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Case report

Extended pancreato-duodenectomy coupled with adjuvant chemotherapy for SMARCB1/INI1 deficient pancreatic carcinoma: A case report and literature review

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ABSTRACT

Introduction: SMARCB1/INI1 gene deletion appears to be associated with a rare, malignant and aggressive form of pancreatic carcinoma whose diagnosis is challenging. Our objective is to illustrate that the tumor may masquerade as a duodenal papillary carcinoma, be difficulty to identify on diagnostic imaging and that making an accurate diagnosis may be challenging, however surgical resection may be possible.

Case report: We present a case of a 24-year old male patient presenting with jaundice and itchy skin, elevated TBIL, AST, ALP and CA125. A 2.2 × 1.7 cm pancreatic nodule, later diagnosed as a SMARCB1/INI deficient pancreatic carcinoma was detected on Endoscopic Ultrasound - Fine Needle Aspiration (EUS-FNA). The patient was successfully treated with extended pancreato-duodenectomy coupled with adjuvant chemotherapy, a 7 × 5 × 5 cm tumor resected.

Discussion: SMARCB1/INI deficient pancreatic carcinoma has been reported in couple of other articles. However, unlike other cases, in our case identification and accurate assessment of the tumor was particularly difficulty both on imaging and during operation. Our patient has thus far had a positive outcome with no recurrence.

Conclusion: For rare forms of pancreatic carcinoma, identification and assessment of the tumor size may be challenging on imaging and during operation. However, careful assessment should be performed before ruling out surgical resection. Furthermore, adjuvant chemotherapy may be beneficial to the patient.

1. Introduction

In recent years, with advancements in and access to genetic testing technology and techniques such as next generation sequencing, more literature has focused on understanding genetic involvement in various neoplasms. The SMARCB1 gene is one such component of interest. SMARCB1 is one of the core sub-unit proteins in the SWItch/Sucrose (SWI/SNF) ATP-dependent chromatin remodeling complex. The gene is located at 22q11.2 and is considered a tumor suppressor. SMARCB1 and related proteins is involved in tumor proliferation and progression through a variety of pathways such as the WNT signaling and p16-RB pathways [1,24]. Although the role of SMARCB1 remains largely unknown, it has been reported to play a role in certain neoplasms including esophageal, renal medullary, pleura and pancreatic carcinoma [2,17–23]. Deficiency of SMARCB1/INI1 appears to be generally associated atypical rhabdoid/teratoid neoplasms. SMARCB1 protein depletion activates the Myc network that has a downstream effect in the extinction of oncogenic Kras signaling and emergency of Kras-independent escaper populations [3]. Agaimy et al. have suggested that loss SMARCB1 expression is restricted to anaplastic monomorphic rhabdoid carcinomas rather than the totality of rhabdoid carcinoma [22].

2. Case report

A 24-year old male patient with a long history of alcohol consumption presented with jaundice for three weeks and itchy skin for one. Laboratory tests revealed elevated TBIL, AST and ALP (479.7 μmol/L, 54 U/L and 348 U/L respectively). Hs-CRP and PT were normal. Both HBV and HIV were negative. CA125 was elevated (63.5 U/mL) while CA19–9 and CEA were both normal, IgG4 was negative. MRCP (Fig. 1) showed a dilated pancreatic duct, dilated hepatic ducts and biliary tree.

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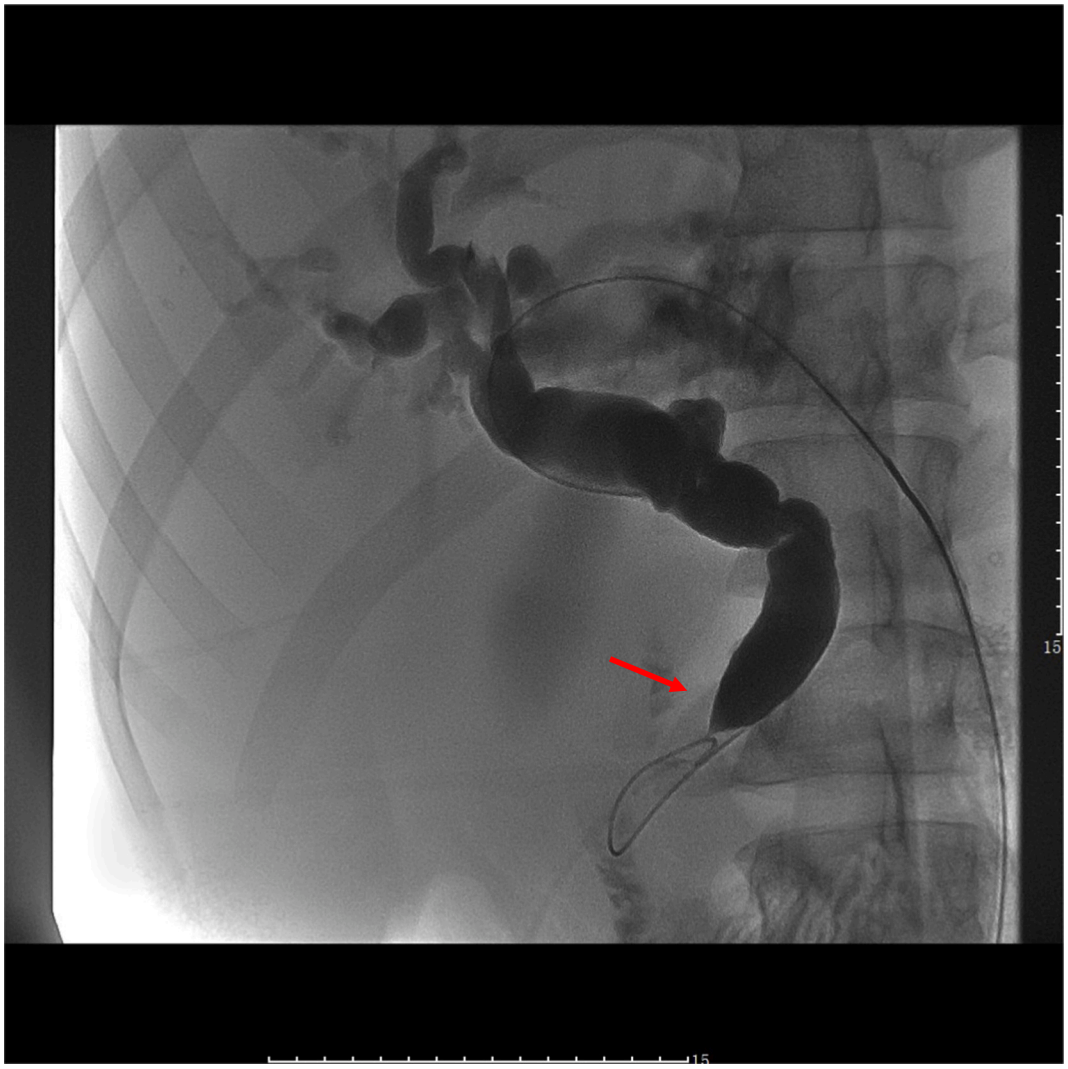

Fig. 1. PTCD imaging showing the common bile duct (CBD) leading into the ampulla of Vater was compressed and obstructed like a beak.

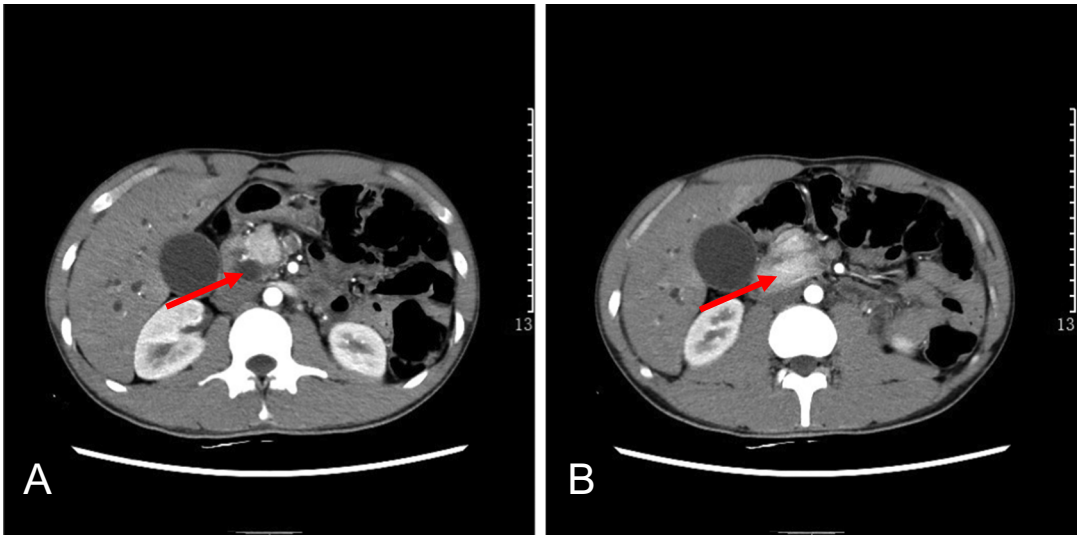

Fig. 2. Axial Computed Tomography showing A: dilated common bile duct. B: Enlarged pancreatic head with no signs of neoplasm.

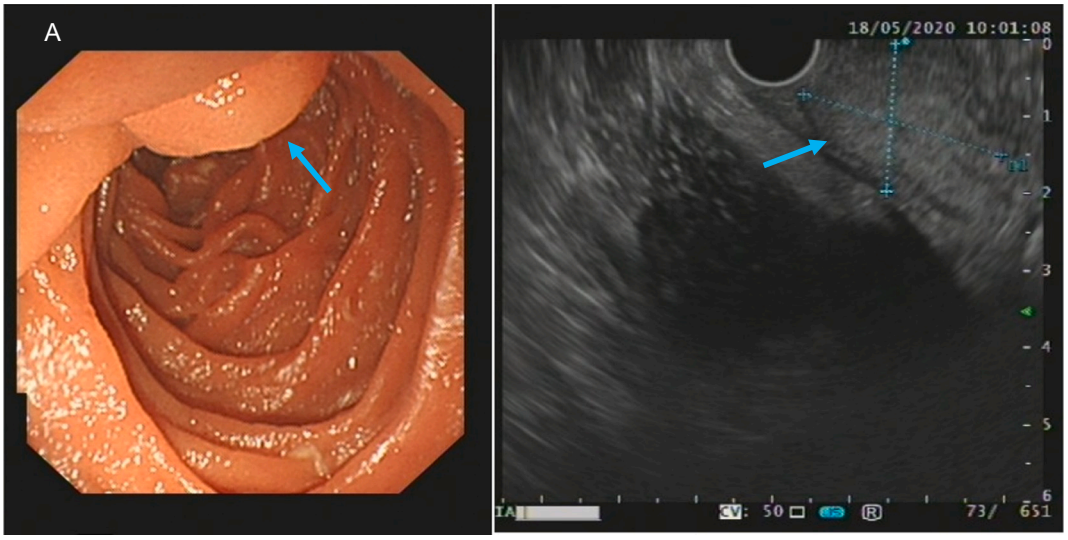

Fig. 3. (a) Endoscopic Retrograde Cholangiopancreatography showing a 3 × 4 cm mass at the location of the major duodenal papilla. (b) A 2.2 × 1.7 cm nodule identified on Endoscopic Ultrasound in the head of the pancreas.

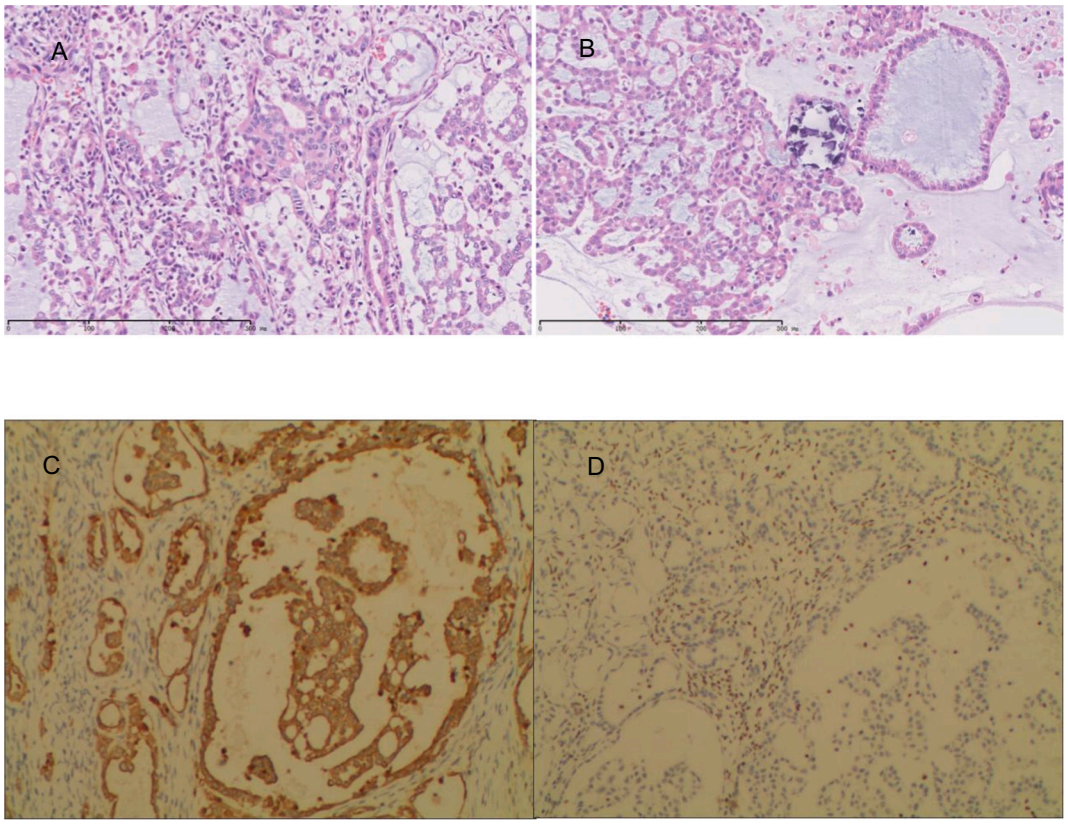

Fig. 4. Pancreatic carcinoma. A: Microcapsules or pseudoadenoids growth pattern, myxoid background, without fibrous stroma (Hematoxylin and eosin stain, HE). B: Focal calcified (Hematoxylin and eosin stain, HE). C, D: Immunohistochemistry stains of CKpan (C) (200×) and SMARCB1/INI1 (D) (200×).

The common bile duct (CBD) leading into the ampulla of Vater was compressed and obstructed. The descending portion of the duodenum was similarly compressed and narrow. On CT imaging, the gallbladder was enlarged, the liver was normal and no signs of duodenal or pancreatic neoplasm were apparent. Findings were consistent with chronic pancreatitis (Fig. 2). ERCP performed at the referring hospital showed a duodenal mass and a diagnosis of duodenal papillary carcinoma and obstructive jaundice was made (Fig. 3). Endoscopic Ultrasound - Fine Needle Aspiration (EUS-FNA) was performed and a 2.2 × 1.7 cm nodule identified in the head of the pancreas. The main pancreatic duct dilated 0.6 cm. (MRCP followed by CT, ERCP and finally EUS). Immunohistochemistry was positive for Bull-2, cyclinD1, Ki-67 and CK19. CEA was negative (Fig. 4). The patient was diagnosed with pancreatic carcinoma.

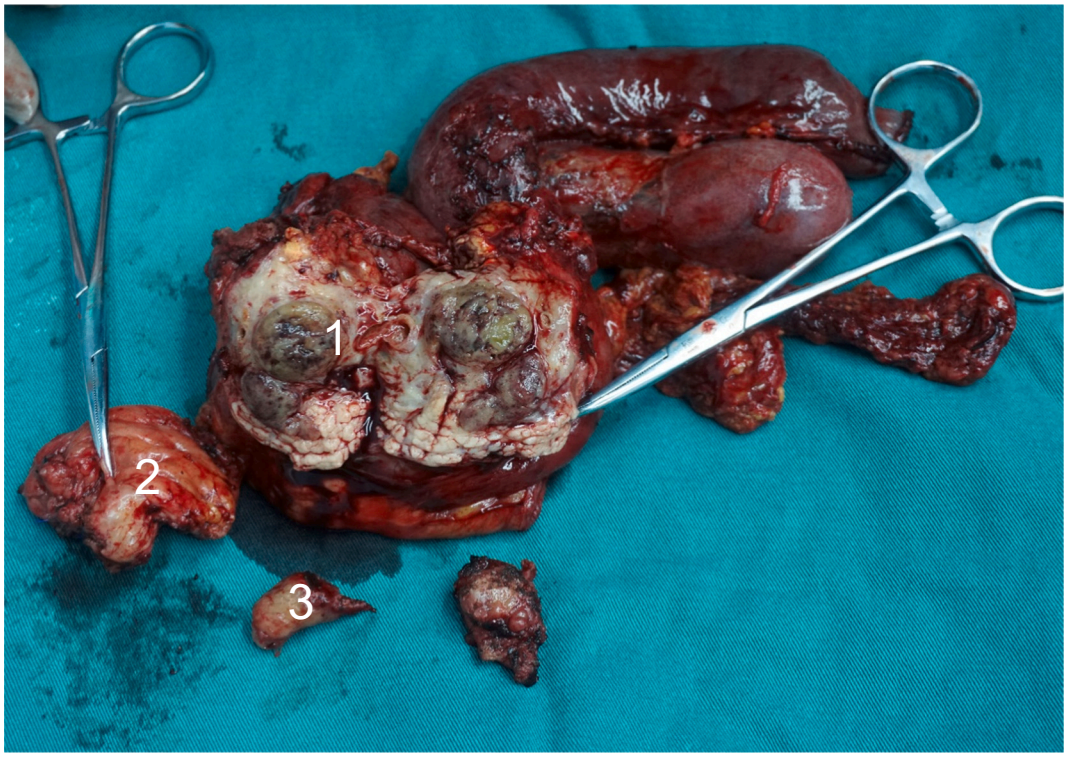

Fig. 5. Resected tumor in head and body of the pancreas. (1) Tumor in the head of the pancreas (2) Resected portion of the body of the pancreas to achieve negative margins (3) embolus from the main pancreatic duct.

3. Treatment

Stent placement via ERCP was attempted with no success. The patent underwent a Percutaneous Transhepatic Bile Duct Drainage (PTCD) procedure to drain the bile and lower the TBIL. TBIL was lowered to 140.6 μmol/L in the subsequent seven days. Following a multidisciplinary team consultation, extended pancreato-duodenectomy (Whipple procedure with child reconstruction) was successfully performed for the patient. During surgery, a large 7 × 5 × 5 cm tumor was found in the head of the pancreas extending to most of the body and inside the pancreatic duct with involvement of 12 out the 20 regional lymph nodes (Fig. 5). Radical resection was performed to achieve negative CBD and pancreas margins. During the operation, identification of the tumor margin was difficult (the margin of the tumor could not be determined by touch) and three attempts were made before negative margins could be achieved. A little over two thirds of the pancreas was resected. Postoperative gemcitabine based adjuvant chemotherapy combined with capecitabine was recommended to and accepted by the patient. Microscopic examination revealed a relatively rare morphology inconsistent with regular adenocarcinoma. Pathological diagnosis was still inconclusive and Next Generation Sequencing (NGS) was performed. NGS identified SMARCB1/INI1 gene deletion without KRAS mutation.

At 9 months post-operation, the patient was in good health with no signs of recurrence. We continue to assess the effectiveness of gemcitabine-capecitabine regimen as choice for adjuvant chemotherapy.

4. Discussion

Patients with pancreatic carcinoma present with non-specific symptoms that may include epigastric and upper quadrant pain, back pain, weight loss, vomiting, diarrhea and in some cases jaundice [4,5]. Jaundice is more often than not a sign of advanced disease. Lipase maybe elevated in about 50% of cases and of these, up to 10% may develop subcutaneous nodules [6]. Patients who present with Schmidt's triad (subcutaneous fat necrosis, polyarthritis and eosinophilia) are associated with a poor prognosis [7]. At the time of identification, rare forms of pancreatic carcinoma are large with a 10 cm diameter, tumors 2 cm or less are rare [4]. Obstruction of the common bile duct (CBD) and jaundice rarely occur (in 12% of cases) and the tumor compresses the neighboring structures rather than infiltrating them. The tumor mass often presents as a solid encapsulated mass that are generally malignant though a few maybe benign [4,8].

While previous papers have detailed the aggressiveness and relatively poor prognosis associated with SMARCB1 deficient pancreatic carcinoma as predominant characteristics of this form of pancreatic neoplasm; our case first collaborates findings by Hua et al. [22] of a pseudo-duodenal papillary (mimicking) carcinoma. Furthermore, we highlight the possibility of the pancreatic tumor not being easily evident on both computed tomography and magnetic resonance imaging. In such situations, where a pancreatic mass cannot be rules out, EUS-FNA may be a useful diagnostic tool.

Pancreatic carcinoma diagnosis utilizes both imaging and biochemical examination. Usually, computed tomography (CT) and magnetic resonance imaging (MRI) are first line and are often adequate to identify the tumor and confirmation of the diagnosis made by biopsy [4], however in some cases, identification via CT and MRI may be difficult as was the case for this patient. Initial imaging by ERCP was consistent with duodenal papillary carcinoma however CT imaging showed no evidence of a duodenal mass. In fact, on CT imaging, only evidence of chronic pancreatitis with homogeneous attenuation was evident. Despite a lack of evidence of a mass on CT, presence of a pancreatic mass should not be ruled out. Scheduling an EUS-FNA and immunohistochemistry can prove helpful.

With EUS-FNA, we were able to identify a small 2.2 × 1.7 cm nodule in the head the pancreas; however, accurate assessment of the size of the tumor may not be possible prior to operation. While the nodule identified during EUS-FNA was small, the actual size of the mass was much larger (7 × 5 × 5 cm). The first two attempts at resecting the mass transected the tumor. A third attempt was made closer to the tail to

Table 1
SMARCB1/INI1 deficient pancreatic carcinoma cases in literature.

Reference	Histology	Location	Age/ gender	KRas mutation	Treatment	Outcome
Ohike et al. [17]	Rhabdoid, diffuse	Head, 6 cm	35 F	Wild type	Chemo	D in 7 mo
Lehrke et al. [18]	Rhabdoid	NR	NR	NR	NR	NR
Tahara et al. [19]	Rhabdoid, solid	Body 1.9 cm	67 F	Wild type	Chemo	D in 6 mo
Sano et al. [20] Yinan et al. [21]	Rhabdoid	Body & tail 10 cm	68 F	NR	Palliative	D in 2 wk
Agaimy et al. [22]	Rhabdoid, angiosarcoma-like	Head, 6 cm	44 F	Positive	Surgery	NR
Agaimy et al. [22]	Rhabdoid	Head, 5 cm	76 M	Wild type	Surgery	D in 1 mo
Agaimy et al. [22]	Rhabdoid, pseudopapillary acantholytic gland-like	Head 4 cm	72 M	Wild type	Surgery	D post-operation
Agaimy et al. [22]	Rhabdoid, prominent neutrophils, focal glandular	Tail 5 cm	61 M	Wild type	Surgery	NR
Joseph et al.[a]	Rhabdoid, microcapsules or pseudoadenoid growth pattern	Head & body, 7 cm	24 M	None	Surgery, adjuvant chemotherapy	No recurrence

M: Male, F: Female, NR: Not reported, D: succumbed to disease. Chemo: Chemotherapy, mo: Month(s), wk: Week(s).
[a] Our case.

achieve R0 resection. The consistence of the tumor was relatively indistinguishable from that nearby normal pancreatic tissue to the touch; this may be due to the atypical nature of SMARCB1 deficiency related neoplasms.

Some reports have indicated a relationship between elevated Alpha Fetoprotein (AFP) and various types of pancreatic carcinoma [9–11]; however, no consensus exists whether it is a signi tumormarker in the case of pACC and rhabdoid pancreatic carcinoma. Elevation of Cancer Embryonic Antigen (CEA) as well as Carbohydrate Antigen (CA) 19-9 may also vary on a case by case basis. In this case, AFP, CEA and CA19-9 were normal while CA125 was elevated. The common histopathological presentation of SMARCB1/INI1 deficient pancreatic carcinomas is their undifferentiated and anaplastic nature and abundance of rhabdoid cells [13,14]. Rhabdoid cells are characteristically large, rich in eosinophilic paranuclear cytoplasmic filamentous inclusions and their nucleus is often displaced to the cell's periphery. The neoplasm has a solid consistence, usually large, malignant and aggressive. In most of the cases reported (Table 1), the loss of SMARCB1 was associated with KRAS mutation predominantly the wild type. However, in our case no KRAS mutation was present. Association between SMARCB1 mutations and pancreatic ductal adenocarcinoma as well as rhabdoid pancreatic carcinoma has also been reported [2,15,16,22] as was the case with this patient.

Surgical resection remains the only curative approach for patients with pancreatic carcinoma, therefore, it is important to properly assess and determine the size and resectability of the tumor. In the 10 cases we know of, surgical resection was performed in 6 (Table 1) and 6 of the 10 patients died within about half year after diagnosis with the outcome not stated in 2. Since most pancreatic tumors are large at the time of identification, most resectable tumors are often not resected [4,12]. In the case of unresectable tumors, chemotherapy can be used as first line treatment, if the tumor shrinks after chemotherapy, in absence of contraindications, adjuvant surgical resection may be performed. This article has been prepared in accordance to SCARE Guidelines 2020 [25].

5. Conclusion

For rare forms of pancreatic carcinoma, SMARCB1/INI1 Deficient pancreatic carcinoma included, identification and assessment of the tumor size may be challenging on imaging and may not be possible prior to surgery. Therefore, since resection is the only viable curative approach, careful evaluation before excluding surgery is crucial. Furthermore, adjuvant chemotherapy following resection of SMARCB1 deficient pancreatic carcinoma may be beneficial to patient prognosis.

Ethical approval

This is case report exempt from ethical approval no experimentation was conducted.

CRediT authorship contribution statement

Joseph Mugaanyi: Conception, and design. Data acquisition, analysis and interpretation, Drafting and revising the work.

Changjiang Lu: Conception, and design. Data acquisition, analysis and interpretation, revising the work & final approval

Caide Lu: Revising the work, Final approval, agree to be accountable for all aspects of the work.

Chunnian Wang: Data acquisition, analysis and interpretation.

Guarantor

Caide Lu, PhD, lucaide@nbu.edu.cn (Corresponding Author)
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Consent

Consent was obtained from the patient to report this case. Signed informed consent form has been attached.

Declaration of competing interest

The authors have no competing interests to declare.

References

[1] R.M.M. Ferreira, R. Sancho, H.A. Messal, et al., Duct- and acinar-derived pancreatic ductal adenocarcinomas show distinct tumor progression and marker expression, Cell Rep. 21 (4) (2017) 966–978, https://doi.org/10.1016/j.celrep.2017.09.093.
[2] Kenichi Kohashi, Yoshinao Oda, Oncogenic roles of SMARCB1/INI1 and its deficient tumors, Cancer Sci. 108 (4) (2017) 547–552.
[3] G. Genovese, A. Carugo, J. Tepper, et al., Synthetic vulnerabilities of mesenchymal subpopulations in pancreatic cancer, Nature 542 (2017) 362–366, https://doi.org/10.1038/nature21064.
[4] P. Chaudhary, Acinar cell carcinoma of the pancreas: a literature review and update, Indian J. Surg. 77 (3) (2015) 226–231, https://doi.org/10.1007/s12262-014-1049-y.
[5] G. Butturini, M. Pisano, A. Scarpa, et al., Aggressive approach to acinar cell carcinoma of the pancreas: a single-institution experience and a literature review, Langenbeck's Arch. Surg. 396 (2011) 363–369, https://doi.org/10.1007/s00423-010-0706-2.
[6] J.Y. Kim, J.A. Brosnan-Cashman, J. Kim, et al., Pancreatic acinar cell carcinomas and mixed acinar-neuroendocrine carcinomas are more clinically aggressive than grade 1 pancreatic neuroendocrine tumours, Pathology. 52 (3) (2020) 336–347, https://doi.org/10.1016/j.pathol.2020.01.437.

[7] A. Al-Hader, R.N. Al-Rohil, H. Han, D. Von Hoff, Pancreatic acinar cell carcinoma: a review on molecular profiling of patient tumors, World J. Gastroenterol. 23 (45) (2017) 7945–7951, https://doi.org/10.3748/wjg.v23.i45.7945.
[8] E.S. Glazer, K.G. Neill, J.M. Frakes, et al., Systematic review and case series report of acinar cell carcinoma of the pancreas, Cancer Control 23 (4) (2016) 446–454, https://doi.org/10.1177/107327481602300417.
[9] Y.C. Lin, P.H. Lee, Y.T. Yao, J.K. Hsiao, J.C. Sheu, C.H. Chen, Alpha-fetoprotein-producing pancreatic acinar cell carcinoma, J. Formos. Med. Assoc. 106 (8) (2007) 669–672, https://doi.org/10.1016/s0929-6646(08)60025-X.
[10] C.Y. Kim, S.H. Lee, H.M. Jeon, H.K. Kim, C.M. Kang, W.J. Lee, AFP-producing acinar cell carcinoma treated by pancreaticoduodenectomy in a patient with a previous radical subtotal gastrectomy by gastric cancer, Korean J. Hepatobiliary Pancreat. Surg. 18 (1) (2014) 33–37, https://doi.org/10.14701/kjhbps.2014.18.1.33.
[11] S. La Rosa, F. Sessa, C. Capella, Acinar cell carcinoma of the pancreas: overview of clinicopathologic features and insights into the molecular pathology, Front Med (Lausanne) 2 (41) (2015), https://doi.org/10.3389/fmed/2015.00041 (Published 2015 Jun 15).
[12] K. Landa, K. Freischlag, D.P. Nussbaum, L.M. Youngwirth, D.G. Blazer 3rd., Underutilization of surgical resection in patients with pancreatic acinar cell carcinoma, HPB (Oxford) 21 (6) (2019) 687–694, https://doi.org/10.1016/j.hpb.2018.10.014.
[13] M.R. Wick, J.H. Ritter, L.P. Dehner, Malignant rhabdoid tumors: a clinicopathologic review and conceptual discussion, Semin. Diagn. Pathol. 12 (1995) 233–248.
[14] J.C. Fanburg-Smith, M. Hengge, U.R. Hengge, et al., Extrarenal rhabdoid tumors of soft tissue: a clinicopathologic and immunohistochemical study of 18 cases, Ann. Diagn. Pathol. 2 (1998) 351–362.
[15] Protein turnover provides pancreatic cancer target, Cancer Discov. 7 (4) (2017) 345–346, https://doi.org/10.1158/2159-8290.CD-NB2017-027.
[16] M. Numata, S. Morinaga, T. Watanabe, H. Tamagawa, N. Yamamoto, M. Shiozawa, Y. Nakamura, Y. Kameda, S. Okawa, Y. Rino, M. Akaike, M. Masuda, Y. Miyagi, The clinical significance of SWI/SNF complex in pancreatic cancer, Int. J. Oncol. 42 (2) (2013 Feb) 403–410, https://doi.org/10.3892/ijo.2012.1723 (Epub 2012 Nov 30. PMID: 23229642; PMCID: PMC3583622).
[17] N. Ohike, R. Suzuki, T. Isobe, T. Norose, A. Shiokawa, T. Kunimura, K. Kohashi, Y. Oda, A case of pancreatic undifferentiated carcinoma mimicking proximal-type epithelioid sarcoma, J. Pancreas 17 (2016) 75–80.
[18] H.D. Lehrke, R.P. Graham, R.R. McWilliams, D.M. Lam-Himlin, T.C. Smyrk, S. Jenkins, H. Dong, L. Zhang, Undifferentiated pancreatic carcinomas display enrichment for frequency and extent of PD-L1 expression by tumor cells, Am. J. Clin. Pathol. 148 (2017) 441–449 (PMID: 29069274), https://doi.org/10.1093/ajcp/aqx092.
[19] S. Tahara, M. Takeyari, E. Morii, Usefulness of cytological analysis in the diagnosis of pancreatic undifferentiated rhabdoid carcinoma, Pathol. Int. 68 (2018) 56–58 (PMID: 29235210), https://doi.org/10.1111/pin.12616.
[20] M. Sano, T. Homma, E. Hayashi, H. Noda, Y. Amano, R. Tsujimura, T. Yamada, B. Quattrochi, N. Nemoto, Clinicopathological characteristics of anaplastic carcinoma of the pancreas with rhabdoid features, Virchows Arch. 465 (2014) 531–538 (PMID: 25031015), https://doi.org/10.1007/s00428-014-1631-5.
[21] Y. Hua, P. Soni, D. Larsen, R. Zreik, B. Leng, D. Rampisela, SMARCB1/INI1-deficient pancreatic undifferentiated rhabdoid carcinoma mimicking solid pseudopapillary neoplasm: a case report and review of the literature, World J. Gastroenterol. 26 (36) (2020 Sep 28) 5520–5526, https://doi.org/10.3748/wjg.v26.i36.5520 (PMID: 33024402; PMCID: PMC7520612).
[22] A. Agaimy, F. Haller, J. Frohnauer, et al., Pancreatic undifferentiated rhabdoid carcinoma: KRAS alterations and SMARCB1 expression status define two subtypes, Mod. Pathol. 28 (2) (2015) 248–260, https://doi.org/10.1038/modpathol.2014.100.
[23] K. Yoshida, Y. Fujiwara, Y. Goto, et al., The first case of SMARCB1 (INI1) - deficient squamous cell carcinoma of the pleura: a case report, BMC Cancer 18 (2018) 398, https://doi.org/10.1186/s12885-018-4321-x.
[24] I. Versteege, N. Sevenet, J. Lange, M.F. Rousseau-Merck, P. Ambros, R. Handgretinger, A. Aurias, O. Delattre, Truncating mutations of hSNF5/INI1 in aggressive paediatric cancer, Nature. 394 (6689) (1998) 203–206.
[25] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, for the SCARE Group, The SCARE 2020 Guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. (2020) 84.