Pancreatic solid pseudopapillary neoplasm

Seung Hyun Lee
Tu Vinh Luong

Abstract

Pancreatic solid pseudopapillary neoplasm (SPN) is a rare low grade malignant tumour. Distinguishing this entity from other pancreatic neoplasms is critical for therapeutic decision making and prognostication. It predominantly affects young female patients <40 years of age, with excellent clinical outcome following surgical removal. The gold standard diagnostic test is cytopathological or histopathological assessment of fine needle aspirate. There are two main difficulties with this. First, SPN can present with morphological and immunohistochemical appearances that can closely mimic other pancreatic tumours, in particular, pancreatic neuroendocrine tumour (NET). Second, the amount of diagnostic material from fine needle aspiration can be limited. Here, we present a cytopathological case with both challenges during the pre-operative investigation of SPN. The case exemplifies the importance of combining morphological features with a targeted panel of immunohistochemistry to arrive at the diagnosis.

Keywords Beta-catenin; fine needle aspiration; Frantz tumour; Hamoudi tumour; papillary cystic neoplasm; papillary cystic neoplasm of the pancreas; solid pseudopapillary tumour; SPN; SPT

Case report

A previously fit and well 20-year-old female patient presented with nonspecific abdominal pain. On CT abdomen, a 5 cm well circumscribed, encapsulated, solid-cystic tumour was identified at the tail of pancreas. The tumour was hypodense and heterogeneously enhancing (Figure 1). To aid in diagnosis, a fine needle aspiration (FNA) of the pancreatic lesion was performed. Notable features on the FNA smears were papillary fronds of monomorphic tumour cells on a haemorrhagic background. The tumour cells were bland and uniform, with oval to round nuclei and a fine chromatin texture. A moderate amount of delicate cytoplasm, occasionally with a wisp of cytoplasmic projection were identified i.e. cercariform cells. Occasional perinuclear vacuoles were seen. Significant nuclear atypia, mitoses and necrosis were not identified (Figure 2). The specimen was processed to obtain a cell block. Further to the similar morphological features, variably sized pseudopapillae and rosette-like clusters of tumour cells were more evident on a background of degenerative changes (haemorrhage, iron pigment and foamy macrophages). In places, larger fragments of tumour were seen, where clefts between detached tumour cells were evident. Nuclear grooves were easily identified in tumour cells on high-power magnification (Figure 3).

In terms of ancillary testing, it was important to limit the number of immunohistochemical markers due to a limited amount of material present. In this case, the following markers were used: neuroendocrine markers (CD56, synaptophysin and chromogranin), low molecular weight keratin marker (CAM5.2) and β-catenin. Interestingly, CD56 and synaptophysin exhibited strong diffuse positive staining but chromogranin A lacked expression. CAM5.2 was negative. Finally, β-catenin showed diffuse positive nuclear expression, which is considered aberrant in epithelial cells (Figure 4).

Taken together morphological, immunohistochemical and clinicoradiological findings, the appearances were in keeping with solid pseudopapillary neoplasm of the pancreas.

Discussion

Pancreatic SPN is a peculiar pancreatic neoplasm of low malignant potential. Its cell of origin remains unclear.[1] It is a rare tumour,

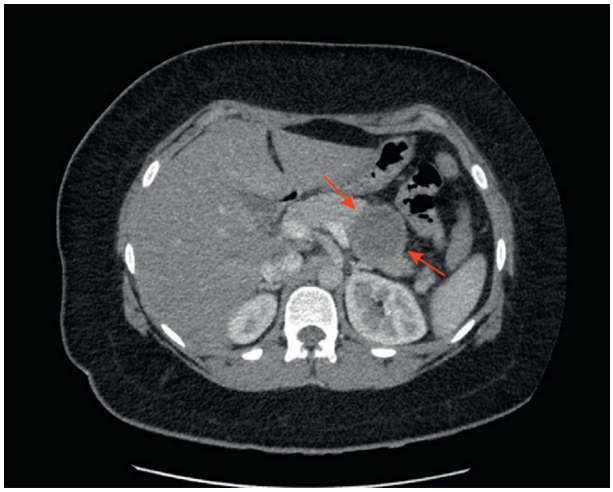

Figure 1 Radiological features of pancreatic solid pseudopapillary neoplasm (SPN). CT abdomen showed a 5 cm well circumscribed, hypodense and heterogeneously enhancing encapsulated mass (marked with arrows). There was no evidence of inflammation, extrapancreatic fluid collection or metastatic disease.

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Seung Hyun Lee *BSc (Hons) MBChB Clinical PhD Fellow Systems Oncology group, Cancer Research UK Manchester Institute, Manchester, UK. Conflicts of interest: none declared.*

Tu Vinh Luong *MD FRCPATH Consultant Histopathologist Royal Free London NHS Foundation Trust, UK. Conflicts of interest: none declared.*

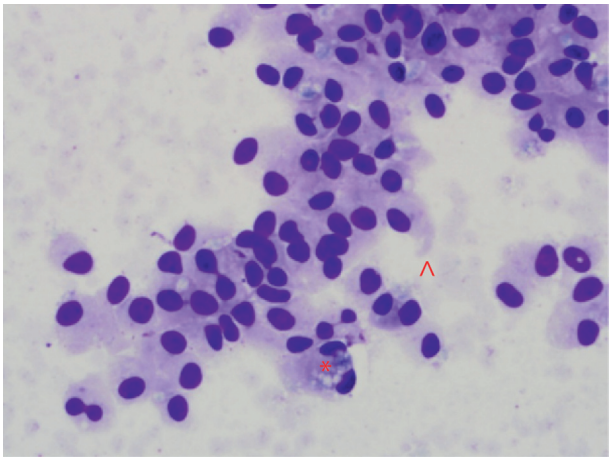

Figure 2 Fine needle aspiration from the pancreatic tumour. Fine needle aspiration of the lesion demonstrated papillary clusters of bland monomorphic cells with a moderate amount of cytoplasm, round to oval bland nuclei and even chromatin. In occasional cells, perinuclear vacuolation (marked with *) and wispy peripheral cytoplasmic projection (marked with ^) were seen. Diff-Quik staining.

accounting for up to 2.7% of all exocrine pancreatic neoplasms.[1] However, it is reported to account for a considerably higher percentage in young patients (approximately 30% of all pancreatic neoplasms in female patients aged <40 years according to Lüttges et al. (2004), n = 8/23).[2] Patients can present with nonspecific gastrointestinal symptoms (e.g. abdominal pain and nausea), but it is most commonly found incidentally on imaging.[1,3]

SPN has a good clinical outlook and effective treatment regime, which makes it critical to differentiate this entity from other pancreatic neoplasms with malignant potential. SPN predominantly affects female patients (88%) in early adulthood (mean age 28 years old).[1,3,4] It is much rarer in the paediatric and male adult (6–17%) populations.[4] Resection confers excellent outcome (>93% 10-year survival rate and 4.4% recurrence rate).[1,3,4] The European Study Group on Cystic Tumours of the Pancreas advises radical surgical resection, irrespective of the presence of local invasion, metastasis and recurrence.[5] There is insufficient data to support the use of neoadjuvant therapy.[4,5]

The gold standard diagnostic test for pancreatic SPN is cellular pathological assessment, often taken via fine needle aspiration

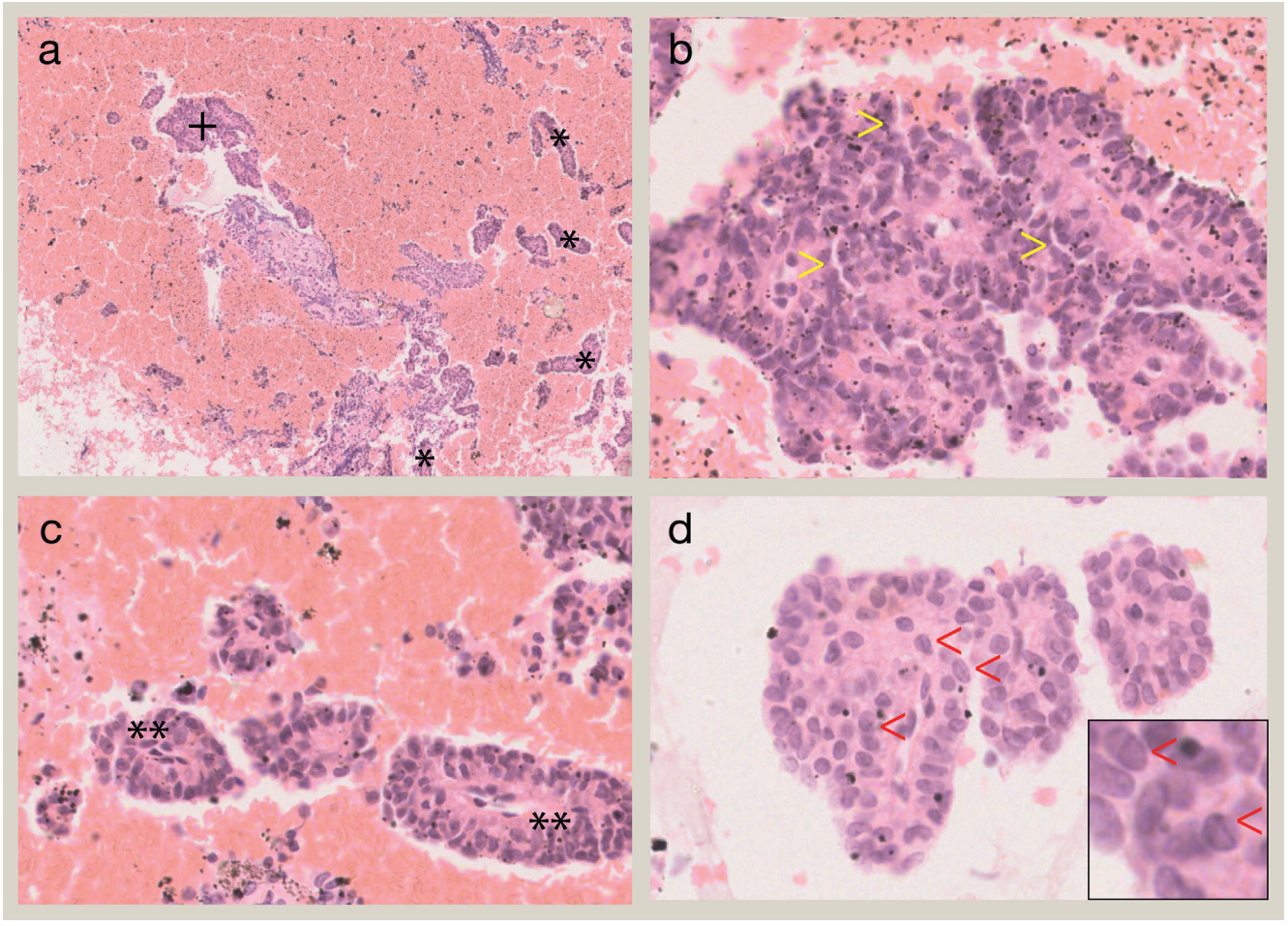

Figure 3 Morphological features of solid pseudopapillary neoplasm (SPN) of the pancreas. (**a**) At low power examination, multiple pseudopapillary structures (some marked with *) were seen. The background was haemorrhagic with abundant iron pigment laden macrophages. One larger cluster (marked with +) was seen, which was connected to hyalinised stromal fragment. (Haematoxylin and Eosin stain, x50). (**b**) On high power examination of the larger cluster, monotonous tumour cells mixed with capillary sized blood vessels were identified. The discohesive nature of the tumour cells was evidenced by the presence of conspicuous clefts between tumour cells (marked with yellow >). (Haematoxylin and Eosin stain, x400). (**c**) Another common architectural pattern was rosette-like structure formation (marked with **) (Haematoxylin and Eosin stain, x400). (**d**) Tumour cells were relatively monotonous with moderate amount of eosinophilic cytoplasm. Nuclei were bland with even chromatin texture. Nuclear grooves were easily identified (inset) (examples marked with red <). (Haematoxylin and Eosin stain, x400).

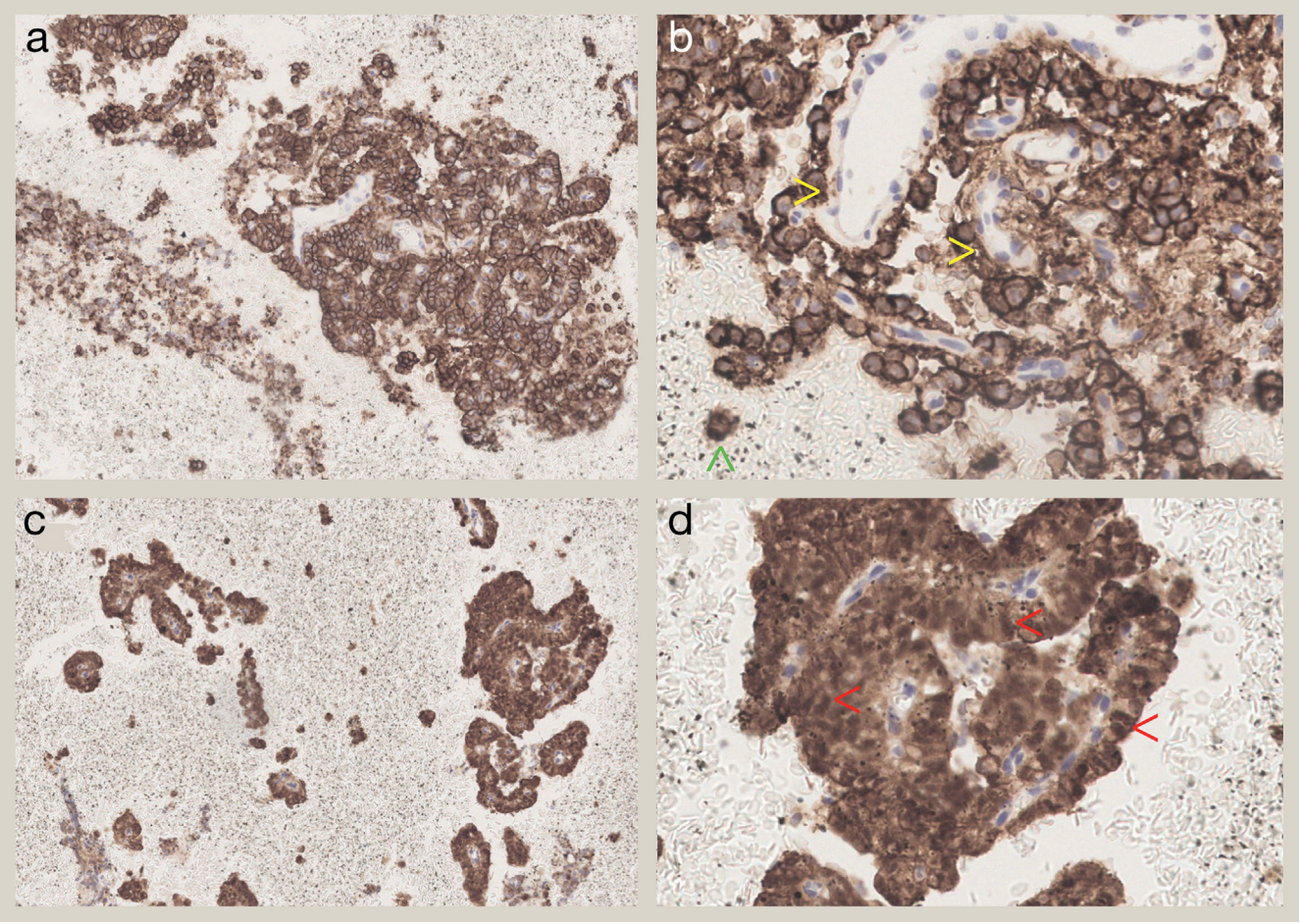

Figure 4 Pertinent immunohistochemical expression of SPN. (**a**) CD56 staining demonstrated diffuse strong positivity (immunohistochemical staining for CD56, x50). (**b**) High power examination of A demonstrated membranous positivity on tumour cells. This staining highlighted individual tumour cells in the background. (Example marked with green ^). Capillary blood vessels closely associated with tumour cells (yellow >) lacked expression. (immunohistochemical staining for CD56, ×400). (**c**) β-Catenin staining showed diffuse block positivity (immunohistochemical staining for β-catenin, ×50). (**d**) High power examination of C showed aberrant localisation of β-catenin within nuclear compartment. Examples are marked with red <. (immunohistochemical staining for β-catenin, ×400).

(FNA) or biopsy (FNB) from the lesion under endoscopic ultrasound guidance. The morphological features can be readily deduced from its name, solid pseudopapillary neoplasm. Specifically, it is associated with a solid pattern of growth. Tumour cells are admixed with capillary sized blood vessels.[1] However, due to poor cell–cell cohesion of the tumour cells, other architectural patterns emerge. They can form pseudo-papillary fronds or rosette-like structures surrounding capillary sized vessels.[6] Cytologic features include tumour cells having a moderate amount of eosinophilic cytoplasm, monomorphic oval to round shaped nuclei and fine chromatin texture.[1,6] These morphological features can closely mimic pancreatic neuroendocrine tumour (NET).

Further, the limited amount of diagnostic material necessitates judicious and effective use of ancillary tests. It is important to note that neuroendocrine immunohistochemical markers can be variably expressed in SPN. CD56 and synaptophysin expression is reported to be positive in 30-70% of cases, while chromogranin expression tends to be absent.[1] Also, the pattern of synaptophysin expression can be varied; it is usually patchy or focal, but it can rarely be diffuse. Therefore, a targeted panel incorporating more than one neuroendocrine marker was used in this case to distinguish it from its main differential: pancreatic NET. Specifically, neuroendocrine markers CD56 and synaptophysin were positive while chromogranin was negative. Also, CAM5.2 was negative. These ancillary test results did not lend support to the diagnosis of NET, which tends to show positive expression of both cytokeratin and neuroendocrine markers (CD56, synaptophysin as well as chromogranin). Hence, incorporating a combination of both key neuroendocrine markers (synaptophysin and chromogranin) acted as a good safety net to distinguish SPN from NET. Finally, β-catenin expression was aberrant in SPN tumour cells (strong diffuse positive nuclear expression) unlike one of NET (membranous expression). This reflects the commonest molecular aberration in more than 90% of cases in SPN that disrupts the Wnt/β-catenin pathway: pathogenic mutation in exon 3 of the *CTNNB1* gene.[1,4] Aberrant β-catenin expression would be a rare finding in NET.[1] Depending on the material available and differential diagnosis (e.g. acinar cell carcinoma), further immunohistochemical markers could be added; a useful table for immunophenotypes of SPN differential diagnosis can be found in La Rosa and Bongiovanni, 2020.[1]

Here we demonstrated a cytopathological case of solid pseudopapillary neoplasm of the pancreas, emphasizing the utility of targeted ancillary studies. One should be mindful of the clinical implications of the correct diagnosis of SPN and be aware of practical approaches to combine diagnostic tools to arrive at a precise differential diagnosis. ◆

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Practice points

- Pancreatic pseudopapillary neoplasm (SPN) is a rare pancreatic tumour of low malignant potential. Its cell of origin is yet to be clarified. It typically presents in a young female patient but can present in children, and rarely in male patients
- Pancreatic SPN is associated with positive clinical trajectory in most cases. It is therefore critical to distinguish pancreatic SPN from other pancreatic neoplasms with similar morphological appearances, including pancreatic neuroendocrine tumour (NET). This can be rendered challenging in a limited amount of material present in fine needle aspiration or biopsy taken from the pancreatic lesion
- A limited but targeted panel of immunohistochemistry is critical to undertake due to overlapping immunophenotype of each marker. Useful markers can include β-catenin, cytokeratin and more than one neuroendocrine marker (e.g. CD56, synaptophysin, chromogranin) to distinguish it from NET

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Self-assessment MCQs

1. Which entities can pancreatic pseudopapillary neoplasm mimic morphologically?

a. Mucinous cystic neoplasm
b. Intraductal papillary mucinous neoplasm
c. Neuroendocrine tumour of the pancreas
d. All of above
e. None of above

Correct answer: c.

2. Which is true from statements below?

a. Solid pseudopapillary neoplasm occurs predominantly in elderly female population
b. All cases of pancreatic solid pseudopapillary neoplasm are benign
c. Pancreatic solid pseudopapillary neoplasm occurs more commonly in children than in adult male patients
d. The most common symptom associated with pancreatic solid pseudopapillary neoplasm is right iliac fossa pain
e. Cytopathological assessment is not a reliable diagnostic modality to diagnose pancreatic solid pseudopapillary neoplasm

Correct answer: c.

3. Which immunohistochemical stain is most useful to distinguish pancreatic pseudopapillary neoplasm from neuroendocrine tumour?

a. β-Catenin
b. CD56
c. Synaptophysin
d. Chromogranin
e. All of above

Correct answer: a.