Malaysian J Pathol 2009; 31(2) : 137 – 141

CASE REPORT

Clear-cell variant of solid-pseudopapillary neoplasm of the pancreas: a case report and review of the literature

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Abstract

Solid-pseudopapillary neoplasm (SPN) of the pancreas is a rare neoplasm reported to have a favourable prognosis because of its slow-growing behaviour. Ignored and misdiagnosed in the past, SPN has recently been increasingly studied. Its clear cell variant creates challenges in distinction from other clear cell tumours in the pancreas. We report a 31-year-old Cambodian woman who presented with abdominal pain and a palpable epigastric mass. Exploratory laparotomy revealed a 5.2 cm well-demarcated tumour in the head of the pancreas, which was treated with Whipple procedure. Microscopically, the tumour showed an extensive solid growth pattern consisting of cells with abundant clear cytoplasm, and papillary areas containing cells with eosinophilic cytoplasm, indicating a clear-cell solid-papillary neoplasm. Perineural and duodenal wall invasion was present. The tumour cells were immunonegative for chromogranin-A and synaptophysin but positive for CD56, cyclin D1, CD10, vimentin, and progesterone receptor. They showed strong nuclear and cytoplasmic expression and reduced membranous expression of beta-catenin protein. In the pseudopapillary area, they showed nuclear E-cadherin localization and absence of membranous staining. The patient was well without local recurrence or metastasis at one year follow-up. Difficulties are recognized in differentiating clear-cell SPN from "sugar" tumours, metastatic renal cell carcinoma, clear-cell variant of pancreatic endocrine neoplasm and ductal adenocarcinoma. When facing such difficulties, nuclear and cytoplamic beta-catenin, nuclear E-cadherin expressions and absence of membranous E-cadherin staining are useful in differentiating clear-cell SPN from other clear cell tumours in the pancreas. Although a rare neoplasm, it is important to recognize this entity for appropriate management.

Keywords: solid pseudopapillary tumour of the pancreas, pancreas tumours, Frantz tumour, solid cystic neoplasm of the pancreas, clear-cell variant of solid pseudopapillary tumour of the pancreas

INTRODUCTION

Solid-pseudopapillary tumour is a very uncommon and ambiguous pancreatic neoplasm which accounts for only about 5% and 1-2% of cystic pancreatic and exocrine pancreatic tumours, respectively.[1, 2] This tumour was first described by Frantz in 1959 and was then termed Frantz tumour.[2] It is also known under the term solid cystic tumour, papillary epithelial neoplasia, solid and papillary epithelial neoplasia, or papillary epithelial tumour. Solid pseudopapillary neoplasm (SPN) is the most recent name advocated by WHO in 1996.[3] Its clear cell variant is even more uncommon with only 3 cases reported in the English literature.[4] Here, we report one case of SPN with predominant clear cell component and, by summarizing the results from previous studies together with those from our case, we suggest key characteristic histological and immunohistochemical features which can be used to distinguish this variant of SPN from its mimics in the pancreas.

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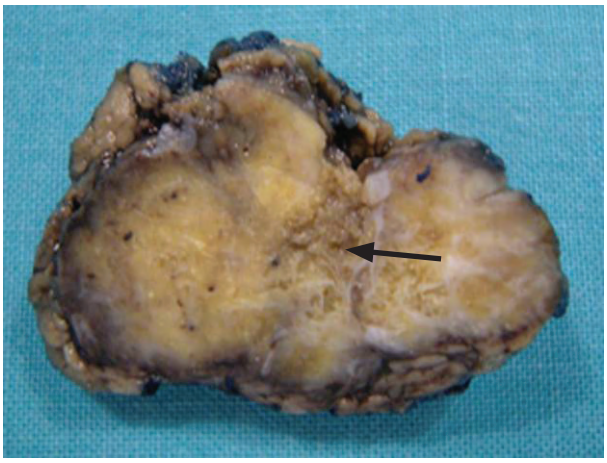

FIG. 1: A well-demarcated tumour containing partly cystic zone (arrow) centrally and yellow solid area peripherally.

CASE PRESENTATION

A 31-year-old Cambodian woman presented with abdominal pain. She was in good condition, without jaundice or anemia. A palpable, mobile mass was observed in the epigastric region during physical examination, confirmed further by ultrasonography. An exploratory laparotomy performed in Siem Reap Provincial Hospital, revealed an unresectable tumour at the pancreatic head, invading into the duodenum wall. The patient was referred to Preah Bat Norodom Sihanouk Hospital in Phnom Penh where a Whipple procedure was performed. The resected specimen was then sent for histopathological examination in a local laboratory in Cambodia, and the diagnosis of 'solid pseudopapillary neoplasm' was suggested in ipath telepathology forum (http://telemed.ipath.ch/ipath/). The paraffin blocks of the tumour were sent to the Pathology Department of Ghent University Hospital, Belgium for further analysis and immunohistochemical staining.

Pathological examination

Grossly, the pancreatic lesion had a diameter of 5.2 centimeters and was well-demarcated. The cut surface showed a partly cystic area at the center and yellow solid area at the periphery (figure 1). Microscopically, the tumour contained both solid and papillary areas (figure 2). The area with solid growth pattern, which consisted of cells with abundant clear cytoplasm, was more extensive than the area with papillary structures that contained cells with eosinophilic cytoplasm. Microscopically, this feature gave the tumour a clear-cell appearance at first glance. Some normal pancreatic parenchyma was entrapped among the tumour cells (figure 3). Perineural and duodenal wall invasion were also present (figure 4).

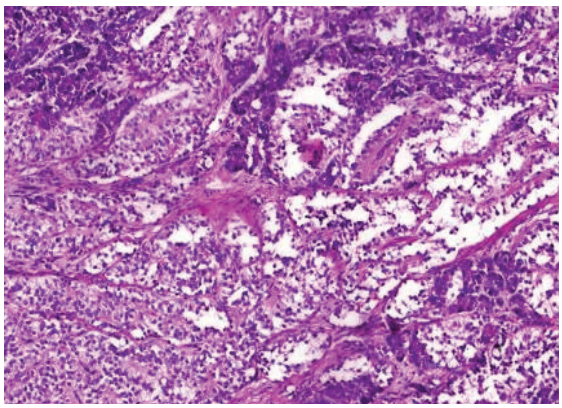

FIG. 2: Solid (left) and pseudopapillary (right) areas in the tumour

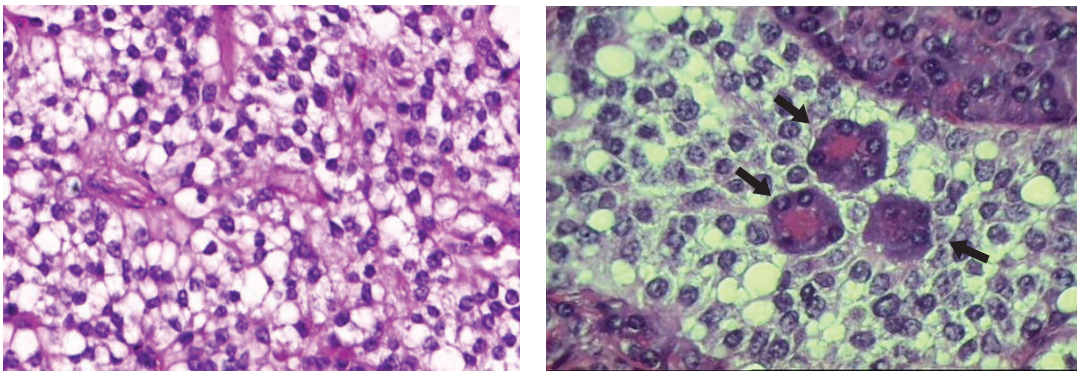

FIG. 3: (A) Predominent clear cell component; (B) trapped normal pancreatic acini (arrows) among tumour cells.

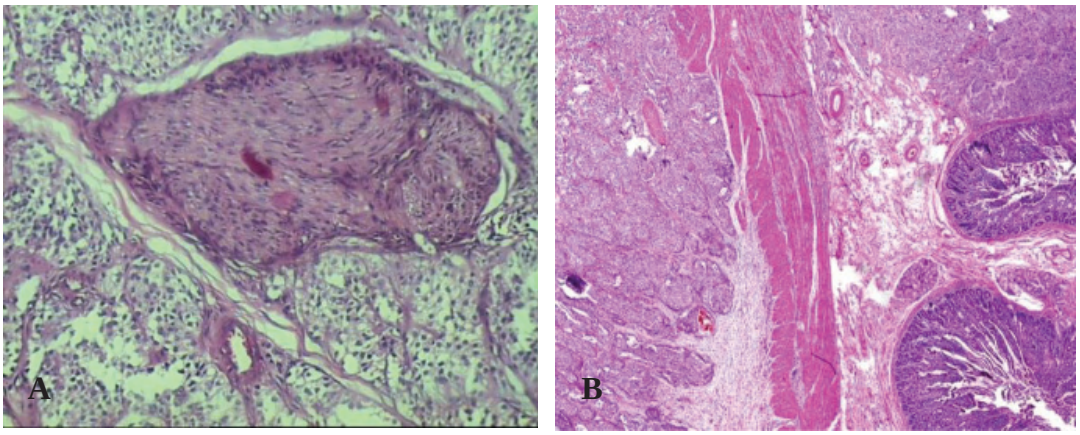

FIG. 4: Perineural (A) and duodenal wall invasion (B).

Immunohistochemistry

The tumor cells were negative for chromogranin-A and synaptophysin but positive for CD56, cyclin D1, CD10, vimentin, and progesterone receptor. They also showed strong nuclear and cytoplasmic expression as well as reduced membranous expression of beta-catenin protein. In the pseudopapillary area, the tumour cells showed nuclear E-cadherin localization and absence of membranous staining (figure 5).

DISCUSSION

Solid pseudopapillary neoplasm (SPN) is an unusual primary tumour of the pancreas with a low potential for malignancy seen mostly in young women, even though some cases in men, children and elderly have been reported.[5, 6, 7, 8] Its clear-cell variant is even more uncommon. The prognosis in SPN is good. A review conducted on 718 patients demonstrated that the 5-year overall survival of patients with SPNs was 95.5%.[9] According to WHO 2002 definition, patients with tumour containing perineural invasion are at high risk of developing metastasis.[10,11] Our patient, however, was still in good health without local recurrence or metastasis upon follow-up at one year after surgery.

The histopathological appearance of SPNs is distinctive among the primary pancreatic neoplasms. The classical neoplastic cells have eosinophilic and vacuolated cytoplasm and are uniform, polygonal, and discohesive in nature. Occasionally, cells contain aggregates of hyaline, diastase-resistant, PAS-positive cytoplasmic globules of varying size which are also sometimes located outside the cells. Small SPN may be primarily arranged in solid sheets with a rich microvasculature. Frequent degenerative changes in larger tumors, however, lend a characteristic pseudopapillary pattern because of residual epithelial cells that form perivascular rosettes. Also found in SPNs are aggregrates of histiocytes and cholesterol clefts.

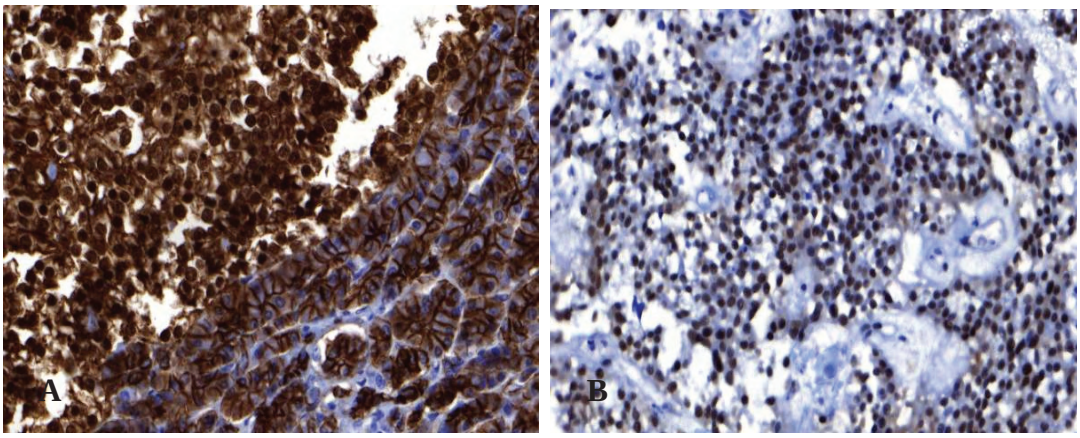

FIG. 5: **(A)** Reduced membranous and the strong nuclear and cytoplasmic beta-catenin staining in tumour cells (left). Note the strong beta-catenin membranous staining of normal epithelium of pancreatic acini on the right; **(B)** Nuclear E-cadherin localization in the pseudopapillary area. Note the loss of membranous staining of the tumour cells.

Difficulties arise, however, in differentiating clear-cell SPN from "sugar" tumours,[12] metastatic renal cell carcinoma,[13] and clear-cell variant of pancreatic endocrine neoplasm (PEN)[14] and ductal adenocarcinoma.[15,16] Unlike clear cells in SPN which results from distended mitochondria or endoplamic reticulum and do not contain mucin, glycogen or lipid, those found in PEN are due to the presence of small lipid droplets and contain chromogranin-positive granules.[4] Clear cell ductal adenocacinoma is different from the other 4 entities in that it has an infiltrative growth pattern and partly consists of intraductal papillary projections, in addition to the solid clear-cell areas. Clear cell "sugar" tumours are characterized by a solid homogeneous perivascular epithelioid cell population, which never shows glandular pattern, necrosis, or mitotic activity. In addition, the coexpression of actin and HMB-45 in sugar tumours combined with the absence of cytokeratins, vimentin, NSE, endocrine and acinar markers rule out the other 4 entities.[12] Clear-cell SPN and metastatic clear cell renal cell carcinoma, although expressing vimentin and CD10, are dissimilar given that the latter does not consist of papillary-like structure.[13] Table 1 summarizes the different immunohistochemical profiles of the five entities. Among the confusing immunohistochemical markers, two appear to be most useful and reliable for making the diagnosis of SPN. Serra *et al*[17] demonstrated the constant

TABLE 1: Immunohistochemical differentiation of clear cell tumours in the pancreas

	SPN	PEN	DAC	Sugar tumour	Metastatic RCC
CK7	+/–	+/–	+	–	+/–
CD10	80% +	10% +	–	–	M +
Vimentin	+	+/–	–	–	+
CD56	At least focally +	25-50% +	–	–	–
Synaptophysin	+/–	+	–	–	–
Chromogranin-A	–	+	–	–	–
ß-catenin	N + & C +	M +	reduced M +	*	M +
E-cadherin	N+ & M –	M +	reduced M +	*	M +
HMB45	–	–	–	+	–

*Key: SPN= solid pseudopapillary neoplasm ; PEN= pancreatic endocrine neoplasm; DAC= ductal adenocarcinoma; RCC= renal cell carcinoma; M + : membranous staining; N + : nuclear staining; C + : cytoplasmic staining; * : have not been studied*

loss of membranous E-cadherin together with the presence of nuclear and cytoplamic beta-catinin and nuclear E-cadherin in neoplastic cells to be the most consistent and unique immunohistochemical profile of SPN.

In summary, we report a case of clear-cell variant of solid-pseudopapillary neoplasm of the pancreas which has a characteristic histomorphology that pathologists can readily recognize with the hematoxylin and eosin stain. In difficult cases, the presence of nuclear and cytoplamic beta-catinin and nuclear E-cadherin expressions and absence of membranous E-cadherin staining suggest the diagnosis of clear-cell SPN rather than other clear cell tumours in the pancreas.

REFERENCES

1. Klimstra DS, Wenig BM, Heffess CS. Solid-pseudopapillary tumour of the pancreas: a typically cystic carcinoma of low malignant potential. Semin Diagn Pathol; 2000; 17:66-80.
2. Frantz VK. Tumours of the pancreas. In: Blumberg CW (editor) Atlas of Tumour Pathology. Series 1, Fascicles 27 and 28. Washington, DC 1959: 32-33.
3. Klöppel G, Solcia E, Longnecker DS, Capella C, Sobin LH. Histological typing of tumours of the exocrinic pancreas. In: WHO International Classification of Tumours. Berlin Heidelberg New York, Springer 1996: 8452/1.
4. Albores-Saavedra J, Simpson KW, Bilello SJ. The clear cell variant of solid pseudopapillary tumor of the pancreas: a previously unrecognized pancreatic neoplasm. Am J Surg Pathol 2006; 30:1237-42.
5. Solcia E, Capella C, Kloppel G. Tumors of the pancreas. In: Atlas of Tumor Pathology, 3rd series, Fascicle 20. Washington, DC, USA: US Armed Forces Institute of Pathology; 1997:120–144.
6. Lam KY, Chung YL, Sheuing TF. Pancreatic solid-cystic-papillary tumor: clinicopathologic features in eight patients from Hong Kong and review of the literature. World J Surg 1999; 23:1045–50.
7. Pettinato G, Di Vizio D, Manivel JC, Pambuccian SE, Somma P, Insabato L. Solid-pseudopapillary tumor of the pancreas: a neoplasm with distinct and highly characteristic cytological features. Diagn Cytopathol 2002; 27:325–34.
8. Faraj W, Jamali F, Khalifeh M, Hashash J, Akel S. Solid pseudopapillary neoplasm of the pancreas in a 12-year-old female: case report and review of the literature. Eur J Pediatr Surg 2006; 16:358–61.
9. Papavramidis T, Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in English literature. J Am Coll Surg 2005; 200:965-72.
10. Nishihara K, Nagoshi M, Tsuneyoshi M. Papillary cystic tumors of the pancreas. Assessment of their malignant potential. Cancer 1993; 71:82-92.
11. 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; 14:960–5.
12. Zamboni G, Pea M, Martignoni G, *et al*. Clear cell "sugar" tumor of the pancreas. A novel member of the family of lesions characterized by the presence of perivascular epithelioid cells. Am J Surg Pathol 1996;20:722-30.
13. Thompson LD, Heffess CS. Renal cell carcinoma to the pancreas in surgical pathology material. Cancer 2000; 89:1076–88.
14. Nunobe S, Fukushima N, Yachida S, Shimada K, Kosuge T, Sakamoto M. Clear cell endocrine tumor of the pancreas which is not associated with von Hippel-Lindau disease: Report of a case. Surg Today 2003; 33:470–4.
15. Ray S, Lu Z, Rajendiran S. Clear cell ductal adenocarcinoma of pancreas: a case report and review of the literature. Arch Pathol Lab Med 2004;128:693–6.
16. Lüttges J, Vogel I, Menke M, Henne-Bruns D, Kremer B, Klöppel G. Clear cell carcinoma of the pancreas: an adenocarcinoma with ductal phenotype. Histopathology 1998; 32:444–8.
17. Serra S, Salahshor S, Fagih M, Niakosari F, Radhi JM, Chetty R. Nuclear Expression of E-Cadherin in solid pseudopapillary tumors of the pancreas. J Pancreas (Online) 2007; 8(3):296–303.