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# SOLID PSEUDOPAPILLARY NEOPLASM: A RARE PANCREATIC TUMOR

Pathology

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## ABSTRACT

Solid pseudopapillary neoplasm is a rare primary pancreatic tumour that usually presents in young women with an abdominal mass. Tumours are often large and resection is usually feasible with long term survival. Solid pseudopapillary neoplasm of the pancreas is generally considered to be of low malignant potential despite their often large size at presentation. The diagnosis of a solid pseudo papillary neoplasm depends on the characteristic histomorphology supported by immunohistochemistry. Grossly, it appears as a large solid, cystic or solid-cystic mass frequently having necrotic and hemorrhagic zones. Histologically, solid pseudopapillary neoplasm is generally characterized by solid areas alternating with a pseudopapillary pattern, and cystic spaces which are the results of degenerative changes occurring in the solid neoplasm. Its immunohistochemical pattern is very distinctive. Many investigators favor the theory that solid-pseudopapillary neoplasm originate from multipotent primordial cells while others suggest an extra-pancreatic origin from genital ridge angle-related cells. It is important to differentiate this neoplasm from other pancreatic tumors, because this type is amenable to cure after complete surgical resection, even in cases with capsular invasion, unlike other malignant tumors of the pancreas. No pathological factors were found to correlate with the prognosis.

## KEYWORDS

Solid, Pseudo Papillary, Neoplasm, Pancreas

## INTRODUCTION

Solid pseudopapillary neoplasm (SPN), an uncommon entity first described by Frantz in 1959[1] reportedly accounts for between 2% and 3% of pancreatic neoplasms and 0.9% to 2.7% of exocrine pancreatic neoplasms.[2,3] Solid pseudopapillary neoplasm primarily affects young females with a mean age of 22 years[4]. Most tumors are located in the pancreatic body and tail.[3-5] Different names for this tumor were reported until it was defined by the World Health Organization (WHO) in 1996 as a "solid pseudopapillary neoplasm " of the pancreas [7]. The origin of solid pseudopapillary neoplasm is unclear. Many investigators favor the theory that SPNs originate from multipotent primordial cells, whereas others suggest an extra pancreatic origin, from genital ridge angle-related cells[6]. Although most Solid pseudo papillary neoplasm exhibit benign behavior, malignancy can occur in about 15% of cases, manifesting as metastases or invasion of adjacent structures [6]. The morphological appearance of SPN varies from solid to cystic components with cellular degenerative changes [7]. Diagnosis is based on characteristic histological features and immunohistochemical study. Microscopically, The SPNs show a combination of solid components that consist of pseudo papillae with vascular stalks and cystic components with hemorrhage, a characteristic architecture. The cells of SPNs demonstrate strong positive staining for beta-catenin, CD10, vimentin, alpha-*1*-antitrypsin, alpha- -1-antichymotrypsin, neuron-specific enolase, and cyclin D1 [5,9]. Solid pseudo papillary neoplasm (SPN) is an unusual tumor that develops from the exocrine pancreas and tumors are often over 10 cm in diameter at presentation. However metastatic disease is rare and complete resection is usually possible with excellent long term survival[10]. Complete surgical excision with a clear margin of normal pancreatic tissue is usually curative [11]. Diagnosis of SPN may be challenging, but careful interpretation of the histologic and cytologic features and immunohistochemical staining patterns usually allows pathologists to make the diagnosis for this uncommon tumor. It is important to differentiate this tumor from other pancreatic neoplasm, because this type is amenable to cure after complete surgical resection, even in cases with capsular invasion, unlike malignant tumors of the pancreas. In this article, we are presenting a case of SPN in a young female which is diagnosed with histomorphological and immunohistochemical study.

## CASE REPORT:

A 23 year old female presented with history of epigastric and right upper quadrant pain abdomen and nausea for 5 years. On examination there was lump in upper abdomen. However, there was no history of jaundice. Ultrasonography showed a cystic mass in pancreatic tail measuring 11.5x10.2cm. CT scan revealed multi locular predominately cystic lesion in pancreatic body and tail measuring 12x10 cm with minimum calcification and multiple irregular septae .Lipase and amylase were mildly increased. Excision of the mass was done and sent for histopathological study. Gross examination of the specimen showed a globular well circumscribed tissue measuring 11.5x10.5 cm .Outer surface was smooth. Cut surface was predominantly cystic with few multi loculated spaces which contain thick chocolate colored fluid. Multiple sections were studied for microscopic examination. Sections revealed circumscribed cystic mass lined by thick fibrous pseudo capsule and composed of monomorphic cells population with round to oval nuclei, inconspicuous nucleoli which arranged as solid and pseudo papillary architecture (Figure-1, 2, 3). Cytoplasm of some of cells showed PAS positive and diastase resistance globules. Areas of degeneration, necrosis and hemorrhage were seen. Cholesterol clefts, fibrosis, macrophages, haemosiderin laden macrophages and F.B body giant cells were also present. Fibrous capsule showed micro calcification. Mitosis was not evident. Immunohistochemical stain showed diffuse positivity for Vimentin, beta catenin and CD-10 (Figure-4, 5 6). Focal positivity for synaptophysin was present (Figure-7). However cells were negative for CK and Chromogranin. Diagnosis of solid pseudo papillary neoplasm of pancreas was done.

### Figures And Legends

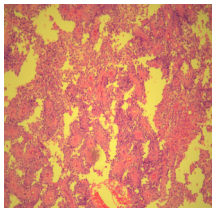

**Figure-1 Histology Of The Neoplasm Showing The Features Of A Solid Pseudo Papillary Neoplasm Of The Pancreas. H &e (10x)**

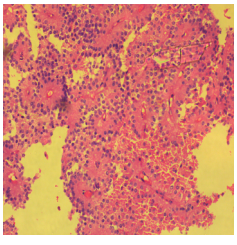

**Figure-2 Histology Of The Neoplasm Showing The Features Of A Solid Pseudo Papillary Neoplasm Of The Pancreas. Papillary Fronds With Fibrous Septae Are Lined By Monotonous Cells. H&e Stain (20x)**

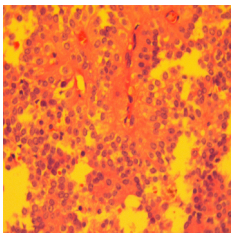

**Figure-3 Solid Pseudo Papillary Neoplasm: Histologically, The Tumor Showing Pseudo Papillary Pattern. Cellular Atypia And Mitoses Are Not Evident. H &e (40x)**

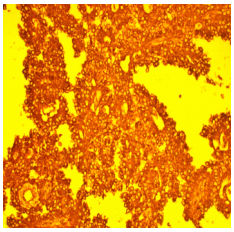

**Figure-4 Immunohistochemical Staining For Vimentin Showing Diffuse Nuclear Positive Staining (20x)**

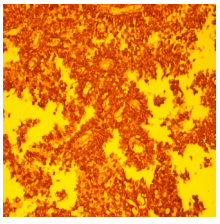

**Figure-5 Immunohistochemical Staining For Beta-catenin Showing Diffuse Nuclear Positive Staining (20x)**

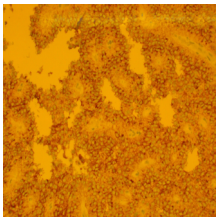

**Figure-6 Immunohistochemical Staining For Cd10 Showing Membranous Positive Staining (20x)**

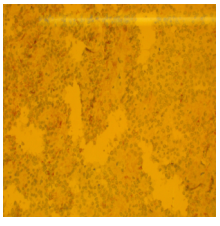

**Figure-7 Immunohistochemical Staining For Synaphtophysin Showing Focal Minimal Positivity(20x).**

## DISCUSSION

Solid pseudopapillary neoplasm (SPN) reportedly accounts for between 2% and 3% of pancreatic neoplasm and 0.9% to 2.7% of exocrine pancreatic neoplasms[2,3]. Solid pseudo papillary neoplasm primarily affects young females with a mean age of 22 years[4] The origin of solid pseudo papillary neoplasm is unclear. Many investigators favor the theory that SPNs originate from multi potent primordial cells, whereas others suggest an extra pancreatic origin, from genital ridge angle-related cells[6]. Although most SPNs exhibit benign behavior, malignancy can occur in about 15% of cases, manifesting as metastases or invasion of adjacent structures[6]. Abdominal pain or mass is the most common presenting clinical symptom or sign. Nonspecific symptoms such as nausea, vomiting, fever, weight loss, and jaundice are other clinical symptoms; a considerable percentage of patient populations are asymptomatic and the neoplasm can be incidentally detected**.** The majority of tumors are diagnosed through ultrasound or CT scan of the abdomen. Computed tomography scan of the neoplasm demonstrates solid and cystic features with regions of hemorrhage and/or cystic degeneration. Calcifications and enhancing solid areas may be present at the periphery of the mass[12]. Magnetic resonance imaging basically shows a well-circumscribed lesion with a mixture of high and low-signal intensity on T1- and T2-weighted images.[28] Most of the tumors are located in the pancreatic body and tail [3, 5]. Echo-endosonography may provide FNA biopsy with the possibility of pre-operative pathologic diagnosis[6]. Typically, SPNs are well-circumscribed masses that demonstrate variable degrees of internal hemorrhage and cystic degeneration, and may be associated with calcifications. When these features are encountered in a young female patient, this neoplasm should be considered as an important differential diagnosis. Solid pseudo papillary neoplasm is an unusual tumor that develops from the exocrine pancreas and tumors are often over 10 cm in diameter at presentation.

This neoplasm is usually a round, circumscribed mass that is separated from pancreas parenchyma by a pseudo capsule. It shows variable appearance with solid, cystic, hemorrhagic, and necrotic areas. Incomplete capsules during gross examination are highly suggestive of a malignant SPN. The larger the tumor, the greater the cystic component that the tumor contains[13]**.** Histological features and immunohistochemical stains are characteristic. Microscopically, The SPNs show a combination of solid components that consist of pseudo papillae with vascular stalks and cystic components with necrosis and hemorrhagic zone. The papillary fronds show central fibrous septae lined by cells exhibiting 'epithelial' morphology. They are monomorphous and lack of cytological atypia. The tumor cells are uniform with round and small nuclei lining a delicate capillary-sized vessel[14]. The nuclei are round or oval, and they are located within the cell center and may exhibit grooves. The nuclei do not have salt-and-pepper features, which are seen in neuroendocrine tumors. The neoplastic cells usually have a moderate amount of amphophilic cytoplasm with focal aggregation of intracytoplasmic and extracytoplasmic hyaline globules[26].These globules are typically periodic acid–Schiff positive and diastase resistant and highly characteristic for diagnosis of SPN. Foam cells (macrophages) and foreign-body giant cells are usually observed adjacent to the cystic spaces. Mitotic activity is either absent or very low.[14] Foci of calcifications, sheets of foamy macrophages and the presence of cholesterol crystals are additional features. The vasculature can be very conspicuous [15].

Areas of necrosis and hemorrhage are commonly found but do not warrant a diagnosis of malignancy.

The cells of SPNs demonstrate strong positive staining for beta-catenin, CD10, vimentin, alpha-1-antitrypsin, alpha-1-antichymotrypsin, neuron-specific enolase, and cyclin D1 [5, 18]. Staining for synaptophysin, usually weak and focal, is reported in as many as 44% of SPNs.[16]19. Keratins is not expressed or is found only focally. Endocrine and pancreatic enzyme markers are absent[17]. Neoplastic cells harbor somatic point mutations in exon 3 of CTNNB1, the gene encoding beta-catenin in Wnt signaling pathway, resulting in nuclear condensation of beta-catenin and cyclin D1, and also loss of E-cadherin receptors on cellular membranes[18]. These changes will be detected by strong nuclear staining of beta-catenin and cyclin D1, and by loss of E-cadherin membranous staining in this tumor cells[19].

Epithelial membrane antigen (EMA) and chromogranin are also not expressed. In fact all expert s agree that if a tumor shows substantial chromogranin expression it is not an SPN[20]. Immunohistochemical patterns suggest that SPNs cannot be regarded as purely epithelial neoplasms[21]**.** In fact, cytokeratin expression, usually associated with epithelial differentiation, is rare (less than 30%) or absent in most cases, and markers of acinar differentiation (trypsin/chymotrypsin) and glycoprotein markers of ductal differentiation are often negative [22].

The differential diagnosis of SPN includes acinar tumors, pancreatoblastoma, and endocrine tumors, adenocarcinoma. However, the immunohistochemical pattern of SPNs is distinctive and differs from that of other primary pancreatic tumors which should be considered in the differential diagnosis [17].Histologically, the closest differential diagnosis is a neuroendocrine tumor (NET) of

the pancreas. Histologic features of pancreatic neuroendocrine neoplasms are very similar to SPNs, and it is often difficult for a pathologist to diagnose either one on the basis only of histology or cytology[13]. However, multiple architectural and cellular features, such as presence of pseudo papillae, hyaline globules, foamy histiocytes, and nuclear grooving, help us to favor SPN.[26] Presence of speckled (salt-and-pepper) chromatin favors neuroendocrine tumor. Immunohistochemistry panel is recommended by most investigators to differentiate, these two entities.[5]

However, SPNs cannot even be regarded as a purely neuroendocrine neoplasm because the presence of neuroendocrine markers is not significant (chromogranin A is not detected, synaptophysin has a patchy immunoreactivity in 22% and NSE is strongly positive in more than 90% but without a certain significance[17]. Most pancreatic neuroendocrine tumor show diffuse strong labeling for chromogranin and keratin, whereas virtually all SPN are negative for these markers[23]. Nuclear expression of beta catenin is consistent in SPN but very uncommon in pancreatic neuroendocrine tumor**.**

It is important to differentiate this tumor from other pancreatic neoplasm, because this type is amenable to cure after complete surgical resection, even in cases with capsular invasion, unlike malignant tumors of the pancreas. Complete surgical excision with a clear margin of normal pancreatic tissue is usually curative[11]. Despite the locally aggressive features, the tumor has a low-grade malignant potential and tends to have a favorable prognosis, even in the presence of metastatic disease. Overall 5-year survival is as high as 97% in patients undergoing surgical resection[24]. No pathological factors including mitotic rate, nuclear pleomorphism and vascular invasion were found to correlate with the prognosis. Neither vascular, or perineural invasion has been a factor for predicting tumor recurrence or overall survival of patients [25]. However metastatic disease is rare and complete resection is usually possible with excellent long term survival [10]**.** Five-year survival rate is as high as 95% to 97%, with an estimated 10-year survival rate of approximately 93%.[16]**.**

Surgery is the treatment of choice, even in the case of distant hepatic metastasis or local recurrence[27].

Conflict of Interests: There is no conflict of interests

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