Peer Review File

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Review Comments:

This case series reported by AlQattan is well documented, however, there are some problems to be dissolved.

Authors response: Thank you!

Comment 1: *The authors should demonstrate some images of MRI to understand the features of the large pancreatic cystic lesion.*

Reply 1 (in agreement with the reviewer): Thank you for this suggestion. However, we did not order an MRI for our patient due to the presence of pathognomonic features of SPNs on two imaging modalities (namely, CT and US). Despite that, we highly valued your comment, so we have extended our discussion addressing the imaging modalities usage. Besides, we have stated that CT and US (cross-sectional imaging) were sufficient to establish the pre-operative diagnosis in our case. We added some data to the revised version of the manuscript as advised (see

Page 7, line 173).

Changes in the text (Note: the blue colored text constitute the added data):

Imaging wise, abdominal CT scan with intravenous contrast has been reported to be the best imaging modality because it provides not only the origin, size, and layout of the tumor but also the presence of local invasion and metastasis (5). As SPNs have a mix of both solid and cystic components, areas of enhancing and non-enhancing lesions are seen and are surrounded by a capsule along with intratumoral calcifications (5). Furthermore, hemorrhage may result due to the growth of the tumor and subsequent internal degeneration (22). The presence of an encapsulated mass consisting of both cystic and solid components and intratumoral hemorrhage are useful factors to distinguish SPNs from its other malignant differentials (5,10,22). **With the presence of these pathognomonic features of SPNs, a CT scan is considered adequate to establish the pre-operative diagnosis (23,24).**

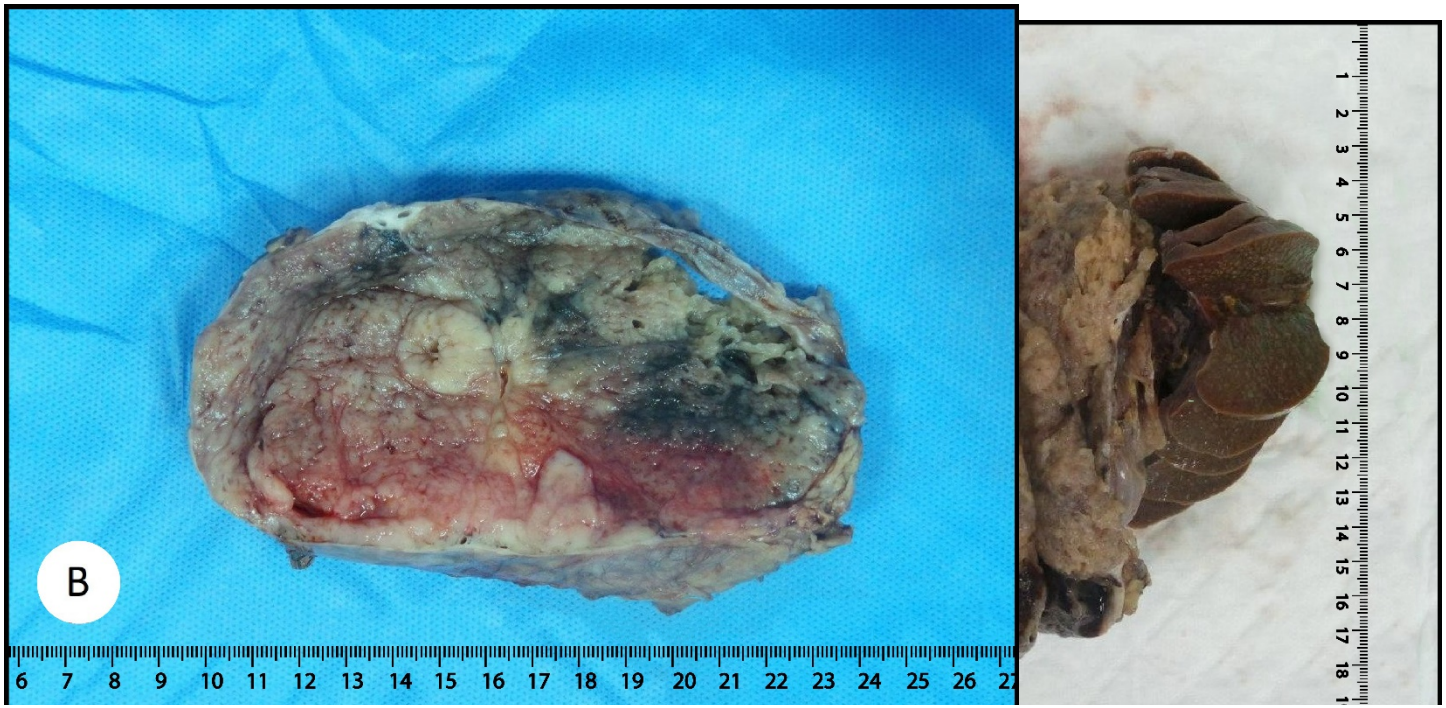
On the other hand, Magnetic Resonance Imaging (MRI), **is considered as a second-line imaging modality as it can demonstrate further information with regards to hemorrhage and necrosis of the tumor's tissue (23,24). Typically, SPNs would** show a vascular, encapsulated mass composed of both mixed cystic and solid components with a high-signal intensity on T1 and low signal intensity on T2 series representing hemorrhagic areas **on MRI** (22,25). **Dan et al. have highlighted that MRI was not necessary in their reported cases of SPNs located in the**

tail of the pancreas, where a CT scan was able to demonstrate the pathognomonic features of SPN (23,24).

23. Rajtar KZ, Sznajder K, Milto KM. Diagnostic imaging of a solid pseudopapillary tumour of the pancreas in a 20-year-old woman - A case study. Prz Gastroenterol. 2016;11(3):214–7.
24. Dan D, Rambally R, Cawich SO, Maharaj R, Naraynsingh V. Solid pseudopapillary neoplasms of the pancreas: A report of two cases. Case Rep Med. 2014;2014.

Comment 2: *The measurement of figure 2 is not visible clearly,*

Reply 2 (in agreement with the reviewer): Thank you for the valuable feedback. The figures' measurement was modified in the revised version of the manuscript as advised by the respected reviewer (see Page 17, line 392).



Changes in the text:

Comment 3: *This SPN may*

have low growth potential with low Ki-67 index, however, the size of this SPN is large one. Why did this SPN show a large size with over 11cm in only 19 y.o. female? The author should discuss about this reason in the discussion session.

Reply 3 (in agreement with the reviewer): Thank you for pointing out this fundamental part of the case. SPNs neoplasms are slowly growing, but with varying growth rates. Specifically, Asari et al. have reported a doubling time of 240 days, Sperti et al. reported 677 days, while Kato et al. reported 765 days. This wide range demonstrates the heterogenicity in terms of growth in SPNs tumors. We totally agree with the reviewer's assessment that this part should be included in the discussion. Accordingly, we have added an additional paragraph, in the revised version of the manuscript, addressing the size of the tumor and growth rate as advised (see Page 6, line 138).

Changes in the text (Note: the blue colored text constitute the added data):

Even though SPNs are slow-growing tumors with a low Ki-67 index, several case reports have shown different growth rates in terms of doubling time starting from 240 to 765 days (18-20). This wide range suggests that although these are collectively slow-growing neoplasms, however, the growth rate varies significantly (19). Despite the unclear pathogenesis and source of the tumor (21), the authors believe that this huge tumor size potentially resulted due to the delayed presentation that lasts for six years.

18. Asari Y, Shimazu S, Nishimura H, Arai Y, Atari H, Owada T, et al. A Case Study of Giant Solid and Cystic Tumor of the Pancreas. Japanese J Gastroenterol Surg. 1991;24:2461–5.

19. Kato T, Egawa N, Kamisawa T, Tu Y, Sanaka M, Sakaki N, et al. A case of solid pseudopapillary neoplasm of the pancreas and tumor doubling time. Pancreatology [Internet]. 2002;2(5):495–8. Available from: http://dx.doi.org/10.1159/000064711.
20. Sperti C, Berselli M, Pasquali C, Pastorelli D, Pedrazzoli S. Aggressive behaviour of solid-pseudopapillary tumor of the pancreas in adults: A case report and review of the literature. World J Gastroenterol. 2008;14(6):960–5.
21. Cuccurullo D, Carbone G, Iovino MG, De Rosa I, Fabozzi M, Corcione F. Solid pancreatic pseudopapillary tumor managed laparoscopically: A case report and review of the literature. Int J Surg Case Rep [Internet]. 2018;45:4–8. Available from: https://doi.org/10.1016/j.ijscr.2017.12.043.

Comment 4: *Recently, the working group of Japan Pancreas Society reported the clinical and pathological features of SPN as follows. The authors should refer this report in the discussion session.*

Hanada K, Kurihara K, Itoi T, et al. Clinical and pathological features of solid pseudopapillary neoplasms of the pancreas: A nationwide multicenter study in Japan. Pancreas. 2018; 47: 1019-1026.

Reply 4 (in agreement with the reviewer): Thank you for this thoughtful comment. We think this is an excellent suggestion. We have added a new paragraph, in the revised version of the manuscript, addressing the notable outcomes that were addressed by Hanada and his colleagues as advised by the respected reviewer (see Page 8, line 190).

Changes in the text (Note: the blue colored text constitute the added data):

Hanada et al. conducted a nationwide, multicentric, retrospective, and questionnaire-based survey study across Japan to assess the clinicopathological features of SPNs (27). The study included 288 patients who were diagnosed with SPN between January 1990 and March 2015 (27). They have evaluated the capability of using a single imaging modality to establish a pre-operative diagnosis, which ranged between 50% to 70%. Additionally, the detection of the cystic component was higher on both MRI and EUS compared to CT scan, while the detection of calcifications on CT scan and EUS was of similar rate (27). Hence, the recommendation was to use a combination of imaging modalities in order to establish a pre-operative diagnosis (27). In our case, due to the typical clinical presentation, along with the presence of the pathognomonic features on CT scan and US, the need for further imaging was waived.

27. 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.