

# A rare case of three different tumors in the same pancreatic specimen: a case report and brief review of the literature

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**Abstract:** Solid pseudopapillary tumors (SPT) of the pancreas are rare neoplasms mainly affecting young women. Pancreatic serous cystadenomas (SCAs) and pancreatic neuroendocrine tumors (PanNETs) account for about 2% of all pancreatic neoplasms. The combination of these three lesions, to our knowledge, has never been described in literature. Here we report a case of combined SPT, SCA and PanNET affecting a 33-year-old woman.

**Keywords:** Solid pseudopapillary tumor (SPT); endocrine neoplasm; serous cystadenoma (SCA); multiple pancreatic tumors

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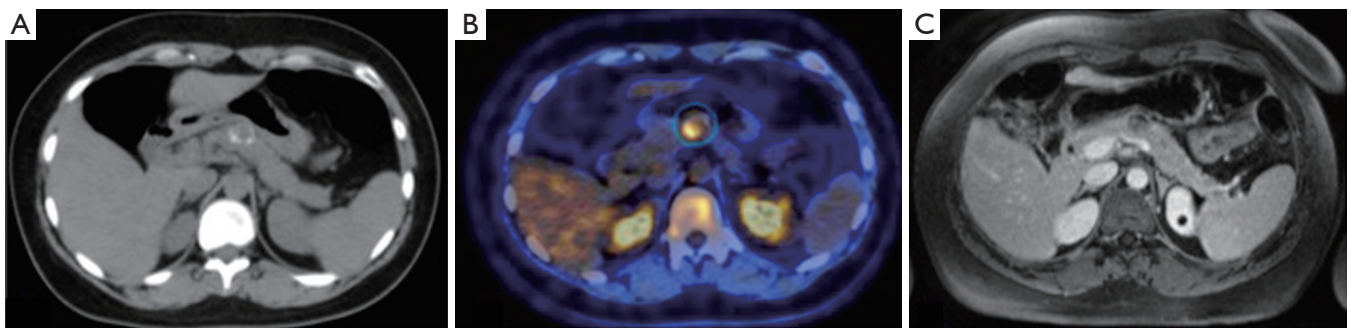
## Introduction

The simultaneous presence of pancreatic exocrine and endocrine tumors, although rare, has been already reported (1-14). We report a case of simultaneous presence in the pancreas of a solid pseudopapillary tumor (SPT), a serous cystadenoma (SCA) and a neuroendocrine tumor (PanNET).

## Case presentation

A 33-year-old Caucasian female was referred to our department for a solid nodule in the body of the pancreas in August 2014. Past medical records revealed several episodes of biliary colic due to gallstones treated surgically with laparoscopic cholecystectomy 1 year before. After a 6 months period of wellness, the patient started suffering from dyspepsia and epigastric nocturnal pain. She had no history of diabetes, smoking or alcohol abuse and did not use any drug on regular basis. There was no family history of pancreatic neoplasms. Biochemical tests did not

reveal abnormalities. CA 19-9 was normal (<37 U/mL). An Ultrasonography confirmed the presence of a solid nodule in the body of the pancreas, which was further investigated with contrast-enhanced CT-scan (CT) (Figure 1A), magnetic resonance (MR) and endo ultrasonography (EUS). All the instrumental findings supported the diagnosis of SPT of the body of the pancreas. After admission, the patient underwent <sup>18</sup>FDG PET/CT scan that revealed a pathologic uptake (Figure 1B) within the body of the pancreas (late maximum SUV was 5.6) with a peripheral calcified rim. To investigate whether the abnormal uptake was due to a neuroendocrine pancreatic tumor a <sup>68</sup>Gallium DOTATOC PET/CT scan was performed. No areas of pathologic uptake were identified. Finally, a magnetic resonance cholangiopancreatography (MRCP) (Figure 1C) showed a hypovascular focal lesion located in the body of the pancreas, hyperintense on T1-weighted and hypointense in T2-weighted sequences. This lesion appeared inhomogeneous due to the presence of a peripheral calcified rim. The main pancreatic duct was lightly compressed and displaced by the lesion with a mild



**Figure 1** Imaging of the SPT at CT-scan (A),  $^{18}\text{F}$ FDG PET/CT (B) and MRCP (C). SPT, solid pseudopapillary tumor; MRCP, magnetic resonance cholangiopancreatography.

dilation upstream. Due to the symptoms and the suspected diagnosis of SPT the patient then underwent laparoscopic distal splenopancreatectomy. Post-operative course was complicated by grade B pancreatic fistula [according to ISGPF (15)], associated with fever, abdominal pain and leukocytosis, treated with parenteral nutrition and broad-spectrum antibiotics. The surgical pancreatic drainage was maintained and a second drainage was inserted for the presence of a fluid collection in the splenic lodge in 8<sup>th</sup> postoperative day. The patient was discharged in 32<sup>nd</sup> postoperative day.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

### **Histopathologic analysis**

Pathological examination revealed a 2-cm SPT of the body of the pancreas (*Figure 2A,B*) without nodal involvement. Grossly, it was a gray-brownish lesion with a firm microcystic appearance. In the remaining pancreatic parenchyma two other neoplasms were discovered, a 7-mm serous cystadenoma (*Figure 2C*) and a 5-mm neuroendocrine microadenoma that grossly appeared as a brown firm nodule (*Figure 2D*).

### **Immunohistochemistry**

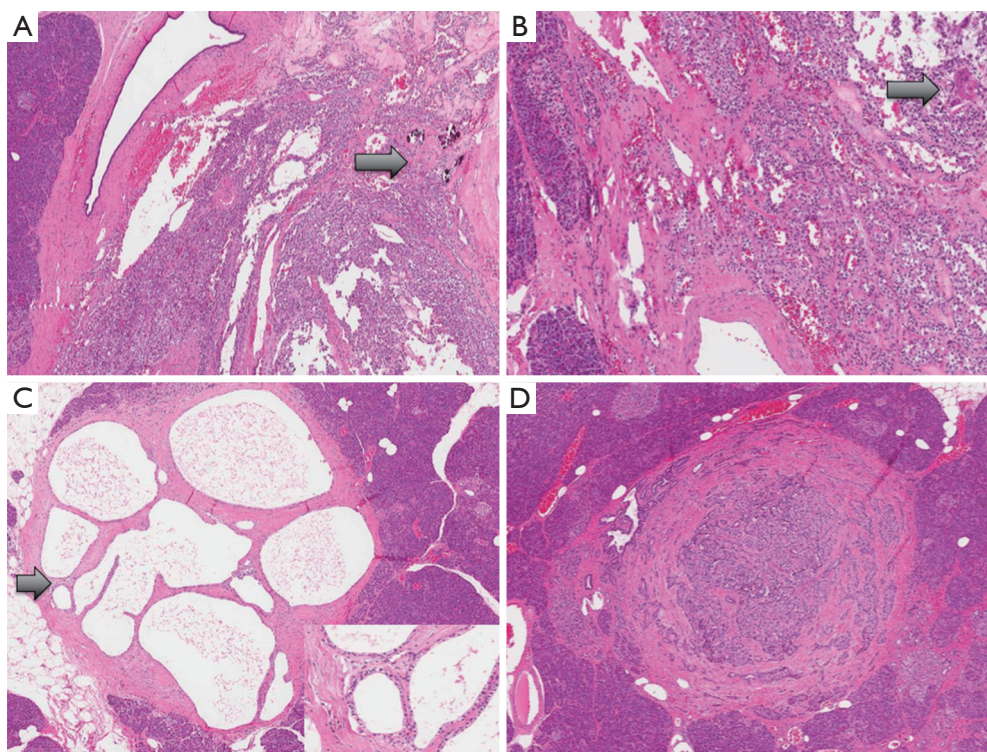
Immunohistochemical analysis was performed as previously described (16,17). Briefly, using 4  $\mu\text{m}$  formalin-fixed paraffin-embedded sections, immunohistochemical analysis was conducted with the standard polymer system and peroxidase methods. After heat-induced antigen retrieval with a heated plate and 0.01 mol/L of citrate buffer, pH 8.9, for 15 min, all samples were processed using a sensitive

‘Bond Polymer Refine’ detection system in an automated Bond immunohistochemistry instrument (Vision-Biosystem, Leica, Milan, Italy). Sections incubated without the primary antibody served as negative controls. Immunostaining confirmed the diagnosis of solid pseudopapillary neoplasm for the main tumor as it showed nuclear positivity for  $\beta$ -catenin (Sigma, clone:15B8, 1:150 dilution) and progesteron-receptor (Dako, clone:PgR636, 1:20 dilution), cytoplasmic positivity for vimentin (Biogenex, clone:V9, 1:50 dilution) and CD10 (Novocastra, clone:56C6, 1:10 dilution), while it was negative for chromogranin A (Dako, clone:DAK-A3, 1:2,500 dilution) and had a scattered positivity for synaptophysin (Novocastra, clone:Snp88, 1:100 dilution). Ki-67 was <1% and 1 mitosis per 50 high power fields was detected (*Figure 3*). The neuroendocrine microadenoma was positive for chromogranin A and synaptophysin, as well as for CD56 (Thermo Scientific, clone:123C3.D5, 1:100 dilution), with a Ki67 proliferative index <1% (Novocastra, clone:MM1, 1:50 dilution).

### **Discussion**

To our knowledge, this is the first report on the simultaneous presence of three different pancreatic neoplasms in a patient.

SPTs are rare pancreatic tumors accounting for 1–2% of all pancreatic exocrine tumors, are usually benign, but metastasis have been described in up to 15% of cases (18). Young women in the second decade are predominantly affected (19). There is no preferential localization within the pancreas, even though some case series report a more frequent localization in the body-tail of the pancreas (20). The origin of SPTs is still controversial. The most diffuse hypothesis is a differentiation from a pluripotential stem cell towards endocrine, acinar or epithelial-cell lineage (21,22). They have an indolent growth, which lead them



**Figure 2** The three pancreatic tumors in the same specimen. The solid pseudopapillary tumor (A, 4× magnification, B, 10× magnification) was characterized by a heterogeneous growth pattern, with a combination of solid areas, typically located at the periphery, and pseudopapillary-microcystic structures with necrotic-hemorrhagic degeneration at the center of the tumor and deposition of calcific material (A, arrow). Furthermore, adjacent to the hemorrhagic areas, there was a classic giant cell reaction to cholesterol crystals, with some foamy histiocytes in the background (B, arrow). The serous cystadenoma (C, 4× magnification) showed a microcystic appearance, with a typical cuboidal mono-stratified epithelium, without any atypia (C, small box: 20× magnification; the arrow indicates the area zoomed in the small box). The neuroendocrine microadenoma (D, 4× magnification) was characterized by a solid-trabecular histologic pattern. The cells are uniform with the typical “salt and pepper” chromatin clumping.

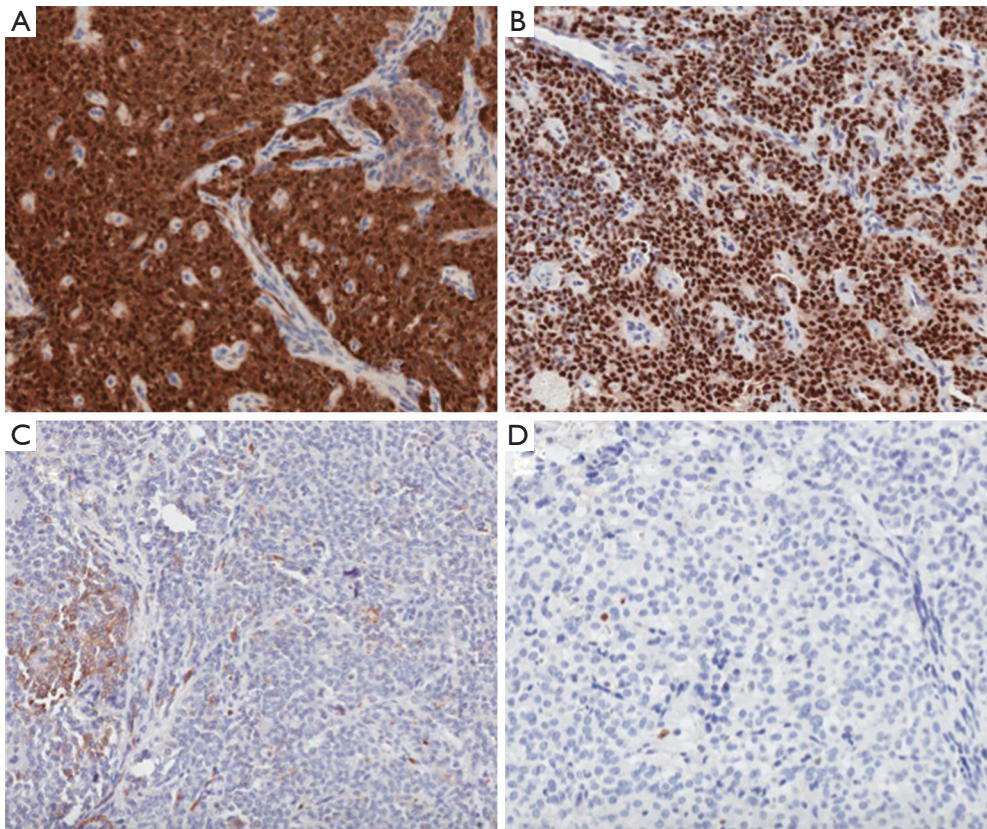
to be discovered mostly incidentally or due to symptoms such as abdominal discomfort, palpable mass or weight loss. SPTs typically present radiologically as a large encapsulated mass with solid-cystic components and often intra-tumoral hemorrhage (23-25). While growing, SPTs can develop cystic changes, mimicking true pancreatic cystic tumors (26). At our Institution we routinely perform contrast enhanced CT-scan of the abdomen and MRCP when a SPT is suspected. With these radiological investigations a 95% preoperative diagnosis can be achieved (27). Surgical resection is the gold standard treatment for SPTs (20,28). Considering the excellent prognosis some reports suggest to resect also recurrences and metastases (26,29,30).

SCAs are rare non-mucinous cystic tumors with a benign behavior, with a stronger prevalence in females, and with a low growth rate (about 0.28 cm/year during the first 7 years

from diagnosis); they are mostly incidentally found and often need differential diagnosis with mucinous cystic tumors. Follow-up of these lesions is the recommended strategy (31).

PanNETs measuring less than 0.5 cm are defined microadenomas and they are considered biologically benign. By definition these early stage PanNETs are nonfunctional (32). While they are common in patients suffering from MEN1 syndrome [so called “microadenomatosis” (33)], their prevalence as sporadic lesions ranges from 1% to 10% in adult population at autopsic findings (34). The diagnosis of endocrine microadenomas usually follows the pathological analysis of a pancreatic specimen resected for other reasons (32).

In conclusion, the association between pancreatic tumors originating from different cell lineages is already known. The most common reported combinations involve SCAs



**Figure 3** Immunohistochemistry showing SPT cells marked by  $\beta$ -catenin (A, 20 $\times$ ), by progesterone-receptors (B, 20 $\times$ ), focally by synaptophysin (C, 20 $\times$ ); Ki 67% was <1% (D, 20 $\times$ ). SPT, solid pseudopapillary tumor.

with PanNETs or ductal adenocarcinoma, and PanNETs with ductal adenocarcinoma (1-14). Yan *et al.* documented a 2-cm SPT of the tail of the pancreas engulfing a 0.7 cm well-differentiated PanNET (22). They postulated that a neoplastic pluripotential stem cell might differentiate in endocrine, epithelial and acinar cell lines.

This case report is unique, since three distinct neoplastic lesions, each derived from distinct cell lineages, have been found in the same pancreatic specimen. Considering the low prevalence of each of these pancreatic neoplasms, the probability to find them simultaneously is exceedingly rare. As a take home message, we want to underline the importance of a careful examination of the whole pancreatic specimen to rule out the possibility of other coexistent tumors.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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