blocks and immunohistochemistry (IHC) for SPN using EUS-FNA specimens without cytological evaluation.

Patients and Methods: We retrospectively analyzed the histopathology records of patients with suspected SPN, who underwent EUS-FNA biopsy between January 1997 and January 2020. Diagnosis based on cell blocks (hematoxylin-eosin staining with complementary IHC) was compared with the definitive surgical diagnosis.

Results: This study included 25 patients (24 were women). Patients' mean age was 33.7 years (range 12–78 years). The most common symptom was abdominal pain. SPN was an incidental finding in 52% of the patients. The mean lesion size was 4.3 cm (range 1.2–11.4 cm), and the most common endosonographic features included solid-cystic (56%) or solid (40%) tumors. Final diagnoses included SPNs (23) and non-functioning neuroendocrine tumors (2). The overall accuracy of EUS-FNA was 80%. Tumor cells showed immunopositivity for beta-catenin, CD10, CD99, and progesterone receptor (PR) in 93.7%, 87.5%, 83.3%, and 66.6% of patients, respectively. No SPN showed immunopositivity for chromogranin A.

Conclusions: Intention-to-diagnose analysis showed that the diagnostic accuracy of EUS-FNA for SPNs using cell blocks and complementary IHC without cytological evaluation was fairly good. Evaluation of beta-catenin, CD 10, CD99, and PR expression must be included in the IHC panel for diagnostic confirmation of SPNs using EUS-FNA biopsy specimens.

Keywords*:* cell block, diagnosis, endosonography, needle biopsy, immunohistochemistry, solid pseudopapillary neoplasm.

Introduction

A pancreatic solid pseudopapillary neoplasm (SPN) is a rare exocrine tumor (less than 2800 cases are reported in the English literature) [1]. Women are more commonly affected (> 90% of the cases), particularly between the second and fourth decades of life. Most patients are asymptomatic or present with nonspecific symptoms, and SPN is usually incidentally diagnosed. SPN commonly presents as a large, well-circumscribed solid mass with cystic areas [2,3,4]. Surgical resection is the treatment of choice, and in contrast to ductal adenocarcinoma, the 5-year disease-free survival rate is as high as 97% [1].

Preoperative diagnostic imaging of SPNs is challenging owing to considerable morphological overlap with pancreatic diseases of particular aggressiveness, treatment and prognosis, specifically non-functioning neuroendocrine tumors (np-NET), serous cystadenoma, and rarely, ductal adenocarcinoma [2,5,6]. Therefore, histopathological evaluation of suspicious lesions is necessary. Considering its high diagnostic accuracy for the detection of ductal adenocarcinoma [7], endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) could be a useful minimally invasive and reliable diagnostic modality for SPN [2,8,9].

We investigated the role of cell blocks (CB) and complementary immunohistochemistry (IHC) without cytological evaluation for the diagnosis of SPNs in specimens obtained by EUS-FNA.

Patients and Methods

Study design

We retrospectively analyzed the histopathology records of patients with surgically confirmed SPNs that were preoperatively diagnosed based on EUS-FNA evaluation between January 1997 and January 2020 in the Endoscopy Unit, Hospital 9 de Julho, São Paulo, Brazil. Patients' charts were reviewed to obtain demographic data, EUS findings, and histopathological and IHC findings. The study protocol was reviewed and approved by the Institutional Review Board (Approval number: 3.518.999), and all patients provided written informed consent for the EUS-FNA procedure.

Endoscopic ultrasound-guided fine-needle aspiration technique

All procedures were performed by two experienced endosonographers (JCA and CVL) using curvilinear array echoendoscopes. The patient was placed in the left lateral position, and deep propofol sedation was administered by an anesthesiologist. EUS-FNA was performed using 22- or 19-gauge aspiration needles (Cook Medical, Bloomington, IN, USA), as well as 20-gauge core biopsy needles (ProCore needle, Cook Medical, Bloomington, IN, USA) depending on the availability of these needles and endoscopist's preferences. A cytopathologist was not present during the procedures. Following puncture of the lesion, negative suction pressure (10 mL) was applied to the needle before performing multiple to-and-fro movements. Non-hemorrhagic small tissue filaments or tissue core samples obtained with this maneuver were considered satisfactory specimens.

Preparation of specimens for histopathological evaluation

Specimens obtained using EUS-FNA were fixed in a 10% formaldehyde solution and subjected to centrifugation. The cell pellet was immersed in a liquid agarose solution and re-centrifuged. Once solidified, the agarose cell block was embedded in paraffin and processed as a routine tissue block. Thin (3 mm) sections were cut from cell blocks and stained with hematoxylin-eosin (HE) [10-12]. Specimens showing histopathological features suspicious for SPN were subjected to IHC evaluation using the avidin-biotin peroxidase method in a fully automated system for IHC staining (BenchMark ULTRA, Roche Tissue Diagnostics). The subset of antibodies selected for analysis included beta-catenin, CD 10, CD99, progesterone receptor (PR), chromogranin A (CG), and Ki-67. Histopathological evaluation of all specimens was performed by a single experienced gastrointestinal pathologist (FEV).

Diagnostic criteria for solid pseudopapillary neoplasms

The classical histopathological findings of SPNs facilitate rapid diagnostic confirmation. SPN typically presents as loosely cohesive cells interspersed with solid nests showing a pseudopapillary arrangement of uniform epithelioid cells surrounding small blood vessels. Eosinophilic cytoplasm may contain hyaline globules and perinuclear microvacuoles. Mitotic figures are rare. Cystic degeneration of the stroma is represented by foamy macrophages, cholesterol clefts, and hemorrhage in varying degrees of organization. Despite these characteristic morphological findings, SPNs may mimic other pancreatic tumors. Therefore, IHC evaluation is also performed. We adopted a concise antibody panel consisting of beta-catenin, CD10, CD99, PR, CG, and Ki-67 to overcome the limitation of inadequate aspirates. The tumor cell nuclei in nearly all SPNs showed strong immunopositivity for beta-catenin, CD10 was primarily expressed in the cytoplasm together with dot-like accentuation, CD99 was observed in the cytoplasm represented by perinuclear dots, and PR expression was observed as a faint dot-like nuclear pattern. We observed Ki-67 expression in < 2% of the tumor cells [13-17].

Statistical analysis

Statistical analysis was performed using the SPSS software, version 20.0 (IBM, New York, USA). Numerical variables were expressed as mean ± standard deviation, and categorical

variables were expressed as simple percentages. The significance level was set to 5% for all statistical procedures.

Results

We investigated 25 patients with suspicious SPNs by image analysis (24 [96%] were women). The mean age of patients in this study was 33.7 years (range 12–78 years). Abdominal pain was the most common symptom among the 12 (48%) patients who were symptomatic. SPN was an incidental finding in 13 (52%) patients. The mean size of the lesions was 4.3 cm (range 1.2–11.4 cm), and the most common endosonographic features included solid-cystic and solid lesions in 14 (56%) and 10 (40%) patients, respectively (**Figure 1**). A single patient had two synchronous lesions in the pancreatic body and tail. Most lesions showed well-defined borders. Large-bore 19-gauge aspiration needles were used for sampling in 64% of patients, with a median of 2.5 passes (range 1–5) for every lesion. Baseline characteristics of patients and the EUS findings are shown in **Table 1**. The definitive surgical diagnoses included SPNs (23) and np-NETs (2).

EUS-FNA could accurately diagnose 19 SPNs and a single case of np-NET; cell block-based evaluation was inconclusive, and specimens obtained were inadequate for IHC evaluation in 4 patients. Based on HE staining alone, SPN was diagnosed in 4 cases, but surgical excision confirmed a SPN in only 3 of these cases; the other patient was a np-NET. Complementary IHC evaluation was performed on the EUS-FNA specimens in 17 (68%) of 25 patients; SPNs were diagnosed in 16 (69.5%) of 23 patients, and np-NETs in 1 of 2 patients. IHC evaluation findings are shown in **Table 2**. The diagnostic yield of CB for SPNs was 82.6% (19/23), and the overall diagnostic accuracy of EUS-FNA was 80% (20/25). The remaining patient diagnosed with np-NET was based on HE and IHC evaluation and surgically confirmed**.**

In regard to the IHC evaluation, SPNs showed immunopositivity for beta-catenin, CD10, CD99, and PR in 93.7% (15/16), 87.5% (14/16), 83.3% (10/12), and 66.6% (8/12) of the patients, respectively. Tumor cells were immunonegative for CG in all 16 patients, and Ki-67 expression was < 2% in all patients. EUS-FNA confirmed the diagnosis of SPNs in 19 (82.6%) of 23 patients; 16 patients were diagnosed using HE staining with complementary IHC, and 3 patients were diagnosed using only HE staining (**Figure 2**).

Intention-to-diagnose analysis showed that the diagnostic accuracy of EUS-FNA for SPNs using cell blocks and complementary IHC without cytological evaluation was good at 69.5% (SPNs were definitively diagnosed in 16 of 23 patients). However, our analysis excluded 8

patients in whom EUS-FNA specimens were insufficient for IHC evaluation. Diagnosis based on cell blocks and IHC evaluation matched the surgical diagnosis in the remaining 17 patients, of which 16 showed SPNs and a single patient showed np-NET.

Discussion

Our findings in this study concur with those reported by previous studies; SPNs typically occur in young women, the lesions are distributed in the pancreatic body and tail, and histopathologically show a characteristic solid-cystic pattern. We suspected SPNs based on this pattern of clinical presentation, and a definitive diagnosis was established after correlation with morphological and IHC findings. However, a few patients in this case series presented with atypical findings. SPN was detected in one man, and 26% of our patients were aged > 40 years. SPN was located in the pancreatic head in 26% of patients, and a solid lesion was observed in 40% of the patients in this study. These unusual presenting features have been previously reported in the literature [1,18,19], which emphasizes that in some patients, SPNs cannot be suspected based on demographics and imaging findings. Microscopic evaluation of tissue specimens is the only method for diagnostic confirmation in such cases.

In this study, we performed EUS-FNA in 25 patients with suspected SPN by image analysis. Satisfactory specimens were obtained for cell blocks in all patients; however, final diagnosis using complementary IHC could be established in only 17 (68%) patients. The diagnostic accuracy of EUS-FNA without cytological evaluation was 80%. The diagnostic accuracy for SPNs was 69.5% in patients in whom histopathological and IHC evaluation of specimens could be appropriately performed.

The diagnostic yield of EUS-FNA for the diagnosis of SPNs ranges between 69.5% and 82.4% [1,2,8]. The results of our intention-to-diagnose analysis based only on histopathological findings were identical to those reported by Law et al.[1] in the largest SPN review published to date (484 studies that investigated 2744 patients). However, several studies have shown that cytological evaluation improves the diagnostic yield for SPNs because cytomorphological and histopathological findings are complementary [2,8,20]. Notably, the diagnosis of suspected SPNs based only on cytological findings without histopathological confirmation can misdiagnose np-NETs as SPNs in up to 36% of the cases. Such misdiagnosis is commonly observed in clinical practice owing to considerable overlap between the radiological and even microscopic features of SPNs and np-NETs [9,17]. Therefore, in addition to both cytological and histopathological evaluation, complementary IHC is widely recommended for the diagnosis of SPNs.

There is lack of consensus regarding the optimal IHC panel for suspicious SPNs. However, the immunoreactivity of some markers is well established; SPNs typically show strong

nuclear staining of beta-catenin with 90%–100% immunopositivity in contrast to np-NETs in which this pattern is extremely uncommon, although cytoplasmic immunopositivity is detected in most cases [3,21-25]. CD10, CD99, and PR are among the other markers used for this purpose. Among the neuroendocrine markers, immunonegativity to CG is common. We observed that EUS-FNA specimens showed beta-catenin immunopositivity in 93.7% of patients, and these findings were similar to those previously reported in the literature [3,21-25]. CD10 immunopositivity was observed in 87.5% of the patients in this study; previous studies have reported immunopositivity rates of CD10 ranging between 83% and 100% for SPNs [13,14,26]. CD99 immunopositivity was observed in 83.3% of our patients. Guo et al.[15] first reported the expression of CD99 in SPNs, and observed immunopositivity of this marker in all 55 patients investigated in the study. Another study that investigated 37 patients with SPNs reported the same pattern of CD99 expression [27]. With regard to PR, its immunopositivity rates in patients with SPNs range between 79% and 100%, and the prognostic value of PR has recently been recognized [3,4,23,28]. We observed PR immunopositivity in 66.6% of our patients. No SPN showed immunopositivity to CG, which concurs with findings of previous studies reported in the literature [21,28]. However, 4 previous studies have reported CG expression in patients with SPNs (immunopositivity in 16 [23.9%] of 67 patients) [14,27,29,30]. Ohara et al.[31] reported the expression of this marker in 6 patients with SPNs, typically with a distinct dot-like staining pattern. These data indicate that CG cannot be used as a single specific IHC marker for the diagnosis of np-NETs to avoid the risk of misdiagnosis of an SPN as a NET.

Following are the strengths of our study: (a) All specimens were obtained from surgically confirmed SPNs using EUS-FNA, which is a well-established safe method for pancreatic sampling in ambulatory settings. (b) This is one of the largest single-center studies that reports the usefulness of this diagnostic method for SPNs. (c) Despite the limited aspirate obtained from SPNs, cell blocks could be appropriately prepared for histopathological evaluation, and complementary IHC could be performed in almost 70% of patients.

Following are the limitations of the study: (a) The small sample size is the most important drawback of the study. However, considering the rarity of this condition, it might not be possible to recruit a large number of patients, except in multicenter studies with a thorough review of patients' histopathological records. Therefore, most knowledge regarding SPNs is based on a limited number of case reports and small case series available in the literature. (b) This case series included the sole use of cell blocks without any cytological evaluation, and adequate cell block

samples for complete IHC evaluation were unavailable in 30% of the patients in this study. In fact, the IHC panel included a limited number of markers owing to an inadequate aspirate, and the markers were selected based on their relevance reported in the literature and at the pathologist's discretion.

In conclusion, the preoperative diagnostic accuracy of EUS-FNA for SPNs using cell blocks and IHC without cytological evaluation was 69.5%. We hypothesize that the addition of cytopathological evaluation would result in higher diagnostic accuracy. We propose that beta-catenin combined with CD10, CD99, and PR must be included in the diagnostic IHC panel for SPNs.

References

1. Law JK, Ahmed A, Singh VK, Akshintala VS, Olson MT, Raman SP, et al. A systematic review of solid-pseudopapillary neoplasms: are these rare lesions ? *Pancreas* 2014;43:331-337.

2. Law JK, Stoita A, Wever W, Gleeson FC, Dries AM, Blackford A, et al. Endoscopic ultrasound-guided fine needle aspiration improves the pre-operative diagnostic yield of solid-pseudopapillary neoplasm of the pancreas: an international multicenter case series. *Surg Endosc* 2014;28:2592-2598.

3. Serrano PE, Serra S, Al-Ali H, Gallinger S, Greig PD, McGilvray ID, et al. Risk factors associated with recurrence in patients with solid pseudopapillary tumors of the pancreas. *JOP* 2014;15:561-568.

4. Nguyen NQ, Johns AL, Gill AJ, Ring N, Chang DK, Clarkson A, et al. Clinical and immunohistochemical features of 34 solid pseudopapillary tumors of the pancreas. *J Gastroenterol Hepatol* 2011;26:267-274.

5. Bhatnagar R, Olson MT, Fishman EK, Hruban RH, Lennon AM, Ali SZ. Solid-pseudopapillary neoplasm of the pancreas: cytomorphologic findings and literature review. *Acta Cytol* 2014;58:347-355.

6. De Robertis R, Marchegiani G, Catania M, Ambrosetti MC, Capelli P, Salvia R, et al. Solid Pseudopapillary Neoplasms of the Pancreas: Clinicopathologic and Radiologic Features According to Size. *AJR Am J Roentgenol* 2019;213:1073-1080.

7. Ardengh JC, Lopes CV, de Lima LF, de Oliveira JR, Venco F, Santo GC, et al. Diagnosis of pancreatic tumors by endoscopic ultrasound-guided fine-needle aspiration. *World J Gastroenterol* 2007;13:3112-3116.

8. Jani N, Dewitt J, Eloubeidi M, Varadarajulu S, Appalaneni V, Hoffman B, et al. Endoscopic ultrasound-guided fine-needle aspiration for diagnosis of solid pseudopapillary tumors of the pancreas: a multicenter experience. *Endoscopy* 2008;40:200-203.

9. Hooper K, Tracht JM, Eldin-Eltoum IA. Cytologic criteria to reduce error in EUS-FNA of solid pseudopapillary neoplasms of the pancreas. *J Am Soc Cytopathol* 2017;6:228-235.

10. Ardengh JC, Lopes CV, de Lima LF, Venco F, Santo GC, Begnami MD, et al. Cell block technique and cytological smears for the differential diagnosis of pancreatic neoplasms after endosonography-guided fine-needle aspiration. *Acta Gastroenterol Latinoam* 2008;38:246-251.

11. Kung IT, Chan SK, Lo ES. Application of the immunoperoxidase technique to cell block preparations from fine needle aspirates. *Acta Cytol* 1990;34:297-303.

12. Choi SJ, Choi YI, Kim L, Park IS, Han JY, Kim JM, et al. Preparation of compact agarose cell blocks from the residues of liquid-based cytology samples. *Korean J Pathol* 2014;48:351-360.

13. Notohara K, Hamazaki S, Tsukayama C, Nakamoto S, Kawabata K, Mizobuchi K, et al. Solid-pseudopapillary tumor of the pancreas: immunohistochemical localization of neuroendocrine markers and CD10. *Am J Surg Pathol* 2000;24:1361-1371.

14. Burford H, Baloch Z, Liu X, Jhala D, Siegal GP, Jhala N. E-cadherin/beta-catenin and CD10: a limited immunohistochemical panel to distinguish pancreatic endocrine neoplasm from solid pseudopapillary neoplasm of the pancreas on endoscopic ultrasound-guided fine-needle aspirates of the pancreas. *Am J Clin Pathol* 2009;132:831-839.

15. Guo Y, Yuan F, Deng H, Wang HF, Jin XL, Xiao JC. Paranuclear dot-like immunostaining for CD99: a unique staining pattern for diagnosing solid-pseudopapillary neoplasm of the pancreas. *Am J Surg Pathol* 2011;35:799-806.

16. Dinarvand P, Lai J. Solid Pseudopapillary Neoplasm of the Pancreas: A Rare Entity With Unique Features. *Arch Pathol Lab Med* 2017;141:990-995.

17. Zalatnai A, Kis-Orha V. Solid-pseudopapillary Neoplasms of the Pancreas is still an Enigma: a Clinicopathological Review. *Pathol Oncol Res* 2019;26:641-649.

18. Papavramidis T, Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in English literature. *J Am Coll Surg* 2005;200:965-972.

19. Reddy S, Wolfgang CL. Solid pseudopapillary neoplasms of the pancreas. *Adv Surg* 2009;43:269-282.

20. Singh P, Kumar P, Rohilla M, Gupta P, Gupta N, Dey P, et al. Fine needle aspiration cytology with the aid of immunocytochemistry on cell-block confirms the diagnosis of solid pseudopapillary neoplasm of the pancreas. *Cytopathology* 2020 Apr 22. doi: 10.1111/cyt.12838. Online ahead of print.

21. Uppin SG, Hui M, Thumma V, Challa S, Uppin MS, Bheerappa N, et al. Solid-pseudopapillary neoplasm of the pancreas: a clinicopathological and immunohistochemical study of 33 cases from a single institution in Southern India. *Indian J Pathol Microbiol* 2015;58:163-169.

22. Harrison G, Hemmerich A, Guy C, Perkinson K, Fleming D, McCall S, et al. Overexpression of SOX11 and TFE3 in Solid-Pseudopapillary Neoplasms of the Pancreas. *Am J Clin Pathol* 2017;149:67-75.

23. Wang F, Meng Z, Li S, Zhang Y, Wu H. Prognostic value of progesterone receptor in solid pseudopapillary neoplasm of the pancreas: evaluation of a pooled case series. *BMC Gastroenterol* 2018;18:187.

24. Kim EK, Jang M, Park M, Kim H. LEF1, TFE3, and AR are putative diagnostic markers of solid pseudopapillary neoplasms. *Oncotarget* 2017;8:93404-93413.

25. Serra S, Chetty R. Revision 2: an immunohistochemical approach and evaluation of solid pseudopapillary tumour of the pancreas. *J Clin Pathol* 2008;61:1153-1159.

26. Salla C, Konstantinou P, Chatzipantelis P. CK19 and CD10 expression in pancreatic neuroendocrine tumors diagnosed by endoscopic ultrasound-guided fine-needle aspiration cytology. *Cancer* 2009;117:516-521.

27. Li L, Li J, Hao C, Zhang C, Mu K, Wang Y, et al. Immunohistochemical evaluation of solid pseudopapillary tumors of the pancreas: the expression pattern of CD99 is highly unique. *Cancer Lett* 2011;310:9-14.

28. Kosmahl M, Seada LS, Janig U, Harms D, Kloppel G. Solid-pseudopapillary tumor of the pancreas: its origin revisited. *Virchows Arch* 2000;436:473-480.

29. Choi YL, Oh YL, Kim SH, Park CK, Ahn G. Comparative study of non-functional islet cell tumors and pancreatic solid and papillary neoplasms: biological behavior and immunohistochemistry. *Pathol Int* 2002;52:358-366.

30. Liu BA, Li ZM, Su ZS, She XL. Pathological differential diagnosis of solid-pseudopapillary neoplasm and endocrine tumors of the pancreas. *World J Gastroenterol* 2010;16:1025-1030.

31. Ohara Y, Oda T, Hashimoto S, Akashi Y, Miyamoto R, Enomoto T, et al. Pancreatic neuroendocrine tumor and solid-pseudopapillary neoplasm: Key immunohistochemical profiles for differential diagnosis. *World J Gastroenterol* 2016;22:8596-8604.

Tables

Table 1. **Patient characteristics and endoscopic ultrasound-guided fine-needle aspiration biopsy findings in suspected solid pseudopapillary neoplasms**

	n	%
Sex		
Female	24	96
Male	1	4
Symptoms *	12	48
Abdominal pain	10	40
Weight loss	6	24
Nausea/vomiting	4	16
Jaundice	3	12
Lesion location		
Neck/Body	13	52
Head/uncinate	6	24
Tail	6	24
Echogenicity		
Solid-cystic	14	56
Solid	10	40
Cystic	1	4
Borders		
Well-defined	22	88
Infiltrative	3	12
Dilated main pancreatic duct	2	8
Needles		
19 G aspiration needle	16	64
22 G aspiration needle	7	28
22 G core biopsy needle	2	8
Surgery		
Distal pancreatectomy with splenectomy	13	52

Pancreaticoduodenectomy	6	24
Distal pancreatectomy	2	8
Uncinectomy	2	8
Enucleation	2	8

* 5 patients with more than one symptom.

Table 2. Immunohistochemical profile of pancreatic tumors

Pcte	Sex	Age	Needle (G)	HE	Beta-catenin	CD10	CD99	PR	CG	Surgery
1	F	20	22	SPN	NA	NA	NA	NA	NA	SPN
2	F	35	22	SPN	NA	NA	NA	NA	NA	SPN
3	F	35	22	SPN	+	+	NA	NA	-	SPN
4	F	57	22	SPN	+	+	NA	NA	-	SPN
5	F	15	19	SPN	+	+	NA	NA	-	SPN
6	F	55	22	INC	NA	NA	NA	NA	NA	SPN
7	F	12	22	SPN	+	+	NA	NA	-	SPN
8	F	26	22	SPN	+	+	+	+	-	SPN
9	F	23	22	SPN	NA	NA	NA	NA	NA	SPN
10	F	23	22	INC	NA	NA	NA	NA	NA	SPN
11	F	32	22	SPN	+	+	+	+	-	SPN
12	F	32	22	SPN	+	-	+	-	-	SPN
13	F	61	19	INC	NA	NA	NA	NA	NA	SPN
14	F	34	19	np-NET	-	+	-	-	+	np-NET
15	F	39	22	SPN	+	+	+	+	-	SPN
16	F	15	19	INC	NA	NA	NA	NA	NA	SPN
17	F	18	19	SPN	+	-	+	+	-	SPN
18	F	49	22	SPN	+	+	+	+	-	SPN
19	F	27	19	SPN	+	+	+	-	-	SPN
20	F	58	20	SPN	+	+	+	+	-	SPN
21	F	25	20	SPN	+	+	+	+	-	SPN
22	F	16	19	SPN	NA	NA	NA	NA	NA	np-NET
23	F	74	22	SPN	+	+	-	-	-	SPN
24	M	38	22	SPN	+	+	+	+	-	SPN
25	F	23	22	SPN	-	+	-	-	-	SPN

SPN: solid pseudopapillary neoplasm; INC: inconclusive; HE: hematoxylin-eosin; PR: progesterone receptor; CG: chromogranin A; np-NET: non-functioning neuroendocrine tumor; NA: non-available

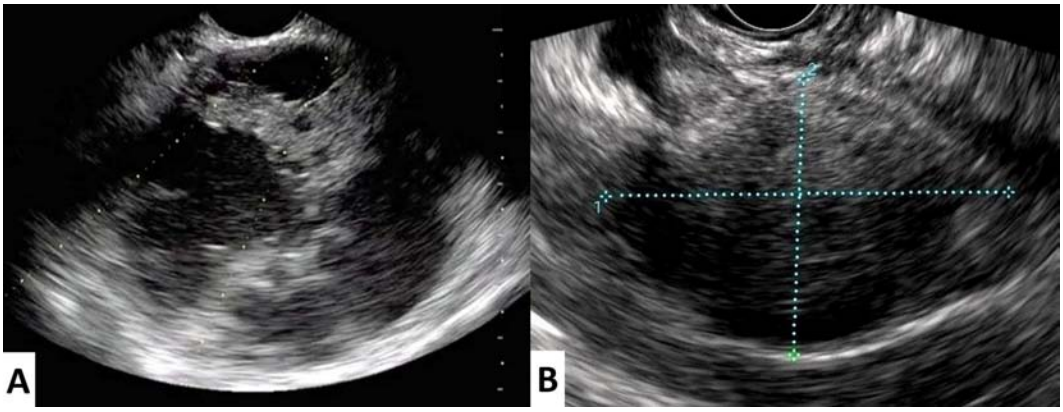
Figure Legends

Figure 1. Endosonographic images showing a suspected SPN: A) Solid-cystic morphology. B) A solid lesion with well-defined borders.

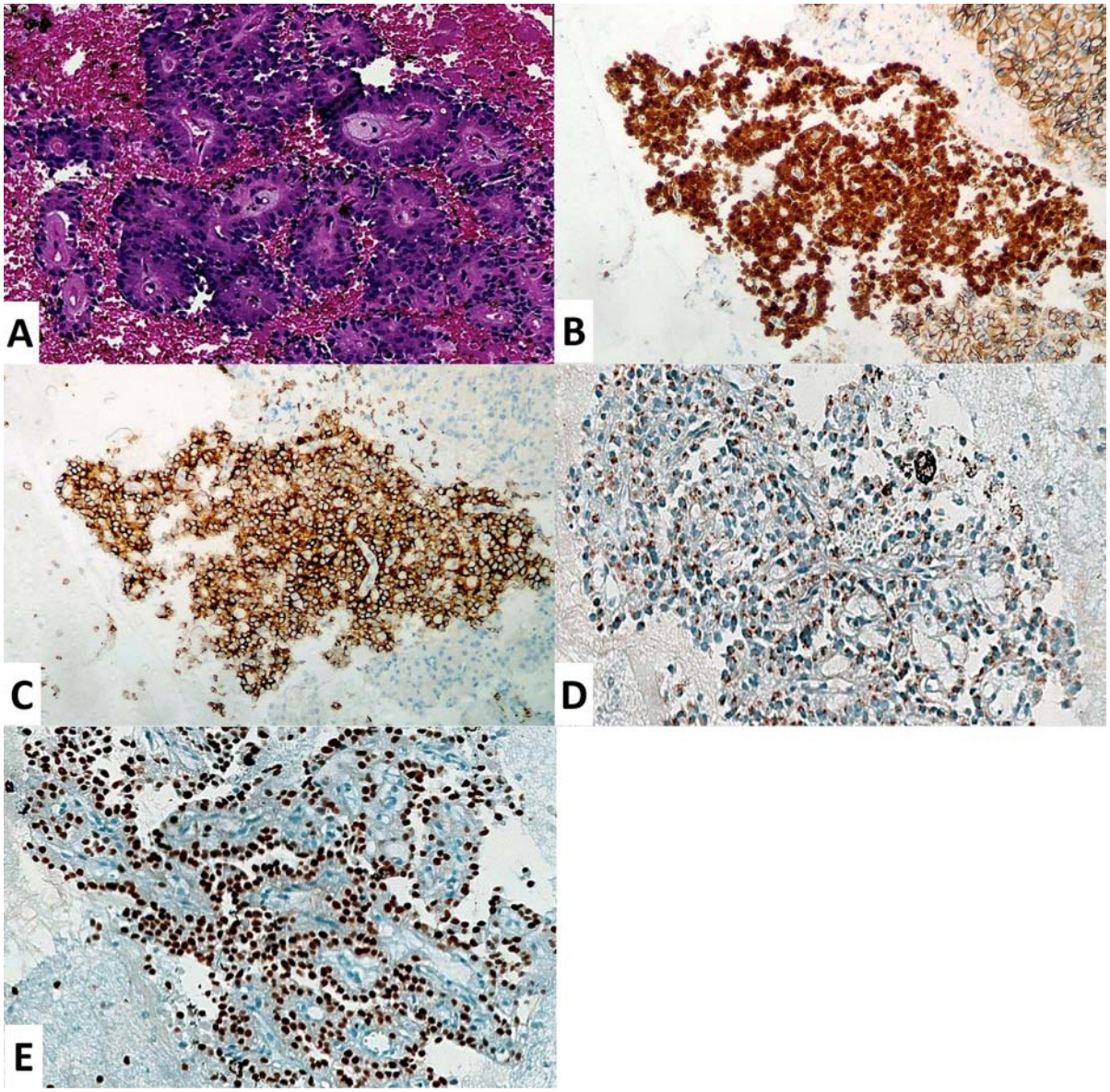
SPN: solid pseudopapillary neoplasm

Figure 2: Histopathological findings of SPNs: A) Pseudopapillae formed by loosely cohesive, short columnar cells with eosinophilic cytoplasm and intracytoplasmic hyaline globules surrounding delicate vessels (HE ×400).
Image showing immunohistochemical markers for SPNs: B) beta-catenin (×200), C) CD10 (×200), D) CD99 (×200) and, E) progesterone receptor (×200).

HE: hematoxylin-eosin, SPN: solid pseudopapillary neoplasm



cyt_12905_f1.jpg



cyt_12905_f2.jpg