

Histopathology of Pancreatic Solid Pseudo-papillary Neoplasm Failed to Predict Metastatic Potential: A Case Report of 2 Cases from a Tertiary Care Centre

Anuradha Sekaran¹, Abid Hussain¹, Partha Pal², Duvuru Nageshwara Reddy²

Departments of ¹Pathology and ²Medical Gastroenterology, Asian Institute of Gastroenterology, Hyderabad, Telangana, India.

Corresponding Author:

Dr Abid Hussain
Email: hussain.abid111@gmail.com

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Abstract

Background: Solid pseudo-papillary neoplasm (SPN) of the pancreas is a rare cystic tumor of pancreas which usually affects young females. Most patients remain asymptomatic for many years prior to diagnosis. Moreover, only rarely, the disease can be locally advanced or metastatic at presentation. **Case Report:** We report our experience with two cases of SPN of the pancreas with metastasis to liver and peritoneum at the time of presentation. Both were young females who presented with intermittent abdominal pain. Tumor's size ranged from 6.3-7 cm in greatest dimension. One case was diagnosed pre-operatively through percutaneous core needle biopsy and the other case had a fine needle aspiration done and later underwent surgery because of high suspicion of SPN based on clinical and radiological findings. By immuno-histochemistry, all cases stained strongly positive for pancytokeratin, vimentin, CD10, beta-catenin (nuclear) and neuroendocrine markers (synaptophysin). However, they were negative for chromogranin and CA19.9. Though these cases showed metastasis, the proliferation index (Ki-67) was very low <3% in both the cases. **Conclusion:** SPN of the pancreas should be considered in the differential diagnosis of any solid and partly cystic pancreatic or upper abdominal mass, particularly in young females. Histopathological features of metastatic potential of SPN have been predicted by several factors however they could not predict metastasis in our cases.

Keywords: Abdominal Pain, Fine Needle Biopsy, Immunohistochemistry, Pancreas, Pancreatic Neoplasms, Peritoneum, Vimentin.

Introduction

Solid pseudo-papillary neoplasm (SPN) of the pancreas is a rare tumor accounting for 1 to 2% of all exocrine pancreatic tumors which typically affects young women (90%). SPN was initially recognized as Guber-Frantz's tumor as it was first described by Frantz Virginia [1] in 1959 as "papillary cystic tumor of the pancreas". Other names are solid cystic pancreatic neoplasm, papillary epithelial neoplasm of pancreas of childhood and solid pseudo-papillary neoplasm. SPN is a low-grade malignant neoplasm [2] with an indolent behavior and only rare cases recur and/or metastasize after complete resection. Metastasis is seen in 5-10% cases. There are many large series of SPN from various countries [3]. However case

reports on metastasis of SPN are very few [4]. We report our experience with two cases of pancreatic SPN with metastasis to liver and peritoneum.

Case Reports

Case 1

A 29-year-old female presented to the hospital with complains of intermittent episodes of pain abdomen for last one year. On computed tomography (CT), there was a heterogenous solid to cystic mass measuring 7×6×5 cms in the body and tail of pancreas with multiple peritoneal nodules suggesting possibility of peritoneal metastasis. FNAC from pancreas showed features of SPN. The patient underwent distal pancreatectomy, splenectomy and metastatectomy.

Gross examination revealed a cystic irregular mass measuring 7×6×5 cms. Cut surface was partly solid and partly cystic. The resected margins of surgical specimen appeared uninvolved by the tumor. On microscopic examination, the tumor was partially encapsulated. Solid areas showed cells predominately arranged in pseudo-papillary pattern, sheets, nodules and islands separated by thin fibrovascular septae. Cells were monomorphic round, with round to oval nucleus, granular chromatin with prominent nuclear grooves and moderate amount of eosinophilic cytoplasm with intra and extracellular hyaline globules. Cystic areas showed spaces lined by flattened to cuboidal cells. Aggregates of foamy macrophages, cholesterol clefts were seen. Areas with marked hemorrhage, necrosis and hyalinization were noted [Fig.1]. The resected margins and lymph nodes were free of tumor. Immunohistochemistry performed showed strong positivity for pancytokeratin, vimentin, nonspecific esterase (NSE), CD 10. Strong nuclear positivity was seen for beta-catenin [Fig.2]. Ki67 labelling index was 2%. The tumor cells were negative for chromogranin and CA19.9. The microscopic findings of the peritoneal nodule were similar to the findings of the pancreatic tumor with similar IHC pattern and low Ki 67 (3%). Microscopic examination of spleen showed congestive splenomegaly. A final diagnosis of SPN of the pancreas with peritoneal metastasis was made.

Case 2

A 13-year-old female presented with complains of pain abdomen and vomiting since two months. On esophagogastro-duodenoscopy (EGD), there was an extrinsic bulge in the antrum and duodenum. CT abdomen showed a large heterogenous mass lesion measuring 6.3×3.7×3 cms in the head and neck of pancreas with multiple heterogenous mass lesions seen in both lobes of liver [Fig.3].

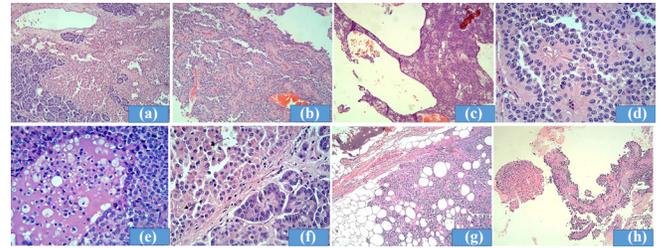


Fig.1: Histopathological examination with H&E stains displaying (a): tumor infiltrating the adjacent normal pancreas (×100), (b): pseudopapillary pattern and (×100) (c): cystic pattern of arrangement of tumor cells (×100), (d): pseudopapillary pattern with tumor cells surrounding the hyalinised fibrovascular core and cells are polyhedral with abundant cytoplasm and oval nuclei with prominent nuclear grooves (×400), (e): cystic areas filled with cystic fluid and cyst macrophages (×400), (f): Oncocytic cells with cytoplasmic globules; at places there is disruption of cytoplasm with extracellular release of hyaline globules (arrow) (×400), (g): peritoneal nodule infiltration by cells arranged in sheets (×100), (h): Liver biopsy with hepatocytes infiltrated by tumor with pseudopapillary architecture (×100).

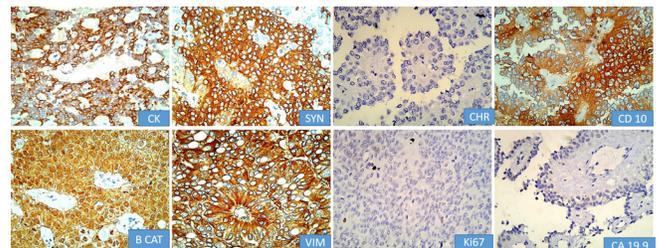


Fig.2: Immunohistochemistry performed with (a): pancytokeratin, (b): synaptophysin, (c): chromogranin, (d): CD10, (e): Beta Catenin, (f): Vimentin, (g): Ki 67, (h): CA19.9.

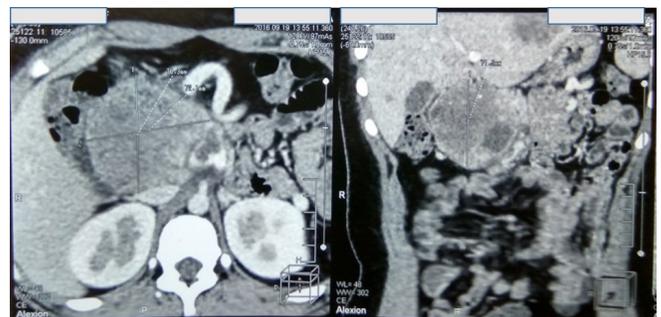


Fig.3: CT abdomen showing a large heterogenous mass lesion measuring 6.3×3.7×3 cms in the head and neck of pancreas with multiple heterogenous mass lesions seen in both lobes of liver.

Table 1: Clinicopathological and radiological findings of the two cases.

Case no.	Age / Sex	Presenting complaint	Site of pancreatic lesion	Size of lesion	Site of metastasis	Radiological findings	Final histopathological diagnosis
Case 1	29 / F	Pain abdomen, vomiting, anemia	Body and tail	7×6 cms	Multiple peritoneal nodules	Heterogenous mass lesion with tiny calcifications	SPN with peritoneal metastasis
Case 2	13 / F	Pain abdomen	Head and neck	6.3×3.7×3 cms	Multiple lesions in liver	Heterogenous mass lesion	SPN with liver metastasis

Biopsies from pancreas and liver showed similar morphology and IHC pattern of staining as described above in case one. Ki 67 labelling index was 3% in both liver and pancreas. A final diagnosis of SPN of the pancreas with liver metastasis was made. She was not operated because she was found to be inoperable and R0 resection was not possible. Chemotherapy was not given as there is no proven role of chemotherapy in SPN.

Discussion

SPN accounts for less than 10% of cystic neoplasms of pancreas and occurs mostly in females (female: male: 10:1). Most cases occur in young female in third decade although older age of onset (>50 years: 5% cases) and pediatric onset has been described (1-18 years: 20%).

Most common clinical presentation are abdominal pain (67-81%) and abdominal mass (35%). A significant proportion of the cases are diagnosed incidentally (15%). Most cases involve body and tail (60%) with size larger than 10 cm. Similar location was found in our cases and the tumors were of 6.3-7 cm in diameter [Table 1]. The close differential of SPN on histopathology is neuroendocrine tumor which can be differentiated by demonstration of CD 10 and Beta-catenin in SPN [Table 2].

Recurrence after curative resection occurs in 10-15% of cases. Mao *et al.* reviewed 292 patients with SPN, of these 14.7% (43 of 292) were diagnosed as malignant due to metastasis (22 of hepatic, lymph node metastasis or peritoneal

Table 2: Histopathological findings and immuno-histochemistry panel of both the cases.

Histopathological Findings	Case 1	Case 2
Pseudo-papillary pattern	+	+
Nuclear grooves	+	-
Eosinophilic hyaline globules	+	-
Necrosis	+	+
Hyalinization	+	+
Cholesterol clefts	+	-
Foamy macrophages	+	+
Immuno-histochemistry		
Pan cytokeratin	Focal +	+
Synaptophysin	+	+
Chromogranin	-	-
CD 10	+	+
Beta-catenin	Nuclear +	Nuclear +
Vimentin	+	+
Ki 67	2%	2%
CA 19.9	-	-

dissemination) or invasion into adjacent organs. Metastasis develops in less than 10% with metastasis to liver being most common. Curative resection for hepatic metastasis is possible if involvement is limited. However, Martin *et al.* [5] suggested that complete resection was associated with long-term survival even in the presence of metastatic disease. In many case report series, even patients with local recurrence as well as liver and peritoneal metastasis have experienced long-term survival after surgical resection [6,7]. Similarly with one of our case, as there were multiple liver metastasis, surgery with resection of liver was advised. However

Table 3: Comparison of several studies predicting clinico-pathological features associated with metastatic SPN.

Features predicting malignant SPN	Nishihara <i>et al</i> ⁸	Klimstra <i>et al</i> ⁹	Woo Seok Nam, <i>et al</i> ¹⁰	Present study
Age (elderly, > 50 years)	-	Elderly, >50 years	-	Young adults (29 and 13 years)
Tumor size (>10 cms)	-	>10 cms	>10 years	<10 cms
Cellular/nuclear pleomorphism	High grade	High grade	No pleomorphism	No pleomorphism
Mitosis	-	Increased	Low (<5%)	Low (3%)
Necrosis	Present	-	-	Absent
Lymphovascular invasion	Present	Present	-	No
Perineural invasion	-	Present	Present	No

the patient refused for surgery. There are several studies showing microscopic features predicting metastatic potential in malignant SPN [Table 3].

The prognosis for SPN is excellent after curative resection in non-metastatic SPN (more than 90% survival at 5 years). Metastatic SPN are frequently amenable to resection. Favorable prognosis with long term survival has been shown in patients with metastasis [8]. Similarly prognosis was good in one of our case (with peritoneal metastasis) after surgical resection of peritoneal nodule, with 100% survival rate after one year of follow-up.

Conclusion

Though SPN possesses a low malignant potential it can rarely metastasize to adjacent sites and should be considered in the differential diagnosis of suspected metastatic pancreatic lesions. Histopathological features of metastatic potential of SPN have been predicted by several studies however they could not predict metastasis in our cases. Pre-operative diagnostic work-up is a cornerstone for surgical approach and complete surgical resection with clear margins is the treatment of choice even after metastasis.

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