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Pancreatoduodenectomy for Malignant Solid Pseudopapillary Neoplasm in a Patient with Chronic Calcifying Pancreatitis, Rheumatoid Polyarthritis and Kidney Stones

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Rezumat

Duodenopancreatectomie cefalică pentru un neoplasm solid pseudopapilar malignizat la o pacientă cu pancreatită cronică calcifiantă, poliartrită reumatoidă și nefrolitiază

Prezentăm cazul unei paciente cu poliartrită reumatoidă, cu istoric îndelungat de pancreatită cronică, diagnosticată incidental în cursul investigațiilor imagistice pentru o colică renală, cu o tumoră cefalopancreatică, cu diagnostic histopatologic şi imunohistochimic de neoplasm solid pseudopapilar. S-a practicat duodenopancreatectomie cefalică cu rezecție laterală de venă mezenterică superioară, cu rezultat histopatologic final de neoplasm solid pseudopapilar malign cu un ganglion pozitiv. Sunt prezentate date clinice, chirurgicale, patologice şi o sinteză a literaturii de specialitate.

Cuvinte cheie: duodenopancreatectomie cefalică, neoplasm solid pseudopapilar, poliartrită reumatoidă

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Abstract

We present the case of a patient with rheumatoid polyarthritis

treated in our department, with a long history of chronic calcifying pancreatitis which was incidentaly diagnosed during a renal colic with a pancreatic tumor. Pancreatoduodenectomy with lateral superior mesenteric vein resection was performed, the final pathological examination revealed a malignant solid pseudopapillary neoplasm with a positive lymph node. Clinical, surgical, pathological and a review of the literature are presented.

Key words: pancreatoduodenectomy, solid pseudopapillary tumor, rheumatoid polyarthritis

Introduction

Solid pseudopapillary neoplasms (SPNs) are rare forms of low-grade pancreatic neoplasia with reported incidence between 0.3% and 2.7% of all pancreatic tumors that most commonly affect young females (1). Once the diagnosis is made, surgical resection is the treatment of choice (2,3). The 5-year survival ranges between 93.6% and 98.8% and the 10-year disease-specific survival rate is 96% (4-8). Despite as being categorized as low malignant potential, between 9-15% of them present with metastases and local invasion (9). In large-scale reviews of adult population the recurrence rate is up to 6.6% (10).

SPNs seem to be unique neoplasm with obscure and intriguing histogenesis witch does not correlate with any common cell lineage: acinar, ductal, epithelial, neuroendocrine or histiocytic (11). SPNs may originate from multipotential primordial cells that may follow different differentiation pathways (12). The neural crest or the genital ridge/ovarian anlage-related cells attached to the pancreatic tissue during the early phase of embryogenesis have been hypothesized as potential origin but further scientific data is needed (11).

We report the clinical and pathological characteristics of a malignant case of SPN managed in our department in a patient with a history of chronic pancreatitis and rheumatoid polyarthritis who was incidentally diagnosed during an episode of renal colic with a pancreatic tumor.

Case Report

A 63-year-old female patient was initially referred to our department in December 2020, due to a newly diagnosed pancreatic head mass. The patient was a heavy smoker with moderate alcohol consumption. The patient was diagnosed in 1997 with seropositive rheumatoid polyarthritis and at that moment she was on methotrexate 7,5 mg per week. At the time of admission, her rheumatoid factor was 6,5 UI/ml (Normal: 0-15UI/ML) and anti-cyclic citrullinated peptide IgG/IgA antibodies level was 2.9 U/ml (Normal: < 20 U/ml). She was diagnosed in 2011 with type 2 non-insulin-dependent diabetes, controlled with oral antidiabetics and diet. In 2013 the patient performed a CT scan which revealed calcifications in the pancreatic head with minimally dilated pancreatic duct and hypotrophy of the body and tail (*Fig. 1*), suggestive of chronic pancreatitis and no suspicion of pancreatic mass. From 2013 she was managed conservatory with pain medication, oral antidiabetics and increasing dosed of pancreatic enzymes. No imagistic controls were performed from the initial CT scan performed in 2013 to December 2020.

In December 2020 she was investigated for right lumbar pain, the ultrasound performed in an emergency department revealed right hydronephrosis and kidney stones. The nephritic colic was treated conservatory and after a few months a double J was placed under cystoscopic control. A CT scan was performed and revealed a 5/5/6 cm pancreatic head mass

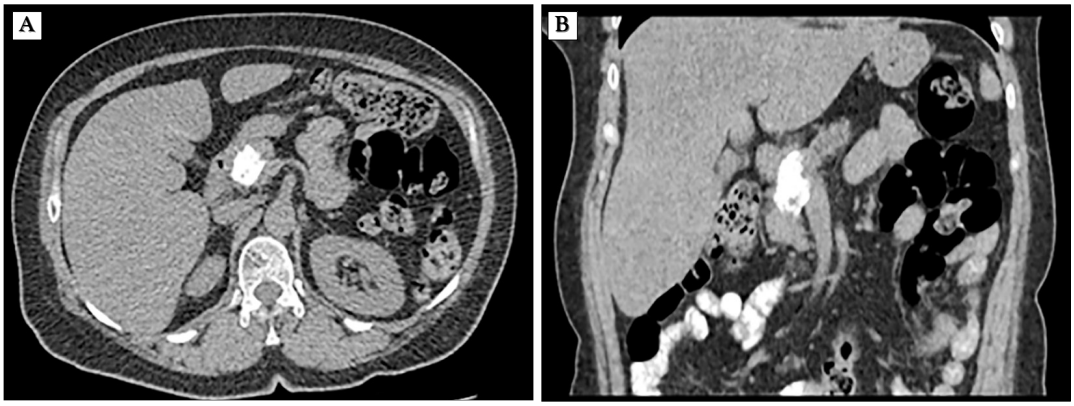

Figure 1. CT scan performed in 2013 (**A** - axial slice and **B** - coronary slice) showing calcification in the pancreatic head with dilation of the Wirsung duct.

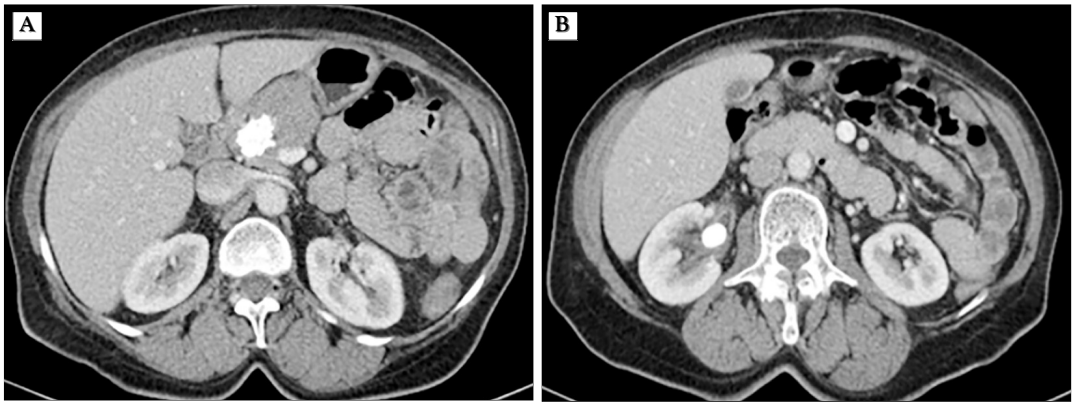

Figure 2. CT scan performed in December 2020, axial venous phase. **(A)** – pancreatic head mass with calcifications in contact with the superior mesenteric vein. **(B)** – right kidney calculus.

with pancreatic head calcifications, and a 7 mm moniliform pancreatic duct (*Fig. 2*).

The patient was scheduled in May 2021 for endoscopic ultrasound evaluation. A 42/46 mm well-defined hypoechoic pancreatic head and isthmic mass, with negative Doppler signal, calcifications and a 7 mm dilatation of the pancreatic duct (*Fig. 3*). Fine needle aspiration was performed with a 19G needle. The histopathologic examination combined with

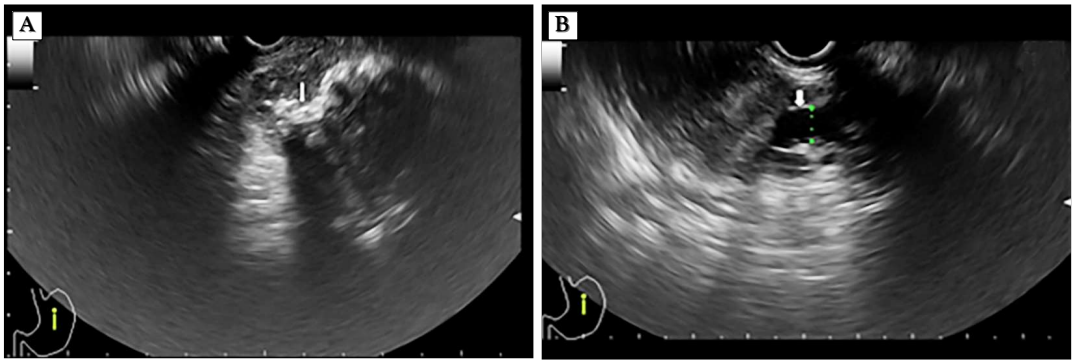

Figure 3. Eco-endoscopic aspect. **(A)** Solid pancreatic head mass with calcifications (white arrow); **(B)** 7 mm dilations of the Wirsung duct (white arrow).

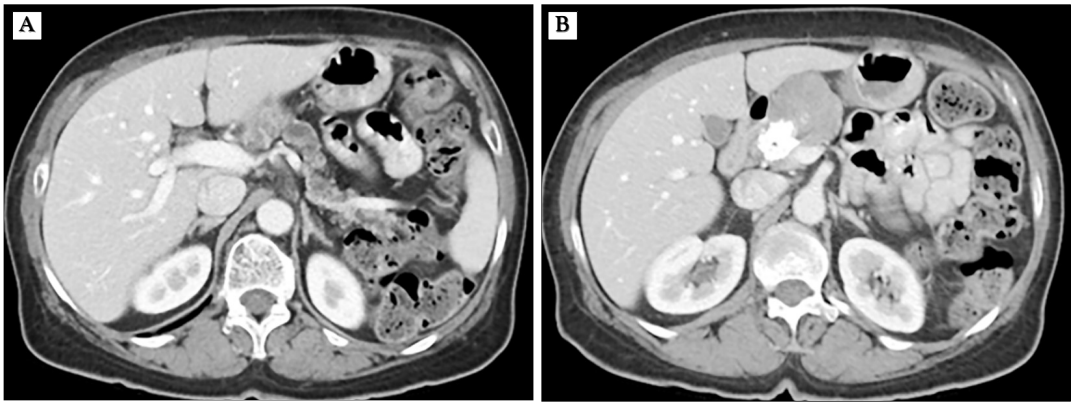

Figure 4. Preoperative CT scan, August 2021, portal phase. **(A)** dilated pancreatic duct with pancreatic body and tail hypotrophy. **(B)** pancreatic head mass with calcifications (solid pseudopapillary neoplasm) in contact with the superior mesenteric vein.

immunohistochemistry tests (positive beta catenin in the nuclei of the tumoral cells, CD10 positive in the tumoral cells, negative chromogranin A, Ki67 positive in 2%) revealed a solid pseudopapillary neoplasm. The tumor markers carcinoembryonic antigen, CA19-9 and alpha-fetoprotein levels were normal.

After appropriate preparation and cessation of methotrexate treatment two weeks before surgery, a CT scan was repeated that revealed minimal growth of the pancreatic tumor (*Fig. 4*). A pancreatoduodenectomy was performed with lateral resection of the superior mesenteric vein with tangential suture. The methotrexate was stopped two weeks before surgery. *Fig. 5A* and *5B* represent intra-operative aspects before and after the resection. A wirsungo-jejunostomy duct to mucosa was performed. The postoperative course was uneventful. Oral antidiabetics were restarted with good glycemic control. The patient was discharged on postoperative day 12.

The final pathologic examination revealed a 4,5/4/3,5 cm malignant solid pseudopapillary neoplasm (*Fig. 6*) with one positive lymph node from 24 peripancreatic and periduodenal lymph nodes that were examined (*Fig. 7*). The resection margins were negative and tumoral cells were identified at the level of the resected superior mesenteric wall but without true

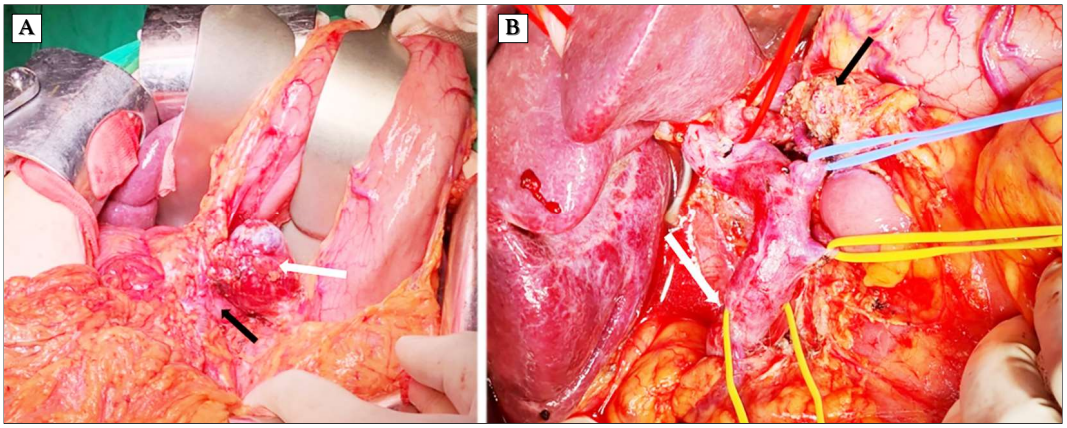

Figure 5. Intra-operative aspects. **(A)** Before the resection; stomach retracted cranially, the colon andd greater omentum retracted caudally; solid pancreatic head and isthmus mass (white arrow) with hemorrhagic cystic component in contact with the superior mesenteric vein (black arrow). **(B)** Intraoperative aspect after pancreatoduodenectomy with lateral superior mesenteric vein resection and primary suture reconstruction (white arrow). Intraoperative frozen section of the pancreatic stump (black arrow) revealed chronic pancreatitis, negative for malignant cells.

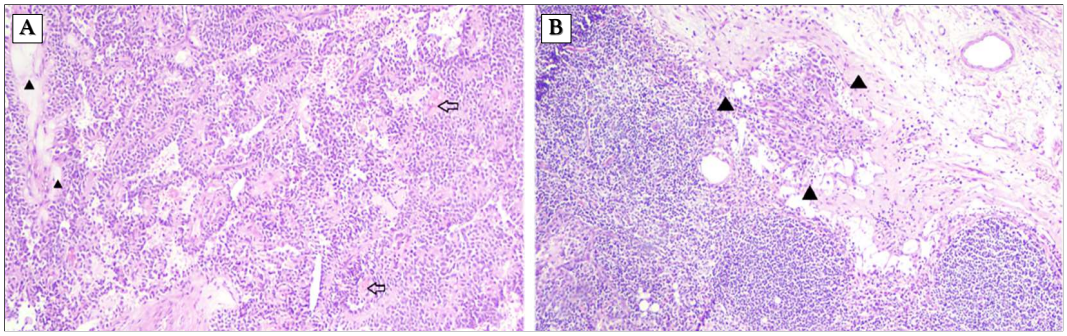

Figure 6. **(A)** Solid and pseudopapillary structures around low-caliber blood vessels (black and white arrows); cells exhibit uniform nuclei with finely dispersed chromatin, inconspicuous nuclei and occasional longitudinal grooves, with a moderate amount of eosinophilic cytoplasm. Stroma (black arrowheads) shows hyalinization and foamy macrophages (H&E, 10x original magnification). **(B)** Subcapsular metastasis of Solid Pseudopapillary Neoplasm (black arrowheads) (H&E, 10x original magnification).

invasion of the vessel wall. The tumor was encapsulated with solid and pseudopapillary architecture and cystic hemorrhagic areas. Lymphovascular and perineural invasion were noted. The normal pancreatic parenchyma showed moderate interlobular fibrosis and moderate lipomatosis. The final staging (8th edition of the AJCC staging system) was pT3pN1 LVI+ and PNI+.

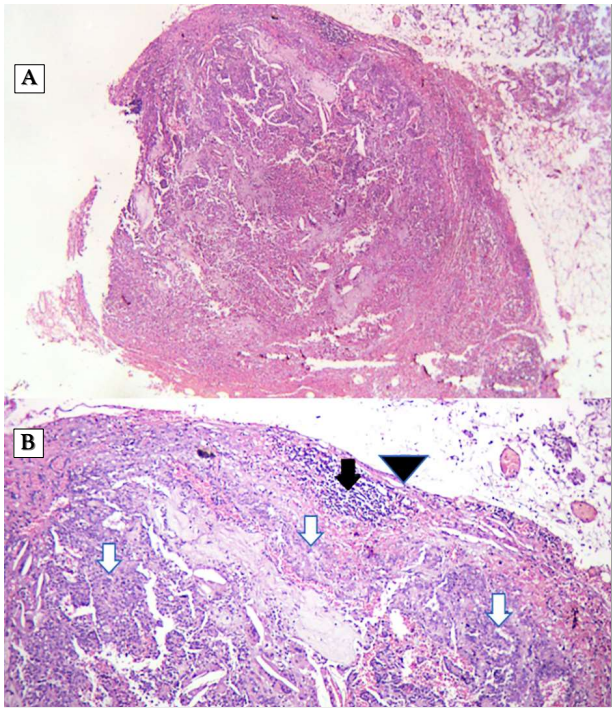

Figure 7. Lymph node architecture completely effaced by malignant proliferation compatible with the diagnosis of Solid Pseudopapillary Neoplasm exhibiting solid and pseudopapillary patterns with hyalinized stroma, cholesterol clefts and giant cell reaction (1 – H&E 4x; 2 – H&E 10x; Black triangle – lymph node capsule; Black arrow – remanent peripheral lymphoid tissue; White arrows – Solid Pseudopapillary Neoplasm metastasis).

Discussion

We report a patient referred to our department who presented both a diagnostic and therapeutic challenge. The patient was diagnosed with rheumatoid polyarthritis and was on chronic medication with methotrexate. In 2011 she was diagnosed with type 2 diabetes mellitus and started on oral antidiabetics. In 2013 a CT scan revealed a pancreatic head calcification with dilated pancreatic duct and pancreatic tail atrophy. Most importantly, no pancreatic mass was noted on the first CT scan. Both clinical and paraclinical factors suggested that the patient suffered from chronic pancreatitis with diabetes and pancreatic exocrine insufficiency. Chronic calcifying pancreatitis is the most common cause of pancreatic calcifications contrary to other types, like obstructive pancreatitis and autoimmune pancreatitis that rarely cause pancreatic calcifications (13).

After approximately 7 years the patient was incidentally diagnosed during a renal colic episode with a pancreatic head tumor. In a population-based cohort study on Taiwanese patients, chronic pancreatitis was associated

with urolithiasis (14). The risk of urolithiasis increased in the cronic pancreatitis cohort as the follow-up duration after the chronic pancreatitis diagnosis increased, but due to the observational nature of the study a causal relationship could not be ascertained (14).

Owing to the increase use of modern imaging in the management of different abdominal symptoms the number of patients diagnosed with SPN has significantly increased (3,15). Almost one fourth of the patients are asymptomatic and the tumor is found incidentally, on imaging performed for unrelated indications (16). Most of the patients complain of non-specific abdominal pain or discomfort which prompts abdominal imaging (16). Jaundice is rare, event when the SPN occurs in the pancreatic head (17).

Although no association has been found between chronic pancreatitis and SPNs, chronic pancreatitis is a well-established risk factor for pancreatic ductal adenocarcinoma (18). It is hypothesized that chronic inflammation generates a microenvironment and through a complicated network of interactions carcinogenesis may occur (19). The cumulative life time risk of pancreatic ductal adenocarcinoma in the setting of chronic pancreatitis is estimated to be between 4%-5%, the history of cigarette smoking and the onset of diabetes may increase the risk further (20).

There are several studies in the literature that address the association between rheumatoid arthritis and pancreatic cancer risk with conflicting results. Most studies have described no association between rheumatoid arthritis and pancreatic cancer risk (21). The study performed by Gomez-Rubio et al on DisGeNET, a knowledge platform on human diseases and their associations with gene alterations, identified a significant association between polymyalgia rheumatic and rheumatoid arthritis with lower pancreatic cancer risk (21,22). In a large retrospective cohort study conducted in the Western population evaluating the risk of pancreatic disease in patients with rheumatoid arthritis the authors found a modestly increased risk of acute pancreatitis, chronic pancreatitis and pancreatic cancer (23). Patients with rheumatoid arthritis seem to have an increased risk of lymphoma and lung cancer and a reduced risk of colon cancer (24). The increase risk of cancer in patients with rheumatoid arthritis does not appear to be related to the use of biological treatments or methotrexate (24).

After adequate diagnosis, surgery is the gold standard treatment (2,3). It appears that tumor related factors like locally aggressive disease, peripancreatic tissue infiltration, adjacent organ involvement or even resectable metastatic disease are not necessarily indication of remote disease or poor patient outcome and should be addressed by radical en-block resection (16). Most centers advocate resection of metastatic disease when feasible (5,16,25, 26-29).

In our patient a lateral resection of the superior mesenteric vein was performed because of tumor adherence. If vascular resection and reconstruction is technically feasible it should be performed in the case of SPN due to the excellent long term survival (15). Other authors reported good outcome after vascular resections for SPNs (9,17).

The pathological examination in our patient identified a positive peripancreatic lymph node. It appears that synchronous lymph node metastases are very rare in SPNs (30). A literature review performed by Rathi et al (31) in 2021 identified two large series of patients with only one patient each with positive lymph nodes: Kang et al (1/351) (25) and Lee et al (1/375) (32). In the analysis performed by Lee et al the median recurrence time after resection was 67 months and was associated with a higher pT category and lymphovascular invasion, features also present in our patient, so longer follow-up is required (32). Perineural invasion seems to not increase the risk of recurrences according to a meta-analysis performed by Gao et al (33).

Conclusion

We presented the case of a complex patient in which multidisciplinary collaboration was the

key aspect in the successful management. Patients with chronic pancreatitis should be referred to specialized centers with follow-up programs including endoscopic ultrasound, due to the risk of pancreatic cancer or other pancreatic neoplasia.

Conflict of Interest and Financial Disclosure

All authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

Ethical Statement

Approved by the hospital ethical committee.

References

1. Kotecha K, Pandya A, Gill AJ, Mittal A, Samra J. Pancreatic solid pseudopapillary neoplasm: a single-institution study. ANZ J Surg. 2021; 91(11):2453–8.
2. Papavramidis T, Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in English literature. J Am Coll Surg. 2005;200(6):965–72.
3. Allam M, Hidalgo Salinas C, Machairas N, Kostakis ID, Watkins J, Fusai GK. Solid Pseudopapillary Neoplasms of the Pancreas: a Single-Center Experience and Review of the Literature. J Gastrointest Canc. 2022;53(2): 460–5.
4. Zalatnai A, Kis-Orha V. Solid-pseudopapillary Neoplasms of the Pancreas is still an Enigma: a Clinicopathological Review. Pathol Oncol Res. 2020; 26(2):641–9.
5. Yu PF, Hu ZH, Wang XB, Guo JM, Cheng XD, Zhang YL, et al. Solid pseudopapillary tumor of the pancreas: a review of 553 cases in Chinese literature. World J Gastroenterol. 2010;16(10):1209–14.
6. Yang F, Yu X, Bao Y, Du Z, Jin C, Fu D. Prognostic value of Ki-67 in solid pseudopapillary tumor of the pancreas: Huashan experience and systematic review of the literature. Surgery. 2016;159(4):1023–31.
7. Hanada K, Kurihara K, Itoi T, Katanuma A, Sasaki T, Hara K, et al. Clinical and Pathological Features of Solid Pseudopapillary Neoplasms of the Pancreas: A Nationwide Multicenter Study in Japan. Pancreas. 2018;47(8): 1019–26.
8. 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(6):561–8.
9. Zhang H, Wang W, Yu S, Xiao Y, Chen J. The prognosis and clinical characteristics of advanced (malignant) solid pseudopapillary neoplasm of the pancreas. Tumour Biol. 2016 ;37(4):5347–53.
10. Hansen CP, Kristensen TS, Storkholm JH, Federspiel BH. Solid pseudopapillary neoplasm of the pancreas: Clinical-pathological features and management, a single-center experience. Rare Tumors. 2019;11: 2036361319878513.
11. Cruz MAA, Moutinho-Ribeiro P, Costa-Moreira P, Macedo G. Solid Pseudopapillary Neoplasm of the Pancreas: Unfolding an Intriguing Condition. GE Port J Gastroenterol. 2022;29(3):151–62.
12. Yan SX, Adair CF, Balani J, Mansour JC, Gokaslan ST. Solid pseudopapillary neoplasm collides with a well-differentiated pancreatic endocrine neoplasm in an adult man: case report and review of histogenesis. Am J Clin Pathol. 2015;143(2):283–7.
13. Javadi S, Menias CO, Korivi BR, Shaaban AM, Patnana M, Alhalabi K, et al. Pancreatic Calcifications and Calcified Pancreatic Masses: Pattern Recognition Approach on CT. American Journal of Roentgenology. 2017; 209(1):77–87.
14. Chen CH, Lin CL, Jeng LB. Association between chronic pancreatitis and urolithiasis: A population-based cohort study. PLoS One. 2018 Mar 9;13(3): e0194019.
15. Coelho JCU, da Costa MAR, Ramos EJB, Torres AR, Savio MC, Claus CMP. Surgical Management of Solid Pseudopapillary Tumor of the Pancreas. JSLS. 2018;22(4):e2018.00032.
16. Lubezky N, Papoulas M, Lessing Y, Gitstein G, Brazowski E, Nachmany I, et al. Solid pseudopapillary neoplasm of the pancreas: Management and long-term outcome. Eur J Surg Oncol. 2017;43(6):1056-1060.
17. Cai Y, Ran X, Xie S, Wang X, Peng B, Mai G, et al. Surgical Management and Long-Term Follow-Up of Solid Pseudopapillary Tumor of Pancreas: A Large Series from a Single Institution. J Gastrointest Surg. 2014;18(5):935–40.
18. Gandhi S, de la Fuente J, Murad MH, Majumder S. Chronic Pancreatitis Is a Risk Factor for Pancreatic Cancer, and Incidence Increases With Duration of Disease: A Systematic Review and Meta-analysis. Clinical and Translational Gastroenterology. 2022;13(3):e00463.
19. Algül H, Treiber M, Lesina M, Schmid RM. Mechanisms of disease: chronic inflammation and cancer in the pancreas--a potential role for pancreatic stellate cells? Nat Clin Pract Gastroenterol Hepatol. 2007;4(8):454–62.
20. Hart PA, Conwell DL. Chronic Pancreatitis: Managing a Difficult Disease. Am J Gastroenterol. 2020;115(1):49–55.
21. Gomez-Rubio P, Piñero J, Molina-Montes E, Gutiérrez-Sacristán A, Marquez M, Rava M, et al. Pancreatic cancer and autoimmune diseases: An association sustained by computational and epidemiological case–control approaches. Int J Cancer. 2019;144(7):1540-1549.
22. Bauer-Mehren A, Rautschka M, Sanz F, Furlong LI. DisGeNET: a Cytoscape plugin to visualize, integrate, search and analyze gene–disease networks. Bioinformatics. 2010;26(22):2924–6.
23. Alkhayyat M, Abou Saleh M, Grewal MK, Abureesh M, Mansoor E, Simons-Linares CR, et al. Pancreatic manifestations in rheumatoid arthritis: a national population-based study. Rheumatology (Oxford). 2021; 60(5):2366–74.
24. De Cock D, Hyrich K. Malignancy and rheumatoid arthritis: Epidemiology, risk factors and management. Best Practice & Research Clinical Rheumatology. 2018;32(6):869–86.
25. Kang CM, Choi SH, Kim SC, Lee WJ, Choi DW, Kim SW, et al. Predicting recurrence of pancreatic solid pseudopapillary tumors after surgical resection: a multicenter analysis in Korea. Ann Surg. 2014;260(2):348–55.
26. Martin RCG, Klimstra DS, Brennan MF, Conlon KC. Solid-pseudopapillary tumor of the pancreas: a surgical enigma? Ann Surg Oncol. 2002;9(1):35–40.
27. Morito A, Eto K, Matsuishi K, Hamasaki H, Morita K, Ikeshima S, et al. A case of repeat hepatectomy for liver metastasis from solid pseudopapillary neoplasm of the pancreas: a case report. Surg Case Rep. 2021;7(1):60.
28. Ranaweera K, Nandasena M, de Silva U, Jayarajah U, Delwatta S, de Silva C, et al. Solid pseudopapillary neoplasm of the pancreas with multiple liver metastases successfully managed with staged resection. SAGE Open Med Case Rep. 2022;10:2050313X221101995.
29. Erguibi D, El Berni Y, Moufakkir A, Boufettal R, Rifki jai saad, Chehab F. Solid pseudopapillary neoplasm of the head of the pancreas: A case report. Annals of Medicine and Surgery. 2021;69:102708.
30. La Rosa S, Bongiovanni M. Pancreatic Solid Pseudopapillary Neoplasm: Key Pathologic and Genetic Features. Archives of Pathology & Laboratory Medicine. 2020;144(7):829–37.
31. Rathi J, Anuragi G, Livin Jose JR, Prabhakaran R, Sugumar C, Naganath Babu OL. Prediction of Recurrence Risk in Solid Pseudopapillary Neoplasm of the Pancreas: Single-Institution Experience. Cureus. 13(8):e17541. eCollection 2021 Aug.
32. Lee G, Sung YN, Kim SJ, Lee JH, Song KB, Hwang DW, et al. Large tumor size, lymphovascular invasion, and synchronous metastasis are associated with the recurrence of solid pseudopapillary neoplasms of the pancreas. HPB (Oxford). 2021;23(2):220–30.
33. Gao H, Gao Y, Yin L, Wang G, Wei J, Jiang K, et al. Risk Factors of the Recurrences of Pancreatic Solid Pseudopapillary Tumors: A Systematic Review and Meta-analysis. J Cancer. 2018;9(11):1905–14.