International Journal of Surgery Case Reports 84 (2021) 106131

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.elsevier.com/locate/ijscr

Case report

Solid bifocal pseudopapillary neoplasm of the pancreas: A case report

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ARTICLE INFO

Keywords:
Solid pseudopapillary neoplasia of the pancreas
Franz's tumor
Solid tumors of the pancreas
Case report

ABSTRACT

Introduction: This neoplasm of the pancreas is an uncommon entity, with a frequency of 0.3–2.7% of all pancreatic tumors and even more so the finding of a synchronous lesion of the same histological lineage. For this reason, we report the atypical presentation of a SPNPs through a clinical case, review of the literature and a classification proposal, from the quantitative point of view.

Case presentation: 21-year-old patient, with incidental finding of two pancreatic tumors. Surgery included a pyloric preserving pancreatoduodenectomy with pancreatojejunostomy, distal pancreatectomy and central pancreas was preserved. The patient presents low output pancreatic fistula and nosocomial infection, treated with antibiotic therapy, being discharged 29 days after the intervention. Pathological and immunohistochemical analysis consistent with two SPNP.

Discussion: Its diagnosis is confirmed with the histological study and two synchronic SPNP are a rare entity and for this, or multiple lesions, an attempt should be made of a conservative resection of the parenchyma to minimize pancreatic insufficiency in a frequently young population, and always look for R0 resection, due to its uncertain behavior.

Conclusion: Bifocal SPNP is rare and for this it is utility classify this entity -from the quantitative point of view- into unifocal, bifocal and multifocal for future medical research.

1. Introduction

Solid pseudopapillary neoplasia of the pancreas (SPNP), first described by Frantz in 1959 [2], is a low-grade malignancy entity composed of poorly cohesive epithelial cells, forming solid and pseudopapillary structures, that lack a specific line of pancreatic epithelial differentiation. Considered for a long time as a benign or borderline pathology, due to its behavior, the WHO reclassified this entity in 2010 with the name it currently bears [3].

SPNP is a rare entity, with a frequency of 0.3–2.7% of all pancreatic tumors [4] and since 2000 its incidence has increased, probably related to a greater use and availability of imaging studies, rather than being a real increase in its incidence [5]. It has a distal location, an average of 7 cm in diameter at the time of its appearance and a propensity for the female gender, showing a bimodal frequency with a peak at 28 years of age and a late one at 62 years of age, while in men shows a single peak at age 64 [6].

Surgical resection, with negative borders, is considered curative in most cases and is associated with an overall survival, at 5 years, of 93.7% [6]. Although the entity may be indolent at the time of appearance, 10–15% of patients show an aggressive form, with invasion of adjacent organs and distant metastases, or both [7].

The objective of this publication is to present a case report, a brief bibliographic review and propose a classification.

2. Clinical case

This work has been reported in line with the SCARE 2020 criteria [1].

Female patient, 21 years old, with no significant morbid history. Evaluated on March 20th, 2020, with a renal doppler ultrasound for suspected renovascular hypertension. Incidentally, a solid tumor is observed, located between the head of the pancreas and the uncinate process, measuring 43 × 40 × 39 mm in diameter, hypoechoic and

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https://doi.org/10.1016/j.ijscr.2021.106131
Received 28 May 2021; Received in revised form 17 June 2021; Accepted 17 June 2021
Available online 25 June 2021

vascularized, with regular contours (Fig. 1).

An MRI of the pancreas is requested in which two solid, rounded lesions with well-defined margins are observed in the head of the pancreas, measuring 40 × 39 mm and another 16 × 15 mm at the junction of the body and the pancreatic tail, of relatively homogeneous signal, slightly hypointense on T1 and hyperintense on T2, with progressive enhancement with intravenous contrast (Fig. 2) and slight diffusion restriction; they do not dilate the main pancreatic duct, nor extra pancreatic lesions are observed (Fig. 2). The study is complemented with a 68-gallium DOTATATE PET/CT, showing two solid pancreatic focal lesions, in which no over-expression of somatostatin receptors is identified, which rules out lesions of neuroendocrine origin.

Surgical intervention was performed by laparotomy on August 8th 2020, revealing upon inspection a tumor lesion in the pancreatic head of 5 cm in diameter and another lesion of the tail of 2 cm, without evidence of metastatic disease. A pancreatoduodenectomy was performed with pyloric preservation and pancreatic intussusception within the jejunum, distal pancreatectomy with Endo GIA and Seamguard stapler. The central pancreas was preserved. She evolved with a low output pancreatic fistula and nosocomial infection, treated successfully with Meropenem and discharged on September 1st, 2021.

In the macroscopic examination of the surgical piece, a solid tumor in the pancreatic head, whitish, partly hemorrhagic, well-defined, measuring 4.5 × 4.5 × 4 cm is observed, and in the distal pancreatic region, a solid tumor, well-defined, with a homogeneous, whitish surface, measuring 2 × 1.6 × 1.5 cm. Both lesions were far from the edges, without compromising the main pancreatic duct (Fig. 3).

In the microscopic analysis, both lesions were compatible with a solid pseudopapillary neoplasm of the pancreas. In addition, 17 lymph nodes are evaluated, all negative for neoplastic cells. Immunohistochemistry was positive for β-catenin and vimentin; negative for CK AE1/AE3. (See Fig. 4).

3. Discussion

SPNP is a tumor with uncertain cell behavior and differentiation, which has led, for many years, to call this entity in various ways [8]. They are mostly asymptomatic and are discovered incidentally on imaging studies; There is a group of patients, however, who may refer nonspecific symptoms, such as abdominal discomfort, nausea, vomiting, asthenia or pain, due to intratumoral hemorrhage [9].

From an imaging point of view, SPNPs are usually located in the tail of the pancreas. On ultrasound, they may present as homogeneous or heterogeneous lesions, predominantly hypoechoic with a hyperechogenic ring. Computed tomography (CT) can show an encapsulated mass with a solid-cystic appearance, areas of necrosis, and hemorrhagic degeneration. These cystic areas are visualized at the center, while solid and calcified areas are located towards the periphery of the lesion [10]. With the use of intravenous contrast, it presents hypovascular kinetics with predominant impregnation in the portal venous phase [11].

The MRI is superior to other modalities in characterizing solid and cystic pancreatic lesions. SPNP are visualized as encapsulated, solid-cystic lesions, with internal bleeding and without internal septa. They can be classified into three types, corresponding to the clinical-pathological findings. Type 1, exclusively solid, diffuse hypointensity in T1 and discreet hyperintensity in T2. Type 2, solid, associated with hemorrhage, with a hypointense signal on T1 and slightly hyperintense on T2 at the central level (solid) surrounded by heterogeneous hyperintense areas on T1 (hemorrhage). Type 3 shows significant bleeding, being predominantly hyperintense on T1 and heterogeneous (hypo/hyperintense) on T2 depending on the evolution of the bleeding time [9].

In the surgical specimen they are visualized as solid lesions with cystic degeneration, well-defined, with hemorrhagic areas that give a yellow-brown color at inspection and are soft and friable on palpation [8].

Its diagnosis is confirmed with the histological study.

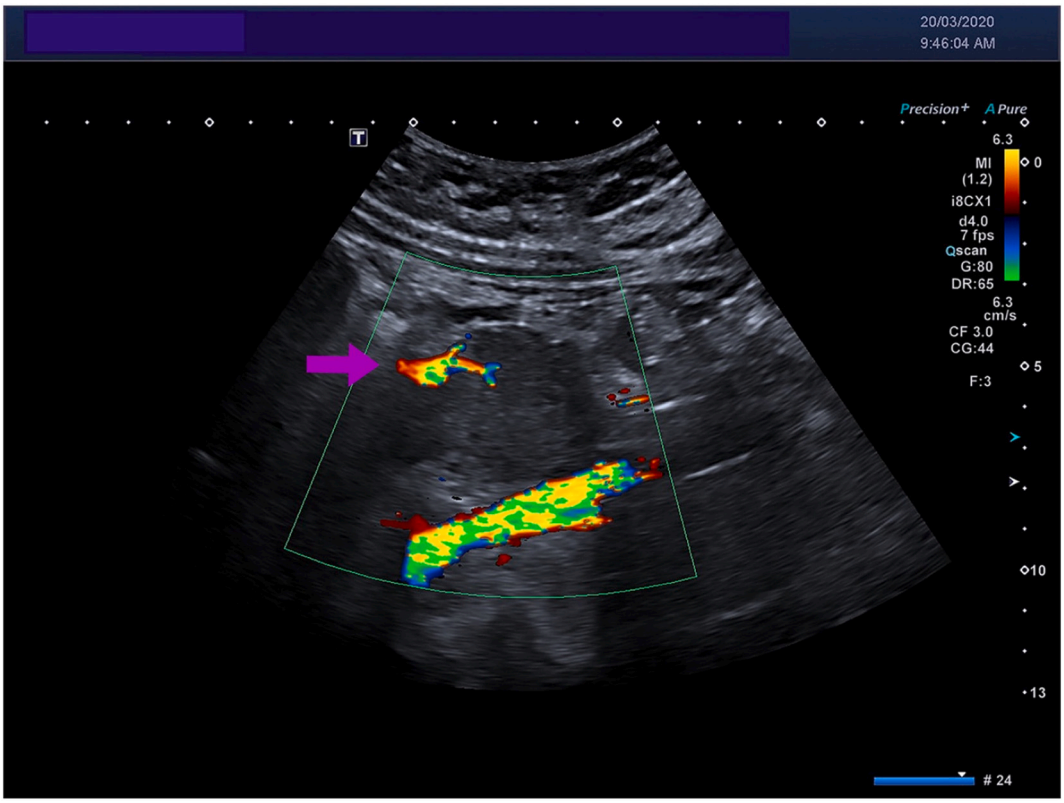

Fig. 1. The arrow shows a relatively well-defined hypoechoic lesion in the head of the pancreas with mild vascularization predominantly in its periphery.

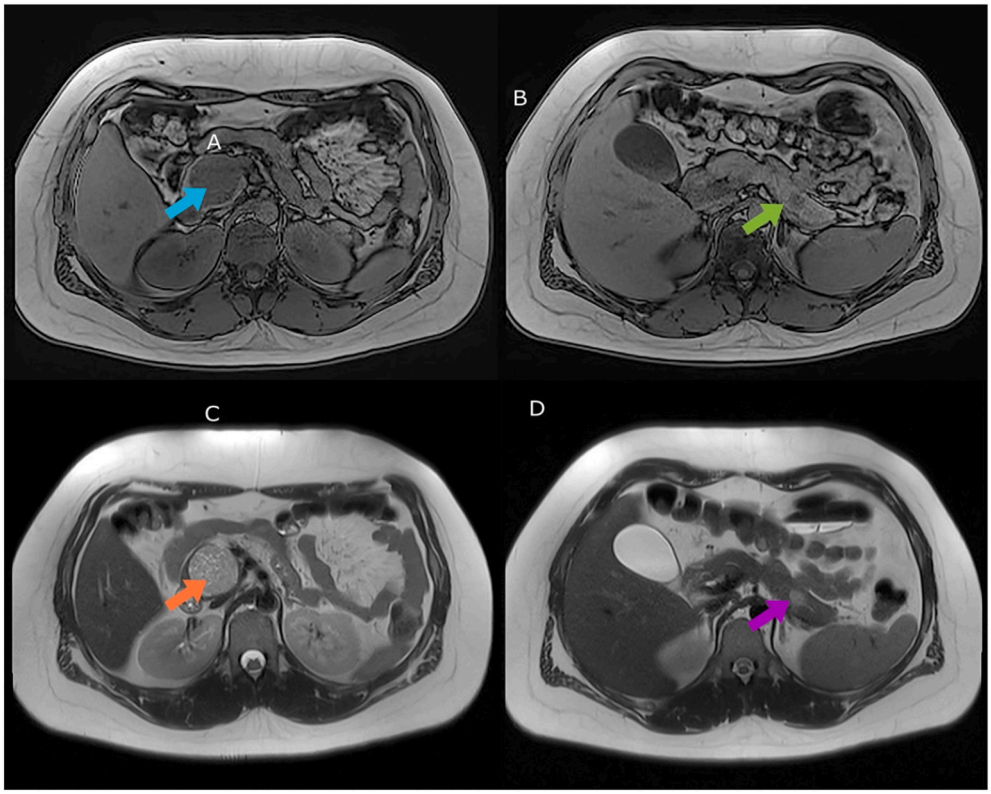

Fig. 2. A) and B) MRI sequence T1, out of phase. Blue and green arrows indicate pancreatic head and tail lesions with a slightly hypointense signal on T1. C) and D) MRI sequence T2, orange and fuchsia arrows indicate lesions in the head and tail of the pancreas.

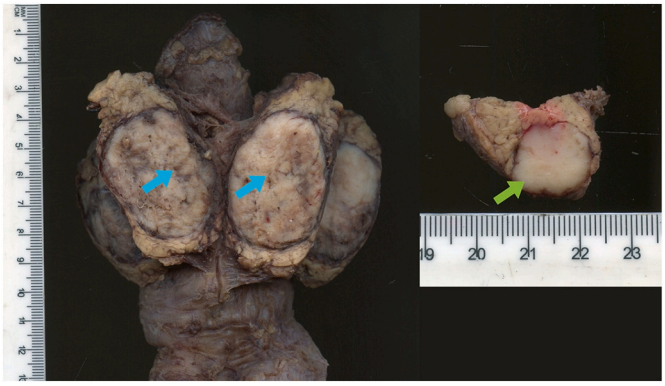

Fig. 3. A) SPNP located in the cephalic region (light blue arrow). B) SPNP located in the distal region (green arrow).

Microscopically they appear as solid nests of cells, with abundant small blood vessels. Cells located distant from the capillaries tend to degenerate and the viable ones, close to them, present pseudopapillary architecture, characteristic of these tumors [12].

They generally show a heterogeneous appearance, including various proportions of solid and pseudopapillary structures. Neoplastic cells, surrounded by a myxoid stroma, fibrous or hyalinized, are quite monomorphic, show hyaline globules, with an eosinophilic or vacuolated cytoplasm, and the nuclei are round to oval, often with nuclear or dentate folds, with finely dispersed chromatin without a prominent nucleolus. Mitoses are rare, and vascular and perineural invasion is rarely found. Additional features that can be observed include areas of hemorrhage, pseudocystic changes, presence of foamy macrophages, and deposits of cholesterol crystals [13]. Despite the well-circumscribed nature of these tumors, at the interface with non-neoplastic tissue, an intimate juxtaposition between normal acinar elements and tumor cell nests is often evident [8].

SPNPs present specific somatic mutations in CTNNB1 exon 3, a gene that encodes β-catenin. These mutations are related to the activation of the Wnt/β-catenin signaling pathway, preventing intracytoplasmic phosphorylation and subsequent degradation of the β-catenin protein, accumulating in the nucleus of neoplastic cells, stimulating the transcription of several genes, such as c -myc and cyclin D1, both involved in cell proliferation. As a result, 90% of SPNPs have an abnormal pattern of nuclear marking of the protein β-catenin, whereas in a healthy pancreas, the marking is on the membrane. B-catenin interacts with E-cadherin, so the deregulation of the former interferes with the expression of the latter and, consequently, no membrane expression of E-cadherin is observed in most SPNP [14].

Despite the foregoing, histogenesis remains poorly understood and is based on hypotheses rather than results, since the latter have not been explanatory. Immunohistochemistry shows a loss of positivity for E-cadherin and positivity for β-catenin, vimentin, alpha-1-antitrypsin, alpha-1-antitrypsin, CD10, CD117 and progesterone receptors, but none of them are specific for a cell line [15], but they are useful to guide the diagnosis, along with the clinical, imaging and histological characteristics (Tables 1–2).

The goal of treatment is a complete resection of the lesion (R0), achieving an overall survival at 5 and 10 years of 96% and 93%, respectively. The optimal approach could be a point of discussion, if it is by laparotomy versus minimally-invasive approach, which could be related to its location, which implies greater or less intra- or postoperative morbidity and mortality; there is also the desire to preserve the greatest amount of pancreatic parenchyma: enucleation, central segmental resection, or combined procedures can be performed if there is more than one tumor, similar to what is done in multiple neuroendocrine tumors associated with multiple endocrinopathies. Therefore, the experience of the surgeon and referral centers is essential to

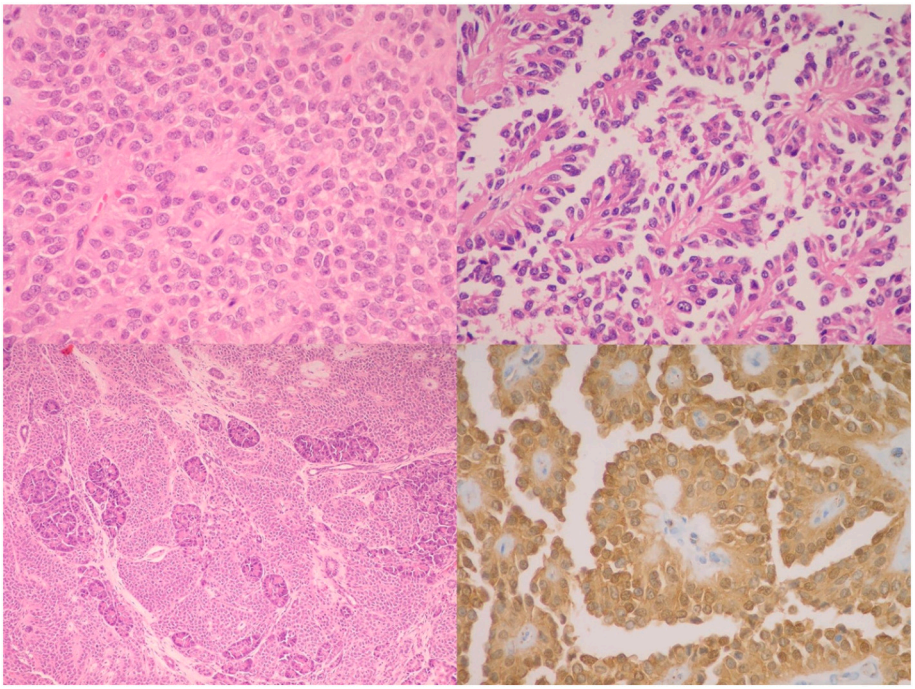

Fig. 4. A) H&E staining. 20×. Solid patterned areas. B) H&E staining. 20×. Areas with a pseudopapillary pattern. C) H&E staining. 10×. Tumor cells surrounding pancreatic acinar structures. D) Immunohistochemistry. 20×. Positive for nuclear β-catenin.

Table 1
Clinicopathological findings of the differential diagnoses for SPNP.

Features	Acinar cell carcinoma	Mixed acinar-neuroendocrine carcinoma	Pancreatoblastoma	Pancreatic neuroendocrine tumor	Solid pseudopapillary neoplasm
Age at diagnosis	Average 58 years	18–75 years	First decade of life. Average age of onset 4 years	30–80 years	Bimodal in women Unimodal in men
Incidence by gender	Men more tan women (3,6:1)	Men more tan women	Boys more tan girls (1,3:1)	Men = Women	Women more tan men
Symptoms	Pain and lipase hypersecretion (10–15%)	Pain	Pain	Dpain, neuroendocrine paraneplasic syndrome	Often asymptomatic
Histology	Highly celular. Solid nest, acinar pattern, sparse stroma.	Solid nest, acini, various degrees of stroma	Highly celular. Well defined solid nest separated by fibrous band. Acinar differentiation and squamous nest.	Solid nest, trabeculae, hyalinized stroma. Round to oval nuclei. Chromatin pattern in salt and pepper. Variable mitosis	Pseudopapillae, lumen deficiency and various degrees of stroma

Table 2
Immunohistochemical findings of differential diagnoses for SPNP.

Features	Acinar cell carcinoma	Mixed acinar-neuroendocrine carcinoma	Pancreatoblastoma	Pancreatic neuroendocrine tumor	Solid pseudopapillary neoplasm
Keratin	++	++	++	++	−/+
Vimentin	−	−	−	−	++
Trypsin	++	++	++	−	−
Chromogranin	−	++	++	++	−
Synaptophysin	−	++	+	++	+
CD56	−	++	+	++	++
Alpha-1-antitrypsin	+	+	+	−/+	++
CEA	−	−	+	+	−
β -catenin (nuclear)	−	−	−	−	++

CEA: Carcinoembryonic antigen; − usually negative; −/+ negative rather than positive; + always positive; ++ consistently positive.

minimize surgical morbidity and mortality.

SPNP is a rare entity and even more so the finding of a synchronous lesion of the same histological lineage. Despite the absence of a formal classification, in relation to the number of SPNP, it is proposed to classify them as follows:

- Unifocal SPNP, when it is a single tumor.
- Bifocal SPNP, when there are two tumors.
- Multifocal SPNP, when they are equal to or greater than three tumors.

In our case, the "bifocal" presentation is an atypical finding, which has not been described in the medical literature and this publication can give certain guidelines to reach a diagnosis, and evaluate the different existing differential diagnoses, relying on immunohistochemistry when the clinical, imaging and histopathological findings are not clear; in addition to how to face this entity from the surgical point of view. Currently, it has been nine months since our patient was operated, with no evidence of loco-regional or distant recurrence.

4. Conclusion

The Solid Pseudopapillary Neoplasia of the Pancreas, described in 1959, is a rare entity, with uncertain behavior and an unknown histogenesis. In women, where the presentation is more frequent, it has a bimodal behavior and, thanks to the imaging progress and the histopathological study, this entity is diagnosed in most cases, and now it can be quantitatively classified as unifocal, bifocal or multifocal for future medical research. R0 surgery is a fundamental pillar in the control of the disease, with an overall survival of 96% at 10 years of follow-up in referral centers [3].

Provenance and peer review

Not commissioned, externally peer-reviewed.

Funding

The authors declared that this study has received no financial support.

Ethical approval

Written informed consent was obtained from the patient for 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.

Consent

Written informed consent was obtained from the patient for 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.

Research registration

Not applicable.

Guarantor

Rubén Lima Flores.

CRediT authorship contribution statement

Rubén Lima: Corresponding author writing the paper.
Adriana Castiblanco: Correction of the paper.
Alejandra Gallardo: Correction of the paper.
Ricardo Rossi: Correction of the paper.
Giancarlo Schiappacasse: Correction of the paper.

Declaration of competing interest

Authors of this article have no conflict or competing interests.

References

[1] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, for the SCARE Group, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.
[2] V.K. Frantz, Papillary tumors of the pancreas: Benign or malignant? Tumors of the pancreas, in: Atlas of Tumor Pathology, Section 7, Fascicles 27 and 28, Armed Forces Institute of Pathology, Washington, DC, 1959, pp. 32–33.
[3] M.J. Kim, D.W. Choi, S.H. Choi, J.S. Heo, J.Y. Sung, Surgical treatment of solid pseudopapillary neoplasms of the pancreas and risk factors for malignancy, Br. J. Surg. 101 (10) (2014) 1266–1271.
[4] T. Papavramidis, S. Papavramidis, Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in English literature, J. Am. Coll. Surg. 200 (2005) 965–972.
[5] J.K. Law, A. Ahmed, V.K. Singh, et al., A systematic review of solidpseudopapillary neoplasms: are these rare lesions? Pancreas 43 (3) (2014) 331–337.
[6] Jiali Wu, Yize -Mao, Yiquan Jiang, Yunda -Song, Yu Ping, shuxin Sun, Shenping Li, Sex differences in solid pseudopapillary neoplasm of the pancreas: a population-based study, Cancer Med. 9 (2020) 6030–6041.
[7] C.M. Kang, S.H. Choi, S.C. Kim, et al., Predicting recurrence of pancreatic solid pseudopapillary tumors after surgical resection: a multicenter analysis in Korea, Ann. Surg. 260 (2) (2014) 348–355.
[8] David S. Klimstra, N. Volkan Adsay, Tumors of the Pancreas. Odze and Goldblum Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas, 2015. Chapter 40, 1081–1119.e8.
[9] G. Lanke, F.S. Ali, J.H. Lee, Clinical update on the management of pseudopapillary tumor of pancreas, World J. Gastrointest. Endosc. 10 (9) (2018) 145–155.
[10] M.H. Yu, et al., MR imaging features of small solid pseudopapillary tumors: retrospective differentiation from other small solid pancreatic tumors, Am. J. Roentgenol. 195 (6) (2010) 1324–1332.
[11] R.C. Martin, D.S. Klimstra, M.F. Brennan, K.C. Conlon, Solid-pseudopapillary tumor of the pancreas: a surgical enigma? Ann. Surg. Oncol. 9 (1) (2002) 35–40.
[12] K.M. Coleman, C.D. Michael, A.B. Steven, Solid-Pseudopapillary tumor of the pancreas, RadioGraphics 23 (2003) 1644–1648.
[13] Stefano La Rosa, Massimo Bongiovanni, Pancreatic solid pseudopapillary neoplasm: key pathologic and genetic features, Arch. Pathol. Lab. Med. (2019), https://doi.org/10.5858/arpa.2019-0473-RA.
[14] Vera Lucia Chagas, Fernando Colonna Rosman, Maria da Gloria da Costa Carvalho, Solid pseudopapillary neoplasia of the pancreas: a review, Rev. Assoc. Med. Bras. 66 (1) (2020) 87–94.
[15] Attila Zalatnai, Viktória Kis-Orha, Solid.pseudopapillary neoplasm of the pancreas is still an enigma: a clinicopathological review, Pathol. Oncol. Res. 26 (2020) 641–649.