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Case Report

Primary mesenteric follicular dendritic cell sarcoma associated with Castleman's disease: a case report and review of literature

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Abstract: Follicular dendritic cell sarcoma (FDCS) is a rare malignant neoplasm of immune accessory follicular dendritic cells and may be associated with Castleman's disease, which is recognized as a known precursor to FDCS. FDCSs in the mesentery are extremely rare. A correct diagnosis can be difficult to make. Clinically, the diagnosis of FDCS relies on the combined clinical examination, radiology, histopathologic features and confirmation with immunohistochemical studies. Here, we reported a case of a FDCS associated with Castleman's disease in a 41-year-old man who presented with a large mesenteric mass, which required a complete resection. Morphologic and immunohistochemical features confirmed the diagnosis of FDCS associated with Castleman's disease.

Keywords: Follicular dendritic cell sarcoma, Castleman's disease, mesentery

Introduction

Follicular dendritic cell sarcoma (FDCS), also known as dendritic reticulum cell sarcoma, is a neoplasm that arises from follicular dendritic cells. FDCS was first described in 1986 in a report of four cases of a non-lymphomatous primary lymph node malignancy [1]. Castleman's disease, which is a benign lymphoproliferative disorder, has been suggested as a precursor lesion for FDCS [2, 3]. As in the hyperplasia-dysplasia-neoplasia sequence proposed for the development of some epithelial neoplasms, FDCS may arise in lymph nodes harboring dysplastic follicular dendritic cell in Castleman's disease. FDCS in mesenteric is extremely rare. In a pooled analysis of 342 cases, primary mesenteric FDCS constituted only 3.8% of all cases [4]. Therefore, the cases of FDCS associated with Castleman's disease are much less, particularly in abdominal lesions [5-9]. Here, we reported a rare case of primary mesenteric FDCS associated with Castleman's disease.

Case report

A 41-year-old man was referred to our hospital because of an abdominal mass. The lesion was found during a routine health screening. The patient's medical history was unremarkable and his physical examination was also not significantly found. Abdominal CT scan showed a large, well-defined homogeneous mass arising from the mesentery. The enhanced CT images revealed marked homogenous enhancement (**Figure 1**). Based on the CT image, the diagnosis of gastrointestinal stromal tumor (GIST) was first constructed. Then the patient underwent an exploratory abdominal surgery.

The gross pathologic examination revealed a cubic mass with diameter of 5 cm. Microscopic examination showed a malignant neoplasm composed of pleomorphic spindle cells admixed with small lymphocytes and plasma cell (**Figure 2A**). In addition, there were areas typical of Castleman's disease, characterized by angiofollicular hyperplasia, small-vascularized germinal centers, and a spectrum of follicular dendritic cell proliferation, along with areas of transition into FDCS (**Figure 2B**, **2C**). The immunohistochemistry results were positive for CD21, CD23, CD35 and negative for cytokeratin (**Figure 2D-F**). Basis on the morphologic and immunohistochemical features, a diagnosis of primary mesenteric FDCS arising in a background of Castleman's disease was made.

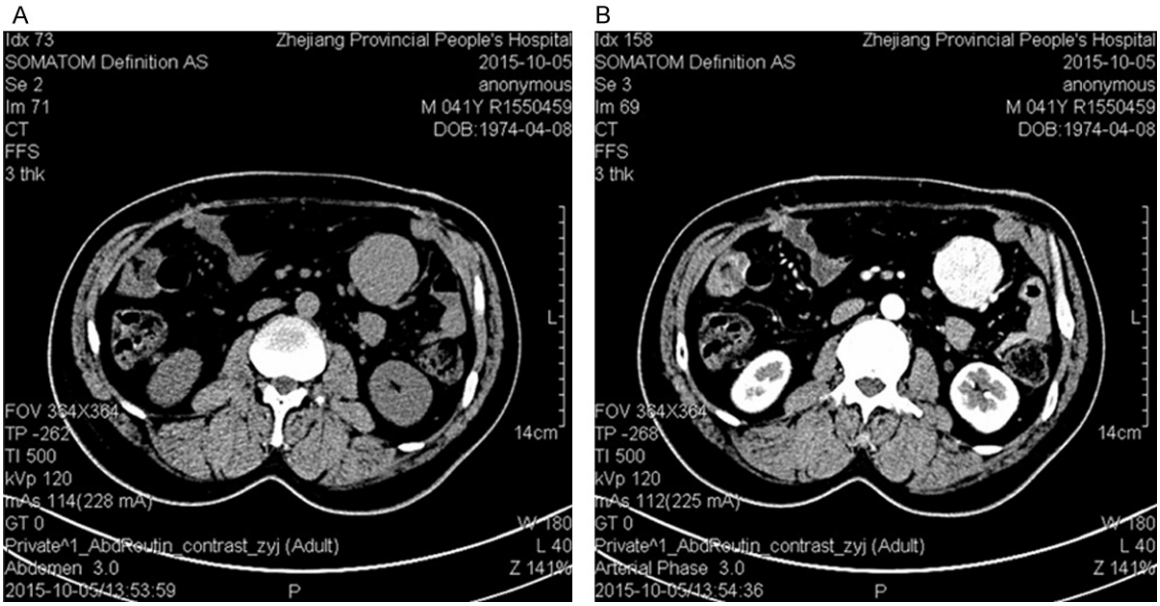

Figure 1. Patient abdominal CT scan (A) The unenhanced abdominal CT scan showed that a round mass with homogeneous density existed in the mesentery. The mass has a smooth border with a clear boundary. (B) Contrast-enhanced CT scan revealed marked homogeneous enhancement.

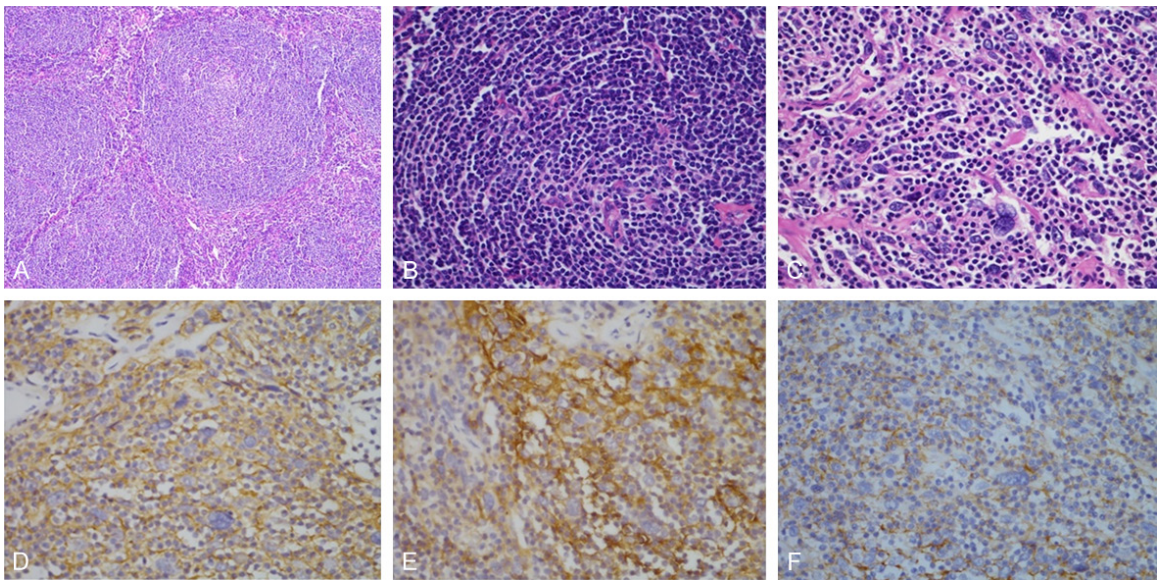

Figure 2. Histological features of the mass. A. The histopathological appearance indicated that the tumor was composed of cells arranged in a storiform pattern and that these cells were admixed with lymphocytes (HE, ×100). B. Tumor cells presented a spindle shape with a vortex arrangement (HE, ×400). C. As well as fascicles of spindle cells with atypical vesicular nuclei and eosinophilic cytoplasm, with admixed lymphocytes (HE, ×400). D. Positive immunohistochemical staining for CD21 (×400). E. Positive immunohistochemical staining for CD23 (×400). F. Positive immunohistochemical staining for CD35 (×400).

Discussion

Follicular dendritic cell sarcoma is an extremely rare malignant tumor of the immune accessory follicular dendritic cells. It was first reported in 1986 by Monda *et al.* [1]. Follicular dendritic cells are normally found in primary follicles and germinal centers, and their primary function is to modulate immune response by presenting antigens to germinal center B cells. Unlike most

cells of the immune system, follicular dendritic cell are derived from nonhematopoetic bone marrow stromal cell and may be increased in lymph nodes in many benign and malignant conditions [2]. Sometimes, this proliferation would lead to neoplastic transformation. One particular example of this transformation is in the hyaline vascular variant of Castleman's disease, which is a form of benign lymphoid hyperplasia with prominent follicular dendritic cell and small-vascularized germinal centers [2]. Approximately 10% to 20% of FDCS cases are associated with antecedent or concurrent Castleman's disease, a benign lymphoproliferative disorder, mostly the hyaline vascular variant [10].

FDCS usually occurs in lymph nodes, especially in the cervical, mediastinal, and axillary areas, but it can also occur in extranodal sites such in the liver, lungs, tonsils, spleen, mediastinum or mesentery [4, 11]. FDCS arising from Castleman's disease within the abdominal cavity, however, is a very uncommon finding, only a handful of cases have been reported in the literature [5].

Clinical presentation varies according to the location of the primary mass. Most cases are asymptomatic, although patients with abdominal mass may present with abdominal pain, and systemic symptoms including weight loss, fatigue, fever, and night sweats [10, 12]. The diagnosis of FDCS associated with Castleman's disease can be challenging, and it mainly depends on the combination of histological and immunohistochemical examinations. Most FDCS are considered low-grade sarcomas. Histologic sections demonstrate a spindle cell proliferation with a varied architectural pattern in storiform or whorled bundles, fascicles, trabecular or diffuse sheets [13]. Notably, Histologic features, such as the presence of Castleman's disease in the background or a mixture of neoplastic cells admixed with lymphocytes, can be extraordinarily facilitate the diagnosis. The diagnosis of FDCS requires confirmation from immunohistochemistry and the combinations of some marker are often necessary [12]. Tumor cells are variably positive for CD21, CD23 and CD35, while clusterin, podoplanin and CXCL13 are more consistently expressed and show high specificity in the differential with tumors that may mimic FDCS [14, 15]. The epithelial growth factor receptor (EGFR) is often positive in FDCS, but its specificity is low[16, 17]. Positivity for epithelial membrane antigen, CD68, S-100 protein, and very rarely for cytokeratin and CD20 have been reported in FDCS [14]. In this case, we found that the immunohistochemistry results are positive for CD21, CD23, CD35 and partially CD20 and negative for EGFR, S100 or Cytokeratin. This immunohistochemistry justified the diagnosis of FDCS associated with Castleman's disease.

Due to small number of cases, the optimal treatment for FDCS associated with Castleman's disease is yet to be found. The current approach is based on the therapeutic guidelines similar to those for the high-grade soft tissue sarcomas [18]. Complete surgical resection remains the mainstay of the treatment, albeit it cannot avoid local recurrences. The most frequently applied chemotherapeutical regimes are mostly referred to non-Hodgkin lymphoma but their effectiveness is difficult to assess [4]. Radiotherapy is frequently applied in these patients [4, 19, 20]. However, in low-stage FDCS, no improvement in term of overall survival was found comparing radiotherapy to surgery alone [4]. Local recurrences and distant metastasis are found in 28% and 27% of cases respectively [4, 19]. The main sites of metastasis are lung [21, 22], liver [23], lymph nodes [24] and bones [25]. In this case, no chemotherapy and radiotherapy were recommended due to the completely resection of the abdominal mass. We follow this patient and no local recurrence and metastasis have been found until now for nearly 10 months.

Basis on this case, we searched in the literature and collected clinical data about FDCS associated with Castleman's disease (**Table 1**). Up to now, only 16 cases of FDCS have been reported to be associated with Castleman's disease, which is mostly hyaline-vascular type and rarely mixed type (**Table 1**). Besides the current case, the FDCS associated with Castleman's disease reveals male predominance (Male:Female=10:6) and affects mostly middle-aged adults, of which average age is 48. The most common site is intra-abdominal (n=6), followed by mediastinum (n=4), neck (3) and other sites (n=3). Surgery is the mainstay of the treatment, 12 cases were treated by complete surgical excision, 3 cases were treated by surgery and chemotherapy and only one case was treated by surgery and radiation.

Table 1. Clinical pathological characteristics, treatments of the cases of FDCS associated with Castleman's disease.

Reference	Age (yrs)	Sex	Site	Immunohistochemical characteristic	Follow up	Outcome	Type of Castleman's disease	Treatment
Lee B.E. et al. [6] (2014)	63	Male	Posterior mediastinal	CD21 (+), CD68 (+), vimentin (-)	None	Unknown	Hyaline-vascular	Surgery
H wang, S.O. et. al. [5] (2013)	51	Female	Intra-abdominal	CD21 (+), CD23 (+), CD68 (+)	9 months	No evidence of recurrence	Hyaline-vascular	Surgery+radiation therapy
Chan, J.K. et al. [12] (1997)	42	Male	Mesocolon	CD21 (+), CD35 (+)	18 months	Recurrence and then died	Hyaline-vascular	Surgery+chemotheray
Wright. Colleen A. [26] (1997)	33	Female	Left side of the neck	CD21 (+), CD35 (+)	6 years	Recurrence in the same area	Hyaline-vascular	Surgery
Saiz, Antonio D. et. al. [27] (1997)	60	Male	Mesentery	CD21 (+), CD35 (+)	7 months	Recurrence	Hyaline-vascular and plasma cells	Surgery
	32	Male	Inguinal lymph node	CD21 (+), CD35 (+)	24 months	Recurrence	Hyaline-vascular	Surgery
Lin, O. et.al. [28] (1997)	31	Male	Anterior mediastinum	CD21 (+), CD35 (+)	11 years	Cervical lymphadenopathy recurrence	Hyaline-vascular	Surgery
	76	Female	Left side of neck	CD21 (+), CD35 (+)	3.5 years	Recurrence	Hyaline-vascular	Surgery
	34	Female	Anterior mediastinum	CD21 (+), CD35 (+)	no data	Alive and well	Hyaline-vascular	Surgery
	53	Female	Retroperitoneum	CD21 (+), CD35 (+)	14 months	Local recurrence	Hyaline-vascular	Surgery
	58	Male	Presternal	CD21 (+), CD35 (+)	No data	Alive and well	Hyaline-vascular	Surgery
Andriko, J.W. [29] (1998)	61	Male	Small bowel mesentery	CD21 (+), CD35 (+), CD68 (+)	2 years	Local recurrence	Plasma cell	Surgery
Chan,A.C. et. al .[8] (2001)	23	Male	Nasopharynx	CD21 (+), CD35 (+)	3 years	Alive and well	Hyaline-vascular	Surgery+chemotherapy
Cakir, E. et. al. [9] (2013)	45	Female	Neck	CD21 (+), vimentin (+)	4 months	No recurrence	Hyaline-vascular	Surgery+chemotherapy
Chang, Z.P. et. al. [30] (2007)	64	Male	Right chest	CD21 (+), CD23 (+), CD35 (+)	15 months	No recurrence	Hyaline-vascular	Surgery
Present case	41	Male	Mesentery	CD21 (+), CD23 (+), CD35 (+)	10 months	No recurrence	Hyaline-vascular	Surgery

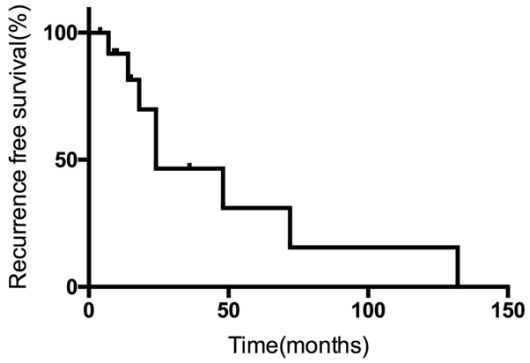

Figure 3. Recurrence free survival of FDCS associated with Castleman's disease.

Finally, we calculated the recurrence free survival basis on the date extracted from literatures and present case. Here we used Kaplan-Meier methods to estimate recurrence free survival and all statistical analyses were performed using Prism, version6.0C. The media recurrence survival of the FDCS associated with Castleman's disease is 24 months (**Figure 3**).

In summary, we reported a rare case of primary mesenteric FDCS associated with Castleman's disease. This case showed sequential pathological changes from Castleman's disease to FDCS. Although this case represents an extremely rare tumor, we should keep in mind that FDCS associated with Castleman's disease should remain in the differential diagnosis for abdominal mass. The final diagnosis still relies on the histology and immunohistochemical techniques. Up to now, complete resection of the mass is still the mainstay of the treatment.

Disclosure of conflict of interest

None.

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