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Pancreatic follicular dendritic cell sarcoma: one case report and literature review

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Abstract

Pancreatic follicular dendritic cell sarcoma (FDCS) is a rare neoplasm with unclear pathological characteristics. In this study, we report one case of pancreatic FDCS and review published cases to summarize the characteristics and treatment of pancreatic FDCS. A man in his early 30 s was admitted for jaundice, abdominal fullness, and weight loss for 15 days. Computed tomography revealed a large capsule solid mass in the pancreatic head together with a dilated bile duct and enlarged retroperitoneal lymph nodes. Serum biochemistry revealed high total bilirubin levels (313.9 μmol/L) and normal tumor marker levels. Pancreatoduodenectomy was performed, but no chemotherapy was administrated at the patient's behest. The pathologic diagnosis was pancreatic FDCS infiltrating the duodenal seromuscular layer and common bile duct. The patient presented with liver metastasis 3 months after surgery and died 8 months after surgery from multiorgan failure. Pancreatic FDCS is a rare disease with high invasiveness. Our previous case exhibited paraneoplastic syndrome together with this disease, and further investigation is needed to confirm whether paraneoplastic syndrome is a typical syndrome of pancreatic FDCS.

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Introduction

Follicular dendritic cell sarcoma (FDCS) is a rare disorder, but its precise incidence is unknown. The disorder was first described by Monda *et al*. in 1986,[1] and some cases have been reported in the medical literature. Conventionally, FDCS is considered to arise in the lymph nodes, whereas extranodal FDCS originating from non-lymph nodes, including the soft palate and tonsils, is currently recognized to be a low-grade sarcoma of mesenchymal dendritic cell origin. Earlier classification schemes had erroneously categorized it as a histiocytic or dendritic cell neoplasm of myeloid origin.[2] There are no known associations with inherited susceptibility, and most reported cases appear to be sporadic. Simultaneously, FDCS has also been reported in digestive organs such as the stomach, liver, and intestine.[3–5]

The first case of pancreatic FDCS was reported by Hollowood *et al*. in 1995.[5] To date, only six cases of pancreatic FDCS have been reported,[5–10] including one case reported by our group that manifested as paraneoplastic pemphigus and myasthenia gravis.[9] However, the pathological characteristics and optimal treatment of this rare disease have not been established. In this study, we report one case of pancreatic FDCS treated recently and review published cases to summarize the characteristics and current treatment of pancreatic FDCS. This manuscript aimed to explore the treatment regimen for future cases.

Case presentation

A man in his 30 s was admitted for jaundice, abdominal fullness, and weight loss for 15 days. He had no special medical history including biliary calculus, cirrhosis, and pancreatitis. The physical examination revealed yellowing of the eyes and skin and a firm and palpable mass located in the right superior abdominal region, but there was no superficial lymph node enlargement. The findings of serum biochemistry were as follows: total bilirubin, 314 μmol/L; direct bilirubin, 202 μmol/L; alkaline phosphatase, 334 U/L; and aspartate aminotransferase, 134 U/L. The levels of serum tumor markers including CA-199, CA-125, carcinoembryonic antigen, and alpha-fetoprotein were in the normal ranges, as were serum autoimmune antibody levels. No special results were obtained in routine blood analysis.

Computed tomography (CT) revealed a 10- × 9-cm^2 well-defined round solid mass with central necrosis in the pancreatic head. The solid inhomogeneous component was enhanced after venous strengthening, and the mass was adjacent to the superior mesenteric artery/vein and right renal vein. The common bile duct was constricted by the mass, inducing biliary tree dilation. In addition, some enlarged retroperitoneal lymph nodes were detected on CT (Figure 1a). The primary diagnosis was pancreatic head neoplasm.

After adequate preoperative preparation, exploratory laparotomy was initiated. A massive occupying lesion ($10 \times 9 \times 8\ cm^3$)

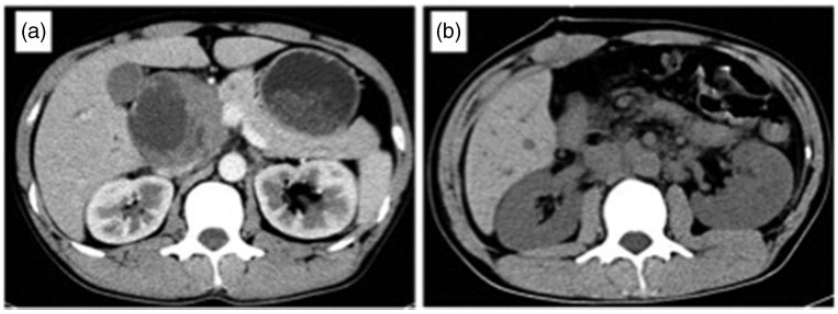

Figure 1. Computed tomography images. (a) Before surgery and (b) After surgery.

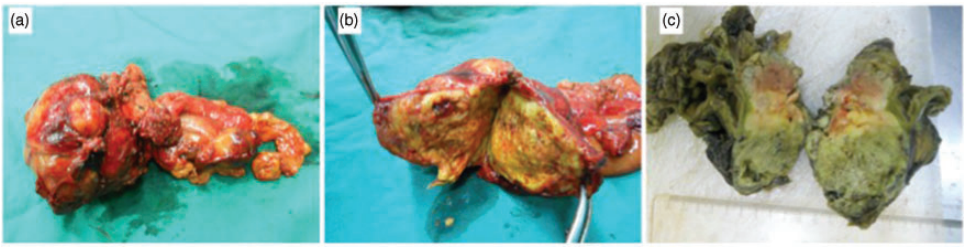

Figure 2. Gross examination of the tumor. (a) The tumor was a well-encapsulated, soft, multilobulated mass. (b) The freshly cut section of this mass was yellow-gray in color, and the tumor featured a fish flesh-like appearance with typical hemorrhagic and necrotic areas and (c) The dissected mass was fixed in paraformaldehyde.

spanning from the hepatic duct to the renal hilum level was detected, and the lesion was mildly adherent to the inferior vena cava and portal vein. The exploration also revealed retroperitoneal lymph node enlargement. Then, pancreatoduodenectomy was successfully performed. Postoperative CT illustrated that this tumor was completely resected, and there were no enlarged lymph nodes in the abdominal cavity or retroperitoneum (Figure 1b). No combined chemotherapy was administrated per the patient's request. His recovery was smooth, and he was discharged from the hospital 16 days after surgery. Liver metastasis was detected 3 months after surgery, and the patient died 8 months after surgery because of multiorgan failure.

The pathological examination revealed that this tumor was well encapsulated, soft, and multilobulated, and the freshly cut section of this mass featured a fish flesh-like appearance, a yellow-gray color, and typical hemorrhagic and necrotic areas (Figure 2). The pathologic diagnosis was pancreatic FDCS infiltrating the duodenal seromuscular layer and common bile duct. Microscopic examination uncovered that the tumor was infiltrated by some lymphocytes, and the tumor was composed of variably sized nodules separated by fibrovascular septae. Within the nodules, ovoid-to-spindle-shaped cells were typically arranged in short fascicular, whorl-like, or storiform patterns (Figure 3a). The boundaries between tumor cells were visible, and the cytoplasm of neoplastic cells was eosinophilic. The nuclei were long-spindle or ovate with prominent nuclear divisive phenomena (Figure 3b). Immunohistochemical

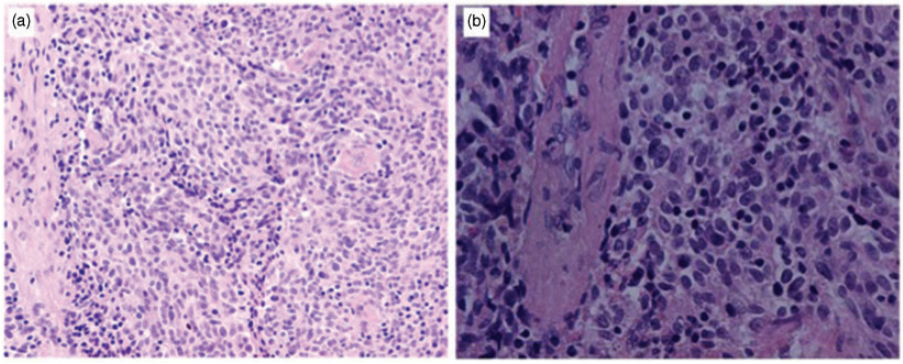

Figure 3. Hematoxylin–eosin staining. (a) The nodules of the tumor were separated by fibrovascular septae, and the ovoid-to-spindle–shaped cells were typically arranged in short fascicular, whorl-like, or storiform patterns within the nodules (×200) and (b) The tumor cell borders were visible, the cytoplasm was eosinophilic, and the nuclei were ovate or long spindle-like in shape with remarkable nuclear divisive phenomena (×400).

staining revealed that the tumor cells were positive for CD21, CD35, and clusterin (Figure 4a–c) and negative for CD30 (Figure 4d). Histologically, typical FDCS must be distinguished from other low-grade sarcomas, other histiocytic neoplasms, melanomas, thymomas, and other tumors.

Literature review

Dendritic cells participate in the immune system through presenting antigens for B-cells, regulating germinal center reaction, and stimulating B-cell proliferation or differentiation.[11,12] As the origin of follicular dendritic cells, FDCS often occurs in the lymph nodes. Extranodal FDCS is rare, and extranodal FDCS originating from the pancreas is even rarer. To date, only six cases of pancreatic FDCS have been reported (Table 1). To date, the etiology of FDCS remains uncertain. Shared overexpression of epidermal growth factor receptor has been suggested as the common pathophysiological link. Some scholars believe that the neoplasm is related to Epstein–Barr virus (EBV) infection. Its clinical presentation includes liver and spleen involvement with systemic symptoms,[3,13,14] but there was no evidence of EBV infection in this case or in previous reports of pancreatic FDCS. In one previous reported case,[9] the patient had high levels of serum autoimmune antibodies including anti-CENP-B antibody, antineutrophil cytoplasmic antibody, anti-acetylcholine receptor antibody, and antineutrophil antibody, indicating that the occurrence of pancreatic FDCS might be relevant to the immune system. However, there were no relevant findings in previous studies or in the present case. Thus, the etiology of this tumor requires further analysis based on additional cases.

Similar to pancreatic carcinoma, pancreatic FDCS has no typical symptoms. In the published papers, the pancreatic location was identified by medical examination in two cases, including one case that was diagnosed inflammatory pseudotumor-like follicular dendritic cell tumor (low-grade sarcoma).[6,10] Possibly, there are some typical symptoms for this disease. Previously, pancreatic FDCS presented with paraneoplastic syndrome including paraneoplastic pemphigus and myasthenia gravis

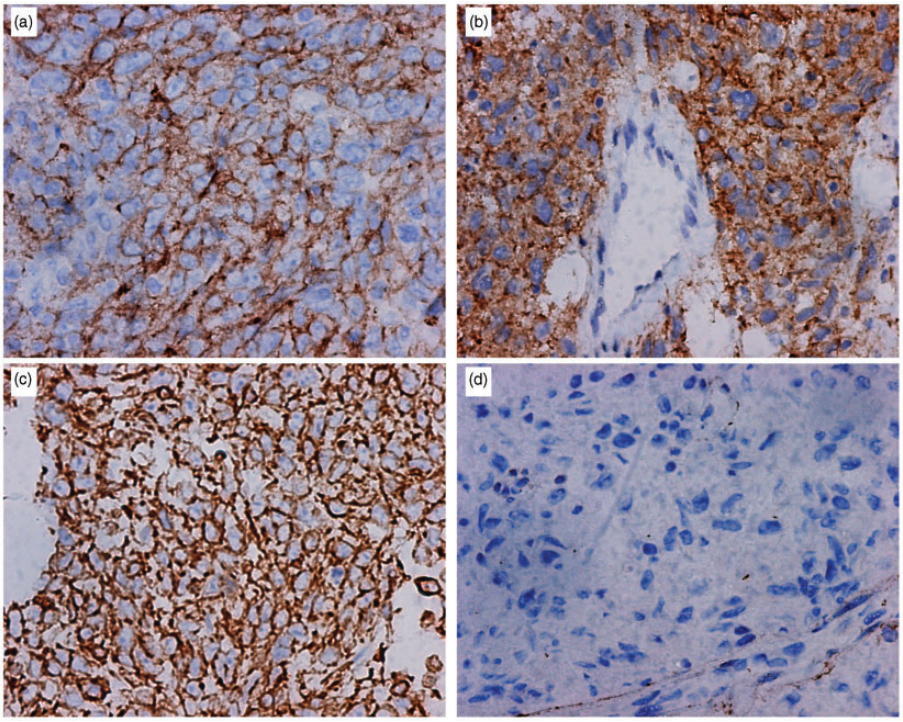

Figure 4. Immunohistochemical staining (×400). (a) CD21 staining. (b) CD35 staining. (c) Clusterin staining and (d) CD30 staining.

Table 1. Previous reports on pancreatic follicular dendritic cell sarcoma.

Reference	Year of publication	Age (years)	Sex	Location	Size	Metastasis
Hollowood *et al.*[5]	1995	63	Male	Head	$15 \times 11.5 \times 9.5\ cm^3$	None
Shen *et al.*[8]	2006	64	Male	Head	$10.5 \times 9.0 \times 6.5\ cm^3$	Liver
Soriano *et al.*[7]	2007	56	Male	–	2 cm	Abdominal lymph node
Liang *et al.*[6]	2016	67	Female	Tail	$3.5 \times 3.6\ cm^2$	None
Lu *et al.*[9]	2019	49	Female	Tail	$6 \times 5\ cm^2$	None
Mograbi *et al.*[10]	2019	70	Female	Tail	$8.5 \times 5.5 \times 3.2\ cm^3$	Spleen

–: The site was not described.

simultaneously,[9] and a report described paraneoplastic pemphigus and myasthenia gravis presenting with FDCS in the axillary region and neck[14]. Therefore, the characteristics of extranodal FDCS, pancreatic FDCS, and inflammatory pseudotumor-like follicular dendritic tumor need to be further clarified.

Discussion

Pancreatic FDCS is frequently misdiagnosed because of its rarity. It is difficult to differentiate pancreatic FDCS from pancreatic solid pseudopapillary tumors. Morphological and immunohistochemical findings are significant for the diagnosis of

FDCS.[15] The typical pathological characteristics of FDCS are spindle- or oval-shaped cells arranged in storiform, whorl-like, or fascicular patterns, individual tumor cells exhibit pale eosinophilic and fibrillar cytoplasm, and some lymphocytes infiltrate the tumor. The nuclei are hyperchromatic and spindle- or oval-shaped with clear nucleoplasm. Additionally, immunohistochemical staining facilitates the diagnosis of FDCS. CD21, CD35, and CD23 are the most specific diagnostic markers for this disease, and podoplanin D2-40 is also a significant marker of FDCS.[16] Furthermore, this tumor is usually positive for vimentin, S-100, CD20, and epithelial membrane antigen. This case and previously reported cases were positive for CD21, demonstrating that CD21 is the most significant immune marker for the diagnosis of pancreatic FDCS.[17,18]

FDCS is viewed as an indolent tumor with a low risk of metastasis, and the 2- and 5-year recurrence-free survival rates are 62.3% and 27.4%, respectively.[19] Given its rarity, the management of localized FDCS primarily involves surgical resection, whereas the optimal treatments for different types of FDCS are not well defined. For instance, Alagheband *et al.* recommend the patients with FDCS arising from the thyroid gland should continue treatment with adjuvant radiotherapy (RT).[20] As a retroperitoneal lesion, the effect of RT on pancreatic FDCS and common adenocarcinoma remains controversial. At present, the role of adjuvant therapy has not been established, and it does not appear to improve progression-free or overall survival following complete surgical resection.[21,22] Radical resection is the primary treatment for relieving the clinical symptoms, whereas recurrence is widely reported.[23] Meanwhile, the role of subsequent RT and chemotherapy during the treatment of FDCS remains unclear.[24] Although Choi *et al.*[11] reported that some patients with FDCS exhibited a partial response after two cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone chemotherapy, whereas research demonstrated that adjuvant chemotherapy did not improve relapse-free or overall survival in patients with resected soft-tissue sarcoma.[25] Overexpression of programmed death ligand-1 and programmed death ligand-2, and the possible involvement of the RAS/RAF/AKT/mTOR pathways have been implicated in the development of pancreatic FDCS, but therapeutic agents that target these abnormalities have not been tested in this disorder.[26] Our patient received no adjuvant therapy after surgery and refused additional chemotherapy. The patient developed liver metastasis and died 8 months after surgery because of multiorgan failure. Thus, the effect of RT and/or chemotherapy on pancreatic FDCS and the difference in response between different organs remain to be illustrated.

FDCS is a low-grade sarcoma of mesenchymal dendritic cell origin that typically presents as a slowly growing painless mass most commonly involving the head and neck or abdominal lymph nodes. The diagnosis is based on laboratory, imaging, and pathological findings, and biopsy of multiple lesions might be necessary to exclude this diagnosis. Radical resection is the basic treatment for this disease. However, additional research is needed to demonstrate the benefit of additional immunotherapy, cytotoxic chemotherapy, and vascular epidermal growth factor receptor-targeted therapy.

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Authors' contributions

XL, YW, and CY designed the study. JG, YW, and XY collected the patient's clinical data. CY,

YW, and YZ analyzed the data. XL and CY wrote the paper. All authors have read and approved the manuscript.

Data availability statement

All data generated or analyzed during this study are included in this published article.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Ethics statement

This work was approved by the Ethical Committee of the Sichuan Provincial People's Hospital (Chengdu, China). Written informed consent for publication was obtained from the patient.

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