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A case report of primary pancreatic leiomyosarcoma requiring six additional resections for recurrences



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ABSTRACT

INTRODUCTION: Primary pancreatic leiomyosarcoma is extremely rare. We report a case in which six additional resections were required to treat recurrent tumors in a 5-year period following the primary operation.

PRESENTATION OF CASE: A 69-year-old man presented with a pancreatic tumor. Abdominal computed tomography scan showed a large heterogeneous mass with a necrotic area arising from the pancreatic body. We performed distal pancreatectomy, splenectomy, and wide resection of the transverse mesocolon. Histopathological examination confirmed the diagnosis of a pancreatic leiomyosarcoma. We repeatedly performed surgery on recurrent tumors.

DISCUSSION: Primary pancreatic leiomyosarcoma is considered to be a highly aggressive malignancy. The most effective treatment is complete surgical resection with tumor-free margins. Even when tumors recur, it is possible to improve the prognosis by further resection.

CONCLUSION: Long-term survival is achievable by repeated resection of recurrent tumors.

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1. Introduction

The first report of pancreatic leiomyosarcoma was described by Ross in 1951 [1], and only 52 cases have been reported in the English literature [2–4]. The tumor is considered to derive from the vasculature or ductal smooth muscle in the pancreas [5–8]. We also discuss the clinical and histological characteristics of primary pancreatic leiomyosarcoma in a brief literature review.

The work in this case has been reported in line with the SCARE criteria [9].

2. Presentation of case

A 69-year-old man was admitted to our hospital for further examinations of a pancreatic tumor. He was asymptomatic and his physical examinations revealed no characteristic features. Except for markedly elevated glucose (205 mg/dL) and hemoglobin A1c (10.5%) levels, all laboratory findings were normal, including his tumor markers (carcinoembryonic antigen, carbohydrate antigen 19-9, Span-1, and duke pancreatic monoclonal antigen type 2). Enhanced abdominal computed tomography (CT) scan showed an

8.2 × 7.2 cm large heterogeneous mass with a central necrotic area in the body of the pancreas (Fig. 1a and b). Ultrasonography revealed a 9.7 × 7.2 cm large hypoechoic mass with cystic change in the pancreatic body (Fig. 1c), and (18F) fludeoxyglucose positron emission tomography (PET)-CT showed strong accumulation in the pancreatic body (maximum standardized uptake value: 6.12; Fig. 1d). This tumor developed markedly outside the pancreas; however, invasion into the surrounding blood vessels was not obvious. Therefore, we suspected a malignant tumor different from a conventional invasive ductal carcinoma. Our differential diagnosis was a non-functioning neuroendocrine neoplasm, acinar cell neoplasm, solid pseudopapillary neoplasm, or mucinous cystic neoplasm.

3. Primary operation

We confirmed the presence of a large tumor measuring 8 cm in its greatest diameter in the body and tail of the pancreas. The border of the tumor invaded the transverse mesocolon, and was slightly attached with the posterior wall of the stomach. The tumor was easily separable from the stomach. Therefore, we performed distal pancreatectomy, splenectomy, and wide resection of the transverse mesocolon (Fig. 2a). The cross-section of the resected tumor was a well-circumscribed whitish mass that had signs of internal hemorrhage and partial myxoid changes (Fig. 2b).

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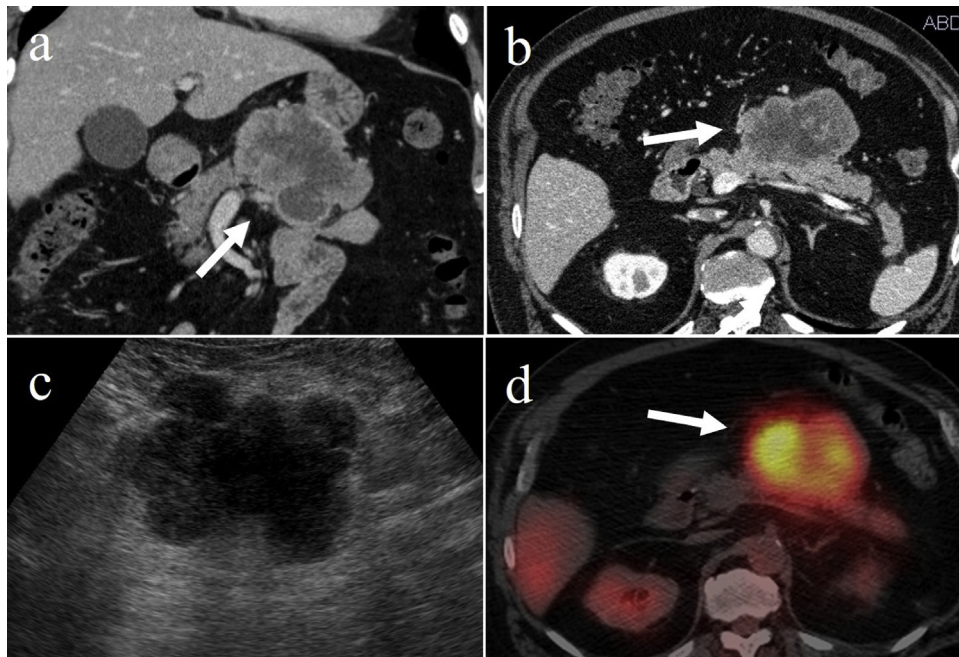


Fig. 1. Radiologic imaging modalities in the diagnosis of leiomyosarcoma.

Coronal (a) and axial (b) abdominal CT scans showing an 8.2 × 7.2 cm large heterogeneous mass with a central necrotic area in the body of the pancreas (arrows). (c) Ultrasonography showing a 9.7 × 7.2 cm large hypoechoic mass with cystic change in the body of the pancreas. (d) PET-CT showing a strong accumulation in the body of the pancreas (arrow).

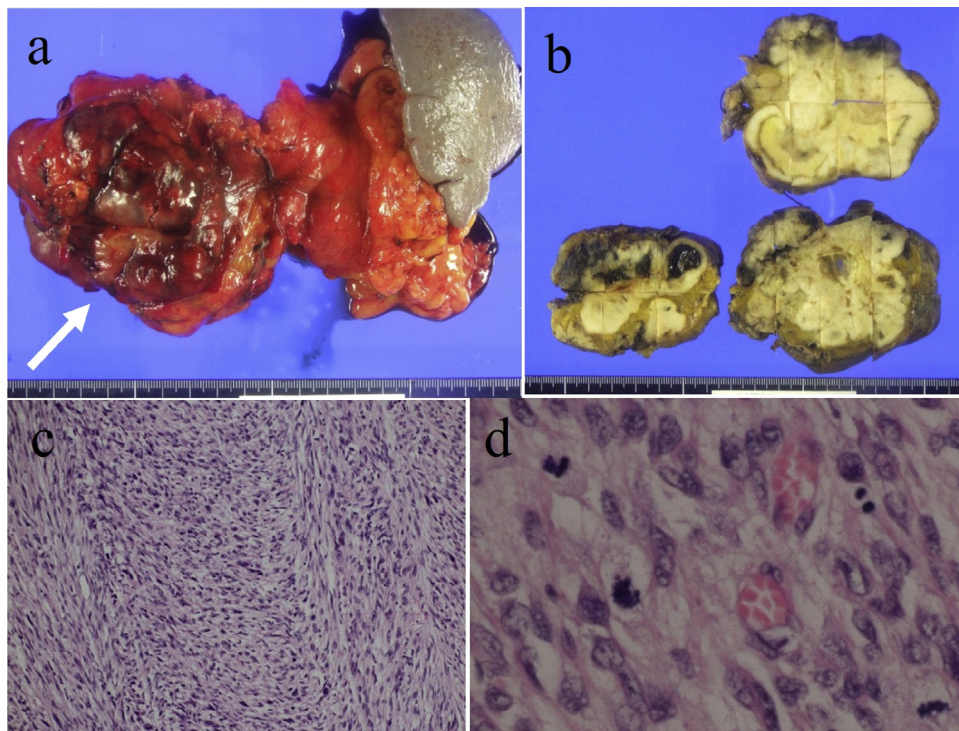


Fig. 2. Resected specimen and histological analysis.

(a) Macroscopically, there was an 8 × 7 cm tumor in the body of the pancreas (arrow). (b) The cross-section of the tumor is whitish and shows signs of internal hemorrhage and partial myxoid changes. (c) Histological examination showing interlacing bundles of spindle-shaped cells (Hematoxylin and Eosin staining x10). (d) Spindle-shaped cells with varying degrees of pleomorphism and a few mitotic figures. (Hematoxylin and Eosin staining x40).

Histological examination of the tumor revealed a composition of interlacing bundles of spindle-shaped cells with varying degrees of pleomorphic nuclei and variable mitotic activity (Fig. 2c,d). Immunohistochemical examination was positive for α-smooth muscle actin, caldesmon, and HHF35 (Fig. 3), but negative for

CD117(c-kit), CD34, desmin, and S100. Given that the main muscle markers were positive, and the MIB-1 labeling index was as high as 14.5%, the tumor was diagnosed as a primary pancreatic leiomyosarcoma. Lymph node metastasis was not observed in the resected specimens. The surgical margins were negative histopath-

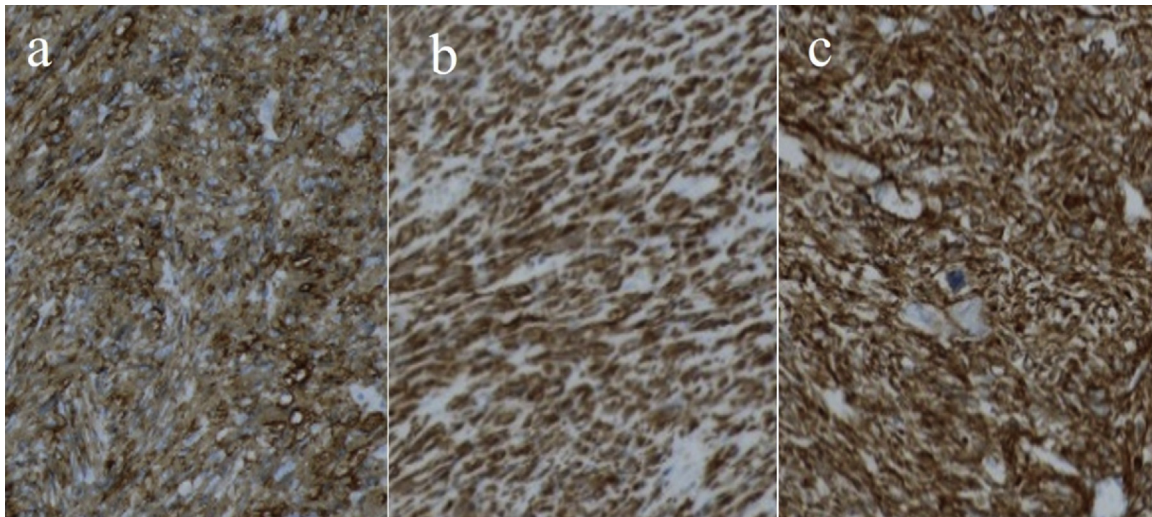


Fig. 3. Immunohistochemical examination.

Immunohistochemical analysis showing positive staining for α -smooth muscle actin (a), caldesmon (b), and HHF35 (c) (a \rightarrow $\times 20$).

logically. The patient was discharged on postoperative day 22 after an uneventful recovery.

3.1. First reoperation

An enhanced abdominal CT scan revealed a tumor measuring 4.5 cm in the caudal region of the stomach of the greater curvature side (Fig. 4a), which led to reoperation 7 months after the primary operation. We confirmed two tumors. One tumor (6 cm in diameter) invaded the stomach, and the other tumor (3 cm in diameter) invaded the small intestine; then, they were totally resected.

3.2. Second reoperation

A year and 8 months after the primary operation, an enhanced abdominal CT scan showed a liver metastasis measuring 5 cm in diameter (Fig. 4b). We resected the tumor 5 months after diagnosis.

3.3. Third and fourth reoperations

Three years and 7 months after the primary operation, a thoracic CT scan showed three metastatic tumors: one each in the upper and lower lobes of the right lung, and one in the lower lobe of the left lung (Fig. 4c, d). We performed partial resection of the lower lobe

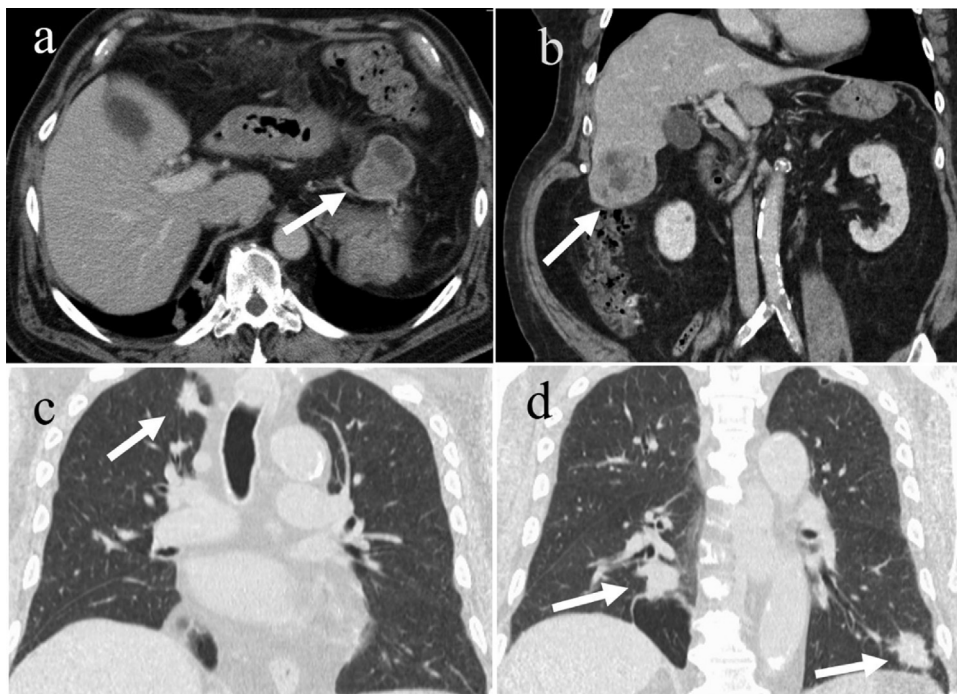


Fig. 4. Thoracic and abdominal CT imaging of recurrent tumors.

(a) Abdominal CT scan revealing a metastatic tumor measuring 4.5 cm in the caudal region of the stomach of middle part of the greater curvature side (arrow) at the time of the first re-operation. (b) Abdominal CT scan showing a liver metastasis measuring 5 cm in diameter (arrow) at the time of the second re-operation. Thoracic CT scan at the third and fourth re-operations shows three metastatic tumors in the upper and lower lobes of the right lung (c,d), and in the lower lobe of the left lung (d) (arrows).

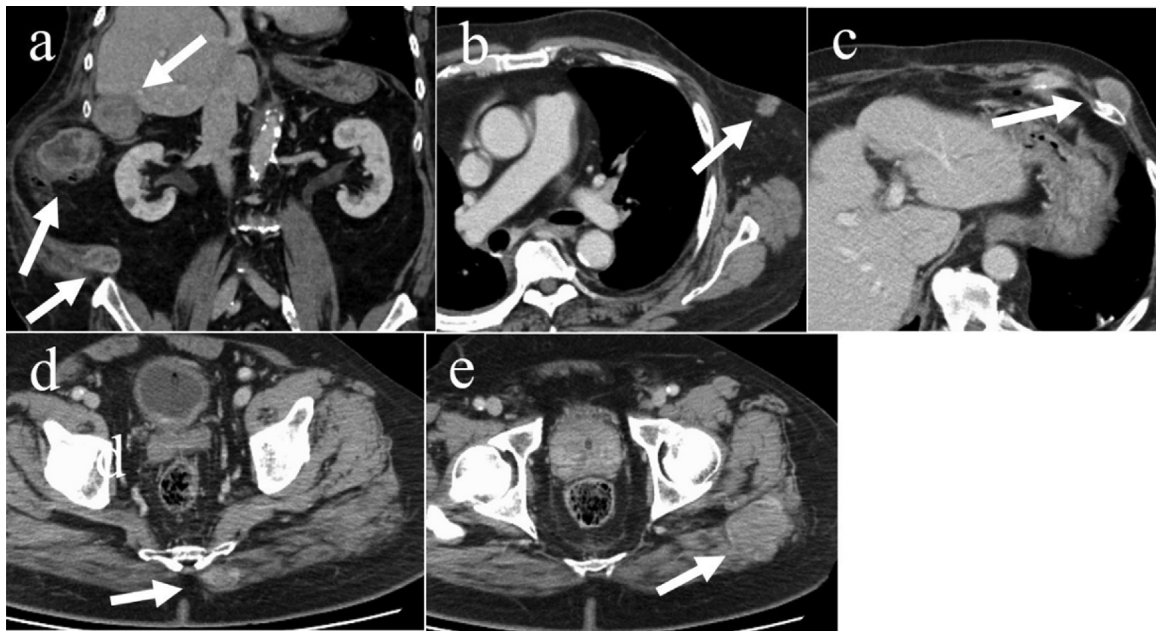


Fig. 5. CT imaging of recurrent tumors.

Thoracic and abdominal CT scans at the fifth and sixth re-operations show multiple metastatic tumors in the abdominal cavity (a), chest wall (b, c), and buttocks (d, e) (arrows).

of the left lung. Furthermore, we performed a lower lobectomy and partial resection of the right upper lobe 1 month later.

3.4. Fifth reoperation

Four years and 4 months after the primary operation, thoracic and abdominal CT scans showed tumors in the abdominal cavity, chest wall, and buttocks (Fig. 5). One of the three intra-abdominal tumors invaded the ascending colon, the other one invaded the liver.

Right hemicolectomy, partial hepatic resection, and two tumor resections in the chest wall were performed (Fig. 5a, b, c).

3.5. Sixth reoperation

Four years and 7 months after the primary operation, an abdominal CT scan showed that the size of two tumors in the buttocks was increasing. We resected both (6 cm and 3.5 cm in diameter) 1 month later (Fig. 5d, e).

These were histologically diagnosed as recurrences. Five years after the primary operation, thoracic and abdominal CT scans uncovered multiple metastases in both lungs, and in the abdominal cavity. He died five years and 10 months after the primary operation.

4. Discussion

Primary pancreatic leiomyosarcoma is rare. Baylor and Berg reported only 5 (0.1%) cases of leiomyosarcoma were present in 5057 histologically confirmed cases of malignant pancreatic tumor [10]. For the diagnosis of primary pancreatic leiomyosarcoma, it is essential to exclude tumors arising from surrounding organs. In our case, the tumor was almost predominantly located in the body of the pancreas with its border invading the transverse mesocolon, and was slightly attached with the posterior wall of the stomach.

However, the tumor was not connected to the stomach. It was strongly suspected to be of pancreatic origin. Immunohistochemical examinations are of great value when evaluating

spindle-shaped cell tumors with prominent cellular pleomorphism and/or focal storiform patterns, supposed to be smooth muscle origin [7,8,11].

In general, when a primary pancreatic leiomyosarcoma is small, ultrasonography shows a regular hypoechoic pattern [12–14]. As the tumor increases in size, necrotic or hemorrhagic changes can occur, as can cystic changes, giving rise to a mixed echoic pattern [8,12,15–17]. It is thought that the degenerative processes that resulting in central necrosis and cyst formation might be associated with the rapid enlargement of the neoplasm [8,17].

It was reported that 25% of patients had distant metastasis, and that 19% had invasion to adjacent organs or vessels at the time of diagnosis [7]. Clinically, the tumors are most likely to metastasize to the liver and lungs, whereas lymph node involvement is rare [2,5,12]. The treatment considered most effective is complete surgical resection with tumor-free margins [5,8,17,18]. Therefore, extended surgical resection by pancreaticoduodenectomy or distal pancreatectomy with splenectomy has been advocated rather than extensive lymph node dissection [8,17]. In our case, we performed distal pancreatectomy, splenectomy, and wide resection of the transverse mesocolon to achieve a macroscopically curative resection. We thought all the tumor tissues could be removed at the primary operation. However, metastatic dissemination had developed initially five months after surgery near the primary site, followed by hematogenous metastasis.

Five years after the primary operation, the patient developed systemic metastases making further radical surgery difficult. We still do not know whether adjuvant therapy would be of benefit after radical pancreatectomy, but there are no data to suggest that chemotherapy or radiation therapy could decrease the risk of local or distant recurrence after complete surgical resection [2,8,12]. Post operative chemotherapy was performed in only 2 reported cases with limited effect [5,15].

Intraoperative dissemination and hematogenous metastasis are thought to predominate as the main mechanisms of recurrence [7]. Prognosis of a primary pancreatic leiomyosarcoma was affected by local recurrence and distant metastasis with hematogenous metastasis. We thought hematogenous metastasis in particular affected

prognosis. The 5-year survival rate was reported to be 43.9% for this tumor type [7].

Tumor size is an important indicator of resectability, but it does not appear to affect the clinical course after surgical resection [2,6,7]. Instead, the quality of the surgical margin is probably the most important factor for predicting local recurrence [18]. Mitotic counts are also considered an important predictive parameter, with counts of more than 10 mitoses per 10 high-power fields being associated with worse outcomes [2,6,8]. However, low mitotic activity can be observed not only in pancreatic leiomyosarcomas, but also in metastatic lesions [7]. Therefore, extensive surgical resection should be advocated, even when morphological results show a low-grade lesion [5,8]. It is particularly important to recognize that complete resectability of the lesion is the only viable hope for improving long-term survival of the patients [2,4,5].

5. Conclusion

There is no evidence to support alternative therapy other than operation in primary pancreatic leiomyosarcoma. Radical resection with a wide tumor-free margin still offers the greatest chance of prolonging survival.

Conflict of interest

The authors have no conflicts of interest.

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Ethical approval

Ethical approval of this study was not required by our ethics committee.

Consent

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

Author contribution

Makimoto S and Tomita M designed this report. Hatano S, Kataoka K, and Yamaguchi T contributed to the collection and interpretation of data. Nishino E performed the pathological diagnosis. Makimoto S drafted the manuscript.

Guarantor

Shinichiro Makimoto.

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