

Jaundice as an Initial Manifestation of Pancreatic Dedifferentiated Liposarcoma

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ABSTRACT

Primary mesenchymal tumors of the pancreas are extremely rare, accounting for 0.3%–0.6% of all pancreatic tumors. Of these, localized liposarcoma of the pancreas constitutes an even rarer form of pancreatic tumors. The clinical presentation reported in almost all cases is abdominal pain and distention, with the body of the pancreas being the most common site of tumor occurrence. We encountered the case of a 77-year-old male presenting with jaundice and upper abdominal pain. Computed tomography revealed a tumor in the head of the pancreas and indicated the dilatation of the main pancreatic duct, similar to invasive ductal carcinoma of the pancreas. We report the findings of this challenging case, with the clinical diagnosis between invasive ductal carcinoma and dedifferentiated liposarcoma; histological findings indicated invasive ductal carcinoma-like growth pattern, which was the dedifferentiated component that invaded the main pancreatic duct and adjacent lesion. The patient did not receive any adjuvant therapy and reported local recurrence after 5 years.

Keywords: Pancreas, Dedifferentiated liposarcoma, Jaundice, Outcome

CASE PRESENTATION

A 77-year-old male was referred to our hospital due to jaundice and upper abdominal pain. His medical history comprised type 2 diabetes mellitus treated with medication (HbA1c, 6.1%). Laboratory examination revealed elevated biliary enzyme levels (γ -GTP, 659 IU/L; ALP, 1724 IU/L; T-bil, 2.0 mg/dL) and slightly elevated CA19-9 levels (45 U/mL). However, the levels of other tumor markers, such as CEA (1.3 ng/mL), DUPAN-2 (<25 U/mL), and Span-1 (18.7 U/mL) were in the normal range. Computed tomography revealed a tumor of approximately 30 mm diameter in the head of the pancreas, with dilatation of the main pancreatic duct of up to 7 mm (**Figure 1A and 1B**). However, there were no signs of extra-pancreatic extension and distant metastasis. Although these findings were not typical of an invasive ductal carcinoma, we suspected malignancy and thus performed pancreaticoduodenectomy. Macroscopic evaluation revealed a grayish white nodular solid tumor (maximum size, 22 mm) occupying the head of the pancreas and exhibiting an expansive growth with common bile duct stenosis. The tumorous and non-tumorous lesions could be clearly distinguished (**Figure 2A and 2B**).

Furthermore, microscopic examination revealed predominantly fusiform tumor cells, with scant cytoplasm and atypical and hyperchromatic nuclei (**Figure 3B**); mitotic

figures were occasionally encountered (3/10 HPF). In addition, the tumor was observed as sticking out of the main pancreatic duct (**Figure 3A**). The following indicated dilation in the main pancreatic duct. The adjacent tissue of the spindle tumor lesion exhibited a variation in the size of adipocytes, including atypical stromal cells (**Figure 3C and D**) and the border region between spindle tumor and adipose tissue was relatively clear. We performed immune histochemical staining of the tumor specimen to facilitate a definitive diagnosis; it demonstrated that spindle cells were positive for vimentin and nuclear positive for MDM2, CDK4, and p16 (**Figure 4A-4C**). In addition, the Ki-67 index was 5%, and atypical stromal cells in the adjacent adipose tissue demonstrated similar immunohistochemical

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reactivity (nuclear positive for MDM2, CDK4, and p16) (Figure 4D–F). However, spindle tumor cells and atypical stromal cells exhibited no reactivity for cytokeratin, CD34,

α -SMA, BCL-6, and STAT-6. Furthermore, we confirmed the *MDM2* gene amplification using fluorescence in situ hybridization (FISH) (Figure 4C, inset).

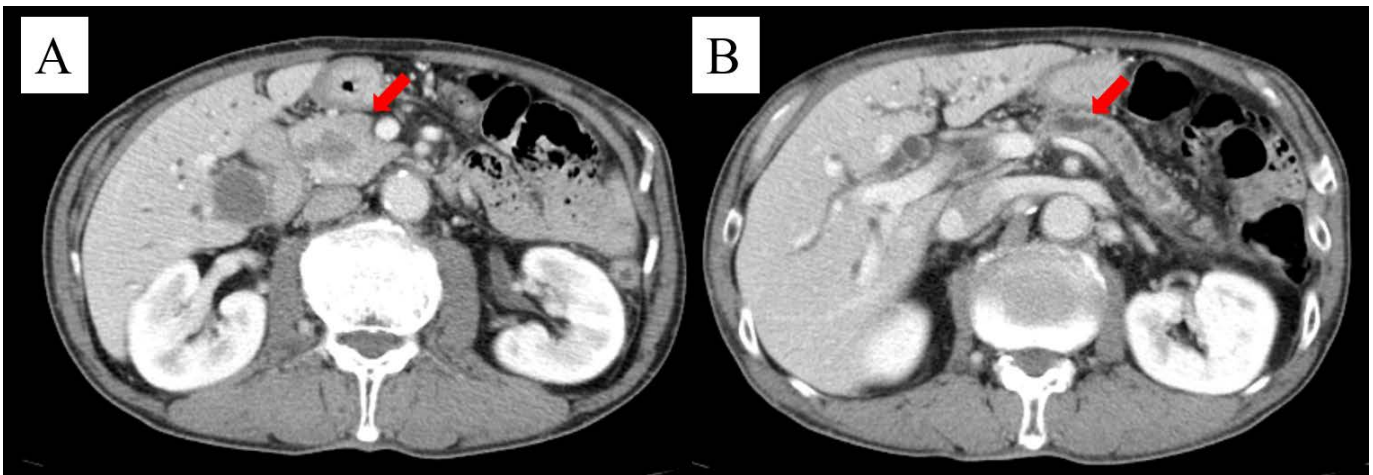


Figure 1. Enhanced abdominal computed tomography showing the primary tumor in the head of the pancreas (A). Dilatation of the main pancreatic duct (B).

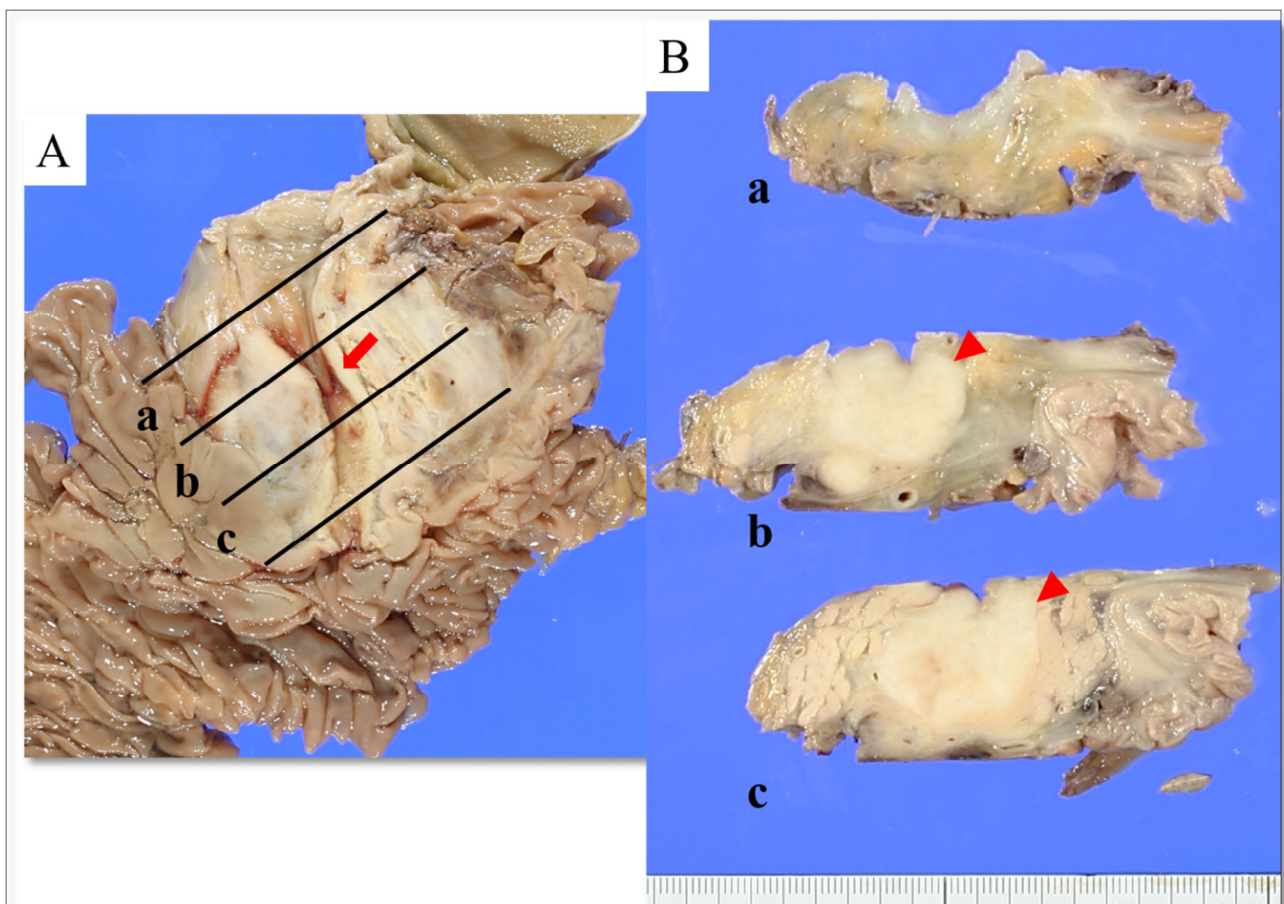


Figure 2. Macroscopically, a grayish white tumor showing proliferation at the pancreatic head (arrowhead) and displacing the common bile duct (arrow) (A and B).

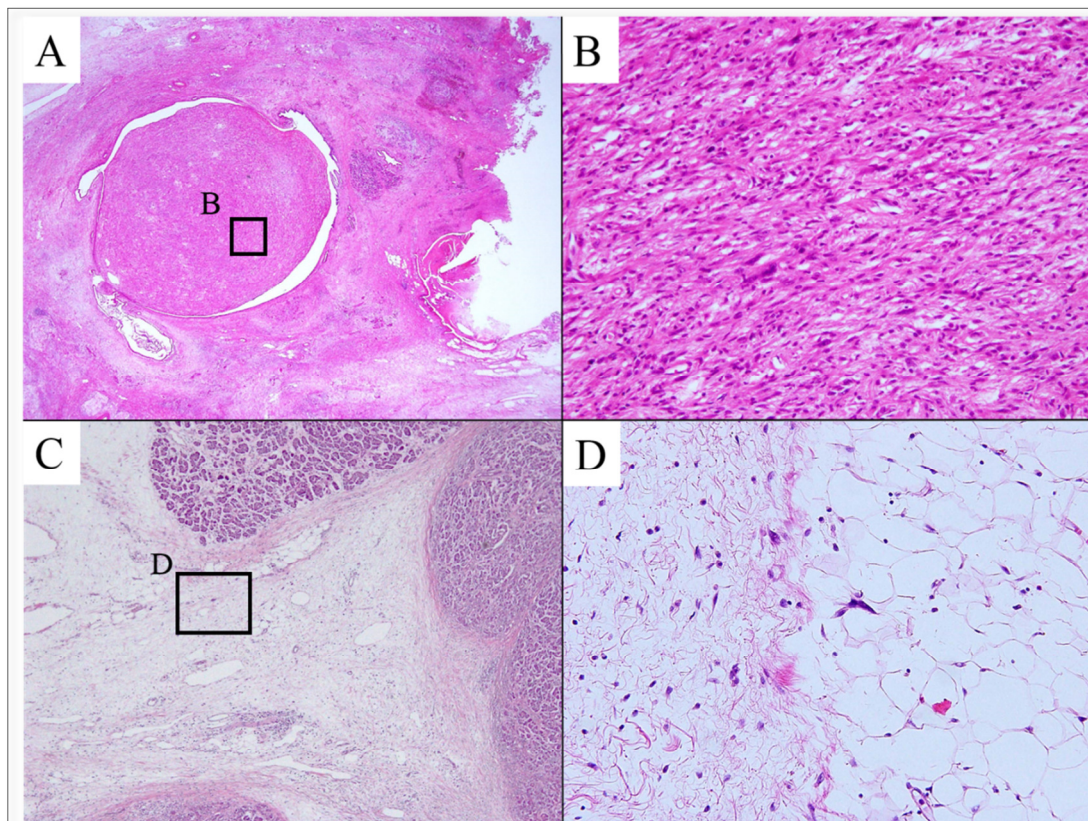


Figure 3. The tumor protruding the main pancreatic duct (A). The tumor cells showing spindle atypical and hyperchromatic nuclei (B). The adjacent tissue of the spindle tumor lesion (C) and apical stromal cells existing in the adipose tissue (D).

The patient's postoperative recovery was uneventful, and he was eventually discharged. The patient did not receive any adjuvant therapy or radiotherapy. However, after postoperative 5 years, the patient experienced a local recurrence, and 6 months later, he died because of pneumonia, which was not related to the primary tumor.

DISCUSSION

Based on the observation of this case, we determined the following two findings: (a) dedifferentiated liposarcomas proliferates in the head of the pancreas; and (b) tumors' invasion into the common bile duct and main pancreatic duct causes jaundice. The following symptoms suggested invasive ductal carcinoma of the pancreas.

First, dedifferentiated liposarcoma was present in the pancreatic head. Reportedly, non-epithelial tumors of the mesenchymal origin are sporadic, accounting for 0.3%–0.6% of all pancreatic tumors [1,6,7]. Of these, little has been reported about primary liposarcoma. To the best of our knowledge, only five cases have been reported in the English literature to date [1-5]. Apparently, the diagnosis of liposarcoma in the pancreas is challenging, because spindle cell tumors of the pancreas are often misdiagnosed as malignant fibrous tumors, and some liposarcomas are

dedifferentiated. The pancreas is a retroperitoneum organ, which is most susceptible to the occurrence of liposarcoma. In addition, the most common pattern of dedifferentiated areas comprises high-grade pleomorphic MFH of storiform fibroblastic MFH [8,9]. Immunohistochemical analysis (MDM2 and CDK4) and genomic hybridization diagnose retroperitoneal sarcoma as dedifferentiated liposarcoma, although the initial diagnosis is MFH (20 of 25 cases) [10]. In our case, the presence of spindle cells comprising an atypical, hyperchromatic nuclei in the pancreatic head resembled MFH; however, the detection of atypical stromal cells in the adipose tissue adjacent to the spindle tumor region ruled out MFH possibility. Immunohistochemical analysis revealed that both stromal cells and spindle cells were positive for MDM2 and CDK4. Furthermore, the *MDM2* gene amplification was confirmed using FISH. Based on these findings, the patient was diagnosed with dedifferentiated liposarcoma. Another problem hindering the definitive diagnosis of dedifferentiated liposarcoma is its origin. Although some mesenchymal tumors primarily occur in the pancreas, most are extrahepatic lesions that have invaded the pancreas. It is a possibility that can never be denied while assessing patients such as our case. In our case, both computed tomography and histological analysis determined that the primary tumor mass occupied the

pancreatic head, and almost all atypical stromal cells in the adipose tissue existed within the pancreas. Although the retroperitoneal surgical margin of our patient's tumor was positive, the positive lesion was the adipose tissue with

atypical stromal cells that occupied a small area. Hence, the definitive diagnosis of our case was primary dedifferentiated liposarcoma of the pancreas.

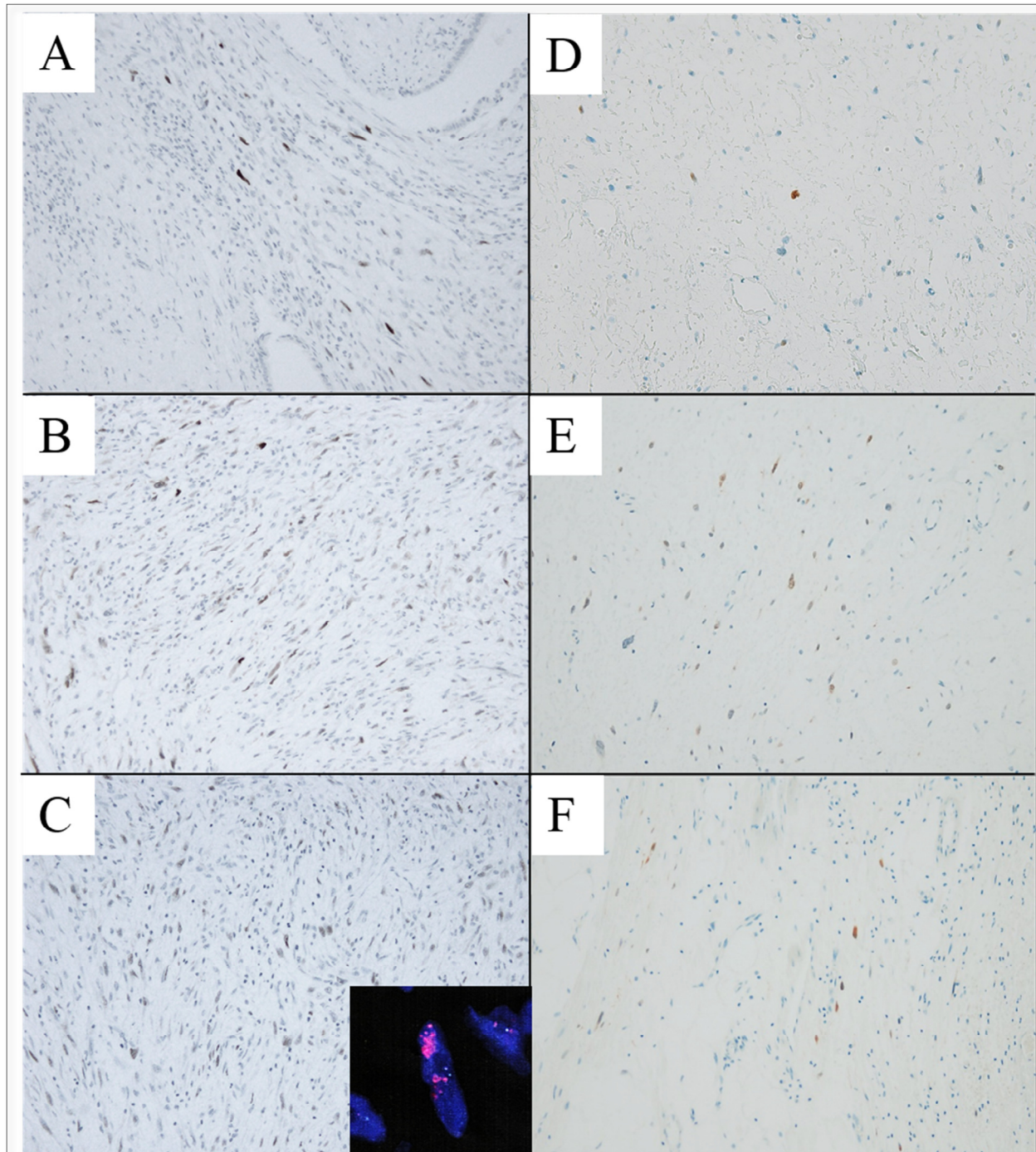


Figure 4. Immunohistochemistry showing partially positive results for MDM2 (A and D), CDK4 (B and E), and p16 (C and F). FISH analysis confirmed the *MDM2* gene amplification (orange signals) in the apical cell (C, inset). Dedifferentiated liposarcoma component (A–C). Well-differentiated liposarcoma component (D–F).

Second, this case presented mass formation in the main pancreatic head and its displacement to the common bile duct, resulting in jaundice. While previous reports have mentioned the clinical presentation of abdominal distention and abdominal pain, this case is the first to report the clinical presentation of jaundice in pancreatic liposarcoma (**Table 1**); the tumor site could be held accountable for this finding. Of the six cases reported to date, including our case, the pancreatic body was the main tumor site in four cases and head and neck in the remaining two. As the pancreatic body mass did not displace the common bile duct and did not indicate jaundice, the expansive growth of the mass revealed

symptoms of abdominal discomfort. The histological subtypes, assessing whether liposarcomas are dedifferentiated, pleomorphic, or myxoid, are variable. Our case experienced a local recurrence after 5 years. The behavior of the liposarcoma affected its subtype such that the dedifferentiated component was more likely to experience local recurrence and metastasize. Notably, the most crucial factor affecting the prognosis is complete resection. Our case had a dedifferentiated component, and a small amount of surgical margin was positive in the well-differentiated liposarcoma component, suggesting the possibility of local recurrence.

Table 1. Pathological features and outcome of pancreatic liposarcoma in case reports

Author	Age/Sex	Chief complaint	Tumor site	Size	Subtype	Outcome
Elliott, et al	59/F	Abdominal distention	Body	16 cm	Pleomorphic	No recurrence (6 years)
Dodo, et al	76/M	Abdominal pain	Body	9 cm	Well-differentiated with dedifferentiated component	No recurrence (26 months)
Kuramoto, et al	24/M	Abdominal distention	Body	25 cm	Mixed	Recurrence (44 months)
Kim, et al	78/F	Asymptomatic	Body	N. A	Well-differentiated	N.A
Machado, et al	42/M	Abdominal pain	Head	6.8 cm	Dedifferentiated	No recurrence (5 years)
Present case	77/M	Jaundice Abdominal pain	Head	2.2 cm	Well-differentiated with dedifferentiated component	Recurrence (5 years)

N.A, not available.

In conclusion, our case presents a sporadic case of pancreatic liposarcoma, wherein the dedifferentiated component invaded the common bile duct and main pancreatic duct, resulting in jaundice. The findings of this case suggest that complete surgical resection might be a potential clinical care option for patients with pancreatic tumors. Hence, in our opinion, the differential diagnosis of dedifferentiated liposarcoma of the pancreas must be considered while examining patients with pancreatic tumor.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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