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Smarcb1/Ini-1-Deficient Pancreatic Carcinoma with Rhabdoid Features: A Case Report and Literature Review

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1. Abstract

1.1. Background: SMARCB1/INI-1-deficient pancreatic carcinoma is a rarely reported entity. So far, only 10 cases have been published in the literature, and most of the reported cases have poor prognosis and mortality rate within six months is extremely high. The clinical presentation, histopathological features, and biologically behaviors are essentially unclear.

1.2. Case Summary: A 53-year-old woman presented with nonspecific non infective gastroenteritis and colitis. Imaging study showed a pancreatic head and uncinate process mass. Biopsy demonstrated carcinoma at outside facility. Patient was then on chemotherapy for 6 months which she tolerated relatively poorly. She came to our institution where she was treated with neoadjuvant therapy and tolerated well followed by pancreatoduodenectomy. The resected neoplasm showed papillary and cystic growth with hyalinized and myxoid stroma, morphologically resembled solid pseudopapillary neoplasm. The cytologic features of the tumor cells included abundant cytoplasm with cytoplasmic clearing, vacuolation, eosinophilic globules, and areas of tumor cells showing plasmacytoid/rhabdoid features. Loss of SMARCB1/INI-1 nuclear staining was observed in tumor cells. A diagnosis of treated SMARCB1/INI-1 deficient carcinoma with rhabdoid features was rendered. The patient tolerated surgical procedure well with only spontaneously resolved vomiting. She has been now well one and half years since the diagnosis.

1.3. Conclusion: In this article, we reported a case of SMARCB1/INI-1-deficient pancreatic carcinoma from a 53-year-old female patient who had an indolent clinical presentation, and the tumor morphologically resembled solid pseudopapillary neoplasm with rhabdoid/plasmacytoid and clear cell features. It is indicated that tumors from patients with an indolent clinical course and showing the above histopathological features may be warranted further investigation of the SMARCB1/INI-1 status.

2. Introduction

Recently, with the development of next gene sequencing, many published literatures have focused on the role of genetic alterations in tumorigenesis. Among these genetic alterations, integrase interactor 1 (INI-1, or hSNF5, SMARCB1, BAF 47) (SMARCB1/INI-1), a tumor suppressor and an integral component of chromatin remodeling complex of the SWItch/sucrose non-fermentable (SWI/SNF), has been attracting attention. The deficiency of SMARCB1/INI-1 was initially reported in malignant rhabdoid tumor (MRT) of infancy. Subsequently, it is also found in the tumorigenesis of other adult tumor types, including renal medullary, esophageal, and pleural carcinoma [1-7]. The mechanism involves various signaling pathways such as canonical WNT (or beta-catenin-dependent), non-canonical WNT [8], and p16-RB pathways [9]. Regardless of anatomical location, the prognosis of MRT is poor with majority of patient die within the first year [10]. Studies have also shown that cofactors of SWI/SNF

play roles in pancreatic cancer [11]. Loss of SMARCB1/INI-1 is reported in pancreatic undifferentiated rhabdoid carcinomas and anaplastic carcinomas with abundant rhabdoid cells [12-18].

3. Case Presentation

A 53-year-old woman presented with non-infective gastroenteritis and colitis more than one and half years ago, which prompted imaging studies.

3.1. Medical History

The patient had a pancreatic head and uncinate process mass, with biopsy proven carcinoma at outside facility in July 2021. She underwent chemotherapy for 6 months and was seen at our institution in January 2022. She received neoadjuvant therapy, then pancreatoduodenectomy in September 2022. The surgery was uneventful, except dehydration secondary to vomiting, which resolved spontaneously. She had done well postoperatively.

3.2. Physical Examination

The abdomen is relatively flat, soft, nontender, nondistended. Normoactive bowel sounds are in all four quadrants. No palpable hepatosplenomegaly.

3.3. Laboratory Findings

CA19-9 remained normal throughout the clinical course.

3.4. Images

The patient underwent multiple computed topography (CT) scans. The initial CT scan in January 2021 showed a 1.1 cm coarse calcified mass within the pancreatic head. CT scan in May 2021 demonstrated stable 1.1 cm calcified mass. CT scan in July 2021 indicated a 3.9 cm hypodense mass in the pancreatic uncinate process, abutting the superior mesenteric artery and possibly the superior mesenteric vein without overt encasement. Biopsy of the mass showed carcinoma at outside facility. There was no evidence of metastatic disease in the chest, abdomen, or pelvis. After chemotherapy, CT study in November 2021 showed a decrease in size of the uncinate process mass, decreased contact of the superior mesenteric artery, and decreased soft tissue thickening along the superior mesenteric artery. There was persistent abutment of the mass to the superior mesenteric vein, and again no evidence of metastatic disease. Repeated CT study in September 2022 showed the pancreatic head and uncinate process mass measuring 4.2 cm with calcification and abutting the duodenum. New hypodense areas within the mass were found, which might represent necrosis. No definitive evidence of metastatic disease was found.

3.5. Pathological Findings

The resection specimen showed an infiltrate pancreatic neoplasm with papillary and cystic growth pattern in a myxoid and focal hyalinized vascular stroma (Figure 1). There was no definitive glandular formation. Special stain for intracellular mucin by mucicarmine was negative. The neoplastic cells were relatively bland. The cytoplasm had clear vacuoles and eosinophilic globules. The nuclei were mostly round to oval, with few areas showing pleomorphism, irregularity, and grooves. In multiple foci, plasmacytoid/rhabdoid tumor cells are seen. Only occasional mitoses were identified. Necrosis, calcification, and ossification were identified. Periodic acid-Schiff (PAS) stain highlighted glycogen granules, and PAS-diastase revealed focal intracellular globules (Figure 2).

Immuno histochemically stains demonstrated that tumor cells were positive for pancytokeratin, E-cadherin (focal), and cyclin D1 (focal); negative for CK7, beta-catenin (membranous), trypsin, progesterone receptor, HepPar1, CK5/6, WT1, D2-40, calretinin, synaptophysin, and chromogranin (Figure 2). SMARCB1/INI-1 immunostaining showed complete loss of nuclear expression in all tumor cells. DNA mismatch repair protein immunohistochemical stains showed intact nuclear expression in tumor cells, indicating MSI-stable. Genetic testing did not show any reportable genetic variants, including APC, ATM, BRCA1, BRCA2, CDKN2A, SMAD4, STK11, TP53, EPCAM, BMPR1A, MEN1, MLH1, MSH2, MSH6, PMS2, NF1, PALB2, TSC1, TSC2, and VHL.

3.6. Final Diagnosis

Treated SMARCB1/INI-1 deficient carcinoma with rhabdoid features.

3.7. Outcome and Follow-Up

The patient tolerated surgical procedure well without complications. She experienced dehydration secondary to vomiting on post-op day 8, which was resolved without intervention. Her case was discussed at the multidisciplinary conference and the consensus was made with surveillance. Until the date of this manuscript the patient has recovered well. Next gene sequencing was sent to molecularly profile the tumor.

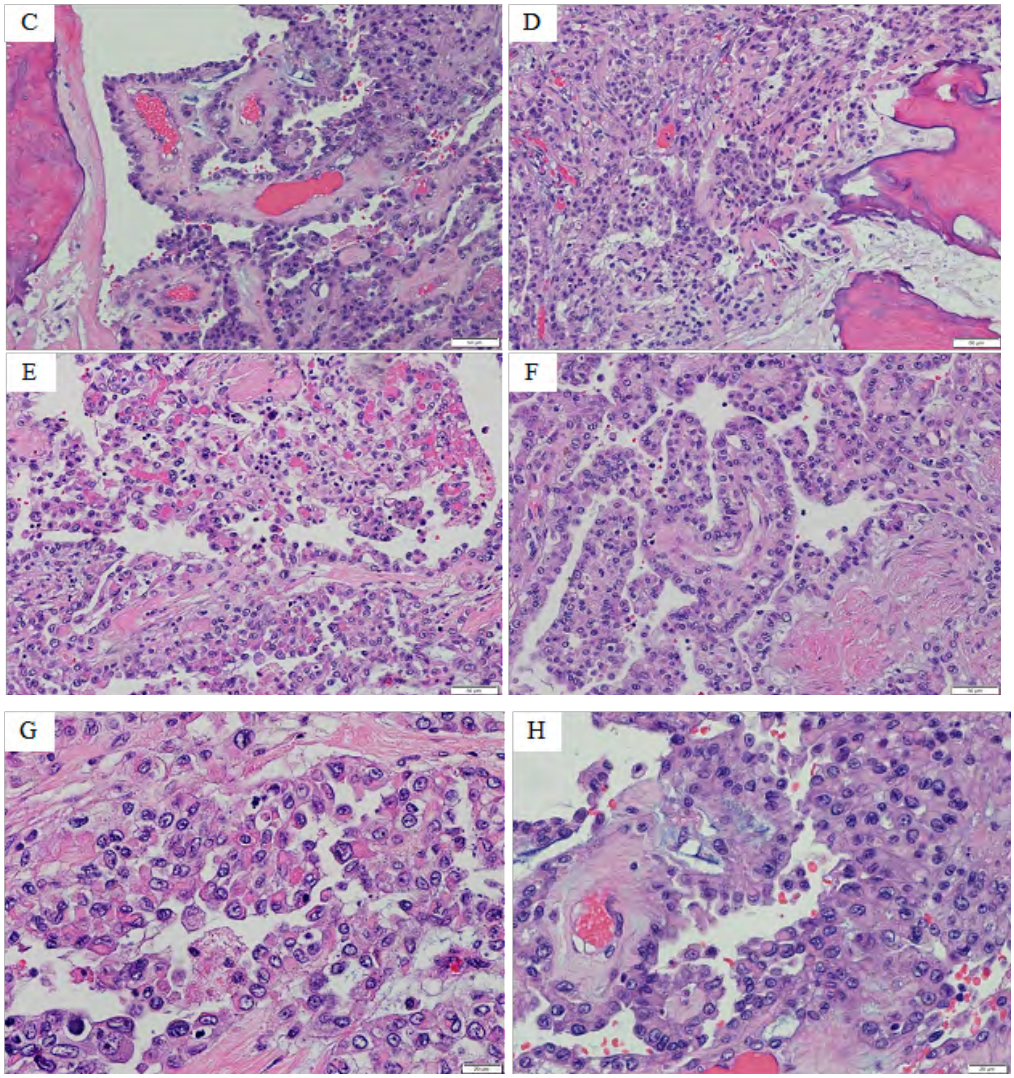
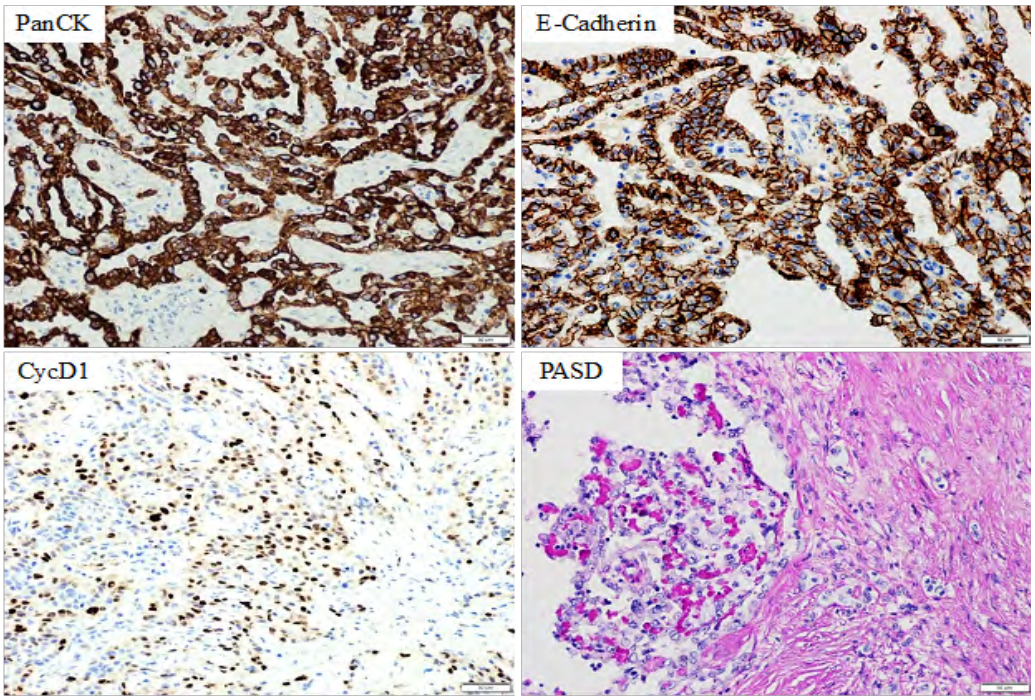


Figure 1: Histology of pancreatic tumor. A and B: Papillary and cystic growth pattern in a myxoid and hyalinized stroma (40x); C and D: Pseudopapillary growth with areas of ossification and hyalinized vascular stroma (200x); E: Intracytoplasmic eosinophilic globules (200x); F: Round to oval nuclei with nuclear irregularity and grooves (200x); G and H: Plasmacytoid/rhabdoid morphology (400x).



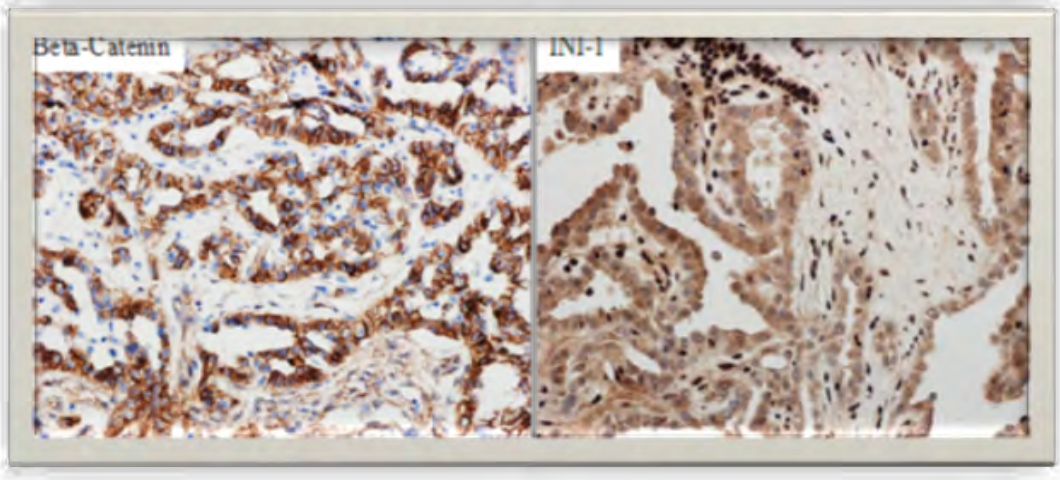


Figure 2: Immunohistochemical and special stains of pancreatic tumor. Tumor cells are positive for PanCK (pancytokeratin), E-Cadherin, and CycD1 (cyclin D1) (patchy); negative for beta-Catenin (membraneous), and INI-1. Intracellular globules are highlighted by PASD. Tumor cells are also negative for CK7, trypsin, progesterone receptor, HepPar1, CK5/6, WT1, D2-40, calretinin, chromogranin and synaptophysin (not shown).

4. Discussion

Here we report a case of SMARCB1/INI-1-deficient pancreatic carcinoma with rhabdoid features. This case is interesting in several aspects: 1) this is a 53-year-old female patient presenting with non-specific clinical symptoms; 2) the pancreatic head/uncinate process mass is an incidentally finding; 3) patient is well after more than one and a half years of the diagnosis; and 4) this mass shows morphological resemblance of solid pseudopapillary neoplasm with areas of rhabdoid/plasmacytoid features. The clinic pathological characteristics of this case implicate that: 1) when tumor mimics pancreatic solid pseudopapillary neoplasm morphologically, but not immunophenotypically (CK7 negative), more generous sampling and searching for plasmacytoid/rhabdoid areas followed by INI-1 study may facilitate further classification of this tumor; and 2) INI-1 deficient tumor with solid pseudopapillary features may represent a subtype of this entity, and have an indolent behavior.

In this current case, although morphologically mimicking solid pseudopapillary neoplasm, immunohistochemical stains do not support such a diagnosis. There are areas demonstrating rhabdoid/plasmacytoid features and further evaluation for SMARCB1/INI-1 expression shows nuclear loss. SMARCB/INI-1 deficiency is reported to be restricted in tumor without KRAS mutation [12,16]. The deficient SMARCB/INI-1 protein activates the downstream Myc signaling pathway of KRAS, leading to a mesenchymal reprogramming in a KRAS-independent manner [19]. In our case, next gene sequencing is pending to further understand the underlying molecular alterations, including KRAS.

To the best of our knowledge, there are 10 cases of pancreatic cancer with rhabdoid features showing SMARCB1/INI-1-deficiency published in the literature [12-18] (Table 1). One case does not have complete clinical characteristic. In the remaining 9 cases, five are female and four are male. The age at diagnosis ranges from 24 to 76. Five lesions are in pancreatic head and four are in body and/or tail, with size ranging 1.9-10 cm. In our case, the patient is a 53-year-old female, has an incidental finding of a 4.2 cm pancreatic head/uncinate mass. An interesting finding is that this tumor is negative for CK7. In the 10 reported cases: 4 are CK7 negative, 2 are positive, and 4 have unknown CK7 status. We speculate that tumors with CK7 negativity may be more likely to be SMARCB1/INI-1 deficient. Furthermore, in our case, the patient is well after more than one and a half years of diagnosis. This is in contrast with a reported case which shows a similar morphology of mimicking solid pseudopapillary neoplasm with a final diagnosis of SMARCB1/INI-1 deficient pancreatic undifferentiated rhabdoid carcinoma [17]. That patient undergoes enucleated surgery of the pancreatic mass and postoperative course is complicated by small bowel ischemia, perforation, intra-abdominal abscess, and upper gastrointestinal bleeding. That patient's dies 3 months later. In contrast, the indolent features of our case are similar to a previously reported case in which the patient receives surgery and adjuvant chemotherapy and shows no recurrent disease [16]. Both cases suggest that although surgery is crucial, adjuvant or chemotherapy following resection of SMARCB1/INI-1 deficient pancreatic tumor may have a positive effect on the overall outcome. However, due to the limited number of cases reported, a definitive conclusion regarding the role of SMARCB1/INI-1 status in predicting the prognosis cannot be made.

Table 1: Summary of SMARCB1 deficient pancreatic carcinoma with rhabdoid features in literature

Case (Ref)	Age/gender	Clinical data	Location	Morphology	CK7	SMARCB1	Treatment	Outcome
1 (13)	68/F	Not available	Body & tail, 10 cm	Rhabdoid	Pos	Loss	Palliative	DOD in 2 weeks
2 (12)	72/M	Not available	Head, 4 cm	Rhabdoid, pseudopapillary gland-like	Neg	Loss	Surgery	DOD post-operation
3 (12)	44/F	Not available	Head, 6 cm	Rhabdoid, angiosarcoma-like	Pos	Loss	Surgery	Not available
4 (12)	76/M	Not available	Head, 5 cm	Rhabdoid	Neg	Loss	Surgery	DOD in 1 month
5 (12)	61/M	Not available	Tail, 5 cm	Rhabdoid, neutrophil-rich, focal glandular	Neg	Loss	Surgery	Not available
6 (18)	35/F	Epigastralgia, backpain, tarry stools, weight loss	Head, 6 cm	Rhabdoid	Neg	Loss	Chemo	DOD in 7 months
7 (15)	Not available	Not available	Not available	Rhabdoid	Not available	Loss	Not available	Not available
8 (14)	67/F	Incidental finding	Body, 1.9 cm	Rhabdoid, solid	Not available	Loss	Chemo	DOD in 6 months
9 (17)	59/F	Abdominal pain, weight loss, nausea, vomiting	Head, 3.1 cm	Rhabdoid, solid pseudopapillary -like	Not available	Loss	Surgery	DOD in 7 months
10 (16)	24/M	Jaundice, itchy skin	Head & body, 7 cm	Rhabdoid, pseudo- adenoid	Not available	Loss	Surgery & Adj	No recurrence *
Current case	53/F	Gastroenteritis, colitis	Uncinate, 3.8 cm	Rhabdoid, pseudopapillary -like	Neg	Loss	Neoadj & Surgery	No recurrence **

Ref: reference; F: female; M: male; Pos: Positive; Neg: Negative; DOD: dead of disease; Chemo: chemotherapy; Adj: adjuvant; Neoadj: neoadjuvant

*: 9 months after operation, the patient was well with no recurrent

**: 2 months post operation (22 months after finding of pancreatic lesion), the patient was well

5. Conclusion

In this article, we report a case of SMARCB1/INI1-deficient pancreatic carcinoma from a 53-year-old female patient who exhibits an indolent clinical course. The neoplasm morphologically resembles but immunophenotypically does not support solid pseudopapillary neoplasm, with rhabdoid/plasmacytoid and clear cell features. We recommend that in cases with indolent clinical behaviors and similar morphologically features, especially CK7 negative, generous sampling and searching for plasmacytoid/rhabdoid features in tumor cells are recommended. Such cases may be warranted further investigation for the SMARCB1/INI-1 status. INI-1 deficient tumor with solid pseudopapillary features may represent a subtype of this entity. Our case also implies that surgery and neoadjuvant treatment may have positive impact for a favorable outcome. However, more studies are needed to better understand the biology, clinical behavior, and outcome of SMARCB1/INI-1 deficient pancreatic carcinoma with rhabdoid features.

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