Korean J Gastroenterol Vol. 62 No. 2, 131-134
http://dx.doi.org/10.4166/kjg.2013.62.2.131
pISSN 1598-9992 eISSN 2233-6869

CASE REPORT

KJG

캐슬만병에서 기원하여 무증상 복강 내 종양으로 발현된 여포성 수상돌기 세포육종

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Transformation of Castleman's Disease into Follicular Dendritic Cell Sarcoma, Presenting as an Asymptomatic Intra-abdominal Mass

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Follicular dendritic cell (FDC) sarcoma is an extremely rare malignant neoplasm arising from FDCs. The exact origin of FDCs remains unclear; both a hematopoietic lineage origin and a stromal cell derivation have been proposed. Proliferation of FDCs can lead to benign reactive lesions or generate neoplastic conditions. The lesions are most commonly found in lymph nodes and usually involve the head and neck area. Castleman's disease is a rare non-neoplasitic lymphoproliferative disorder. Rare cases of hyaline-vascular Castleman's disease have been associated with FDC sarcoma, but a clonal relationship has not been convincingly demonstrated. A pathway toward tumor evolution, beginning with hyperplasia and dysplasia of FDCs, has been proposed. Despite this known association between Castleman's disease and FDC sarcoma, there have only been few reported cases of sarcoma arising as a complication of pre-existing Castleman's disease, especially in abdominal lesions. We describe here a 51-year-old female with an FDC sarcoma arising from unicentric, hyaline-vascular type Castleman's disease in an intra-abdominal mass. Pathologically, the lesion showed a series of changes during the process of transformation from Castleman's disease to FDC sarcoma. **(Korean J Gastroenterol 2013;62:131-134)**

Key Words: Follicular dendritic cell sarcoma; Castleman's disease

INTRODUCTION

Follicular dendritic cell (FDC) sarcoma is an extremely rare neoplasm arising from the FDCs of germinal centers.[1] FDC sarcoma has a low-to-intermediate risk of recurrence or metastasis, and such events may occur many years after the initial diagnosis.[2] Castleman's disease, which is a rare non-neoplasitic lymphoproliferative disorder, is classified into two subtypes according to histological features; a hyaline-vascular type and a plasma cell type.[3,4] Hyaline-vascular Castleman's disease (HVCD) has been identified as a possible predisposing factor for FDC sarcoma in a minority of cases. A pathway toward tumor evolution, beginning with hyperplasia and dysplasia of FDCs, has been proposed.[5] Despite this known association between Castleman's disease and FDC sarcoma, there have been only few reported

Received November 26, 2012. **Revised** January 28, 2013. **Accepted** January 31, 2013.

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Financial support: None. Conflict of interest: None.

cases of sarcoma arising as a complication of pre-existing Castleman's disease, particularly in abdominal lesions.[1,2,5,6] To our knowledge, a case showing sequential tissue transformation has been reported once in Korea.[2,7]

We report an unusual case of sequential transformation of an FDC sarcoma starting from Castleman's disease which presented as an asymptomatic intra-abdominal mass in a Korean female.

CASE REPORT

A 51-year-old female was referred to our hospital because of a pancreatic mass. The lesion was found during a health-screening abdominal ultrasound scan. The patient's medical history was unremarkable except for hypertension, and she had no symptoms. Her physical examination was normal. Blood laboratory tests including hemoglobin, erythrocyte sedimentation rate, CRP, γ-globulin and tumor markers, were within normal ranges. Chest and abdominal X-rays had non-specific findings.

On abdominal CT scan, a well-enhanced mass of about 4 cm was detected. The lesion was located in the anterior and superior aspects of the pancreatic head (Fig. 1A). MRI revealed a 4.4-cm heterogeneous high-signal intensity mass on the T2 weighted image at the hepatic hilum. The lesion abutted the caudate lobe of the liver and the pancreas (Fig. 1B). Sequential EUS was performed to determine the origin of the mass, and revealed a 4-cm heterogeneous hypoechoic mass on the anterior portion of the head and body of the pancreas. A pancreatic or liver origin seemed unlikely. On PET-CT, other abnormal findings, such as lymph node enlargement, were not detected. Based on the imaging results, we considered a disease of neuroendocrine origin or a mesenchymal tumor, and surgical exploration was planned to confirm this.

During surgery, a 5-cm tumorous lesion originating from a lymph node was found around the head of the pancreas and portal vein; there was no connection with adjacent organs. The mass was completely removed by surgical excision. Macroscopically, the tumor was partially encapsulated by a membrane. On sectioning, the cut surface showed a pale yellowish-to-brownish homogeneous appearance, with multifocal hemorrhagic spots (Fig. 2). Histopathological analysis of the mass revealed a tumor composed of spindle cells, atypical vesicular nuclei, and eosinophilic cytoplasm, in accordance with Castleman's disease (Fig. 3). Immunohistochemistry was positive for FDC markers (CD21, CD23, CD68). All other markers investigated (CD20, CD79a, CD3, CD45RO, CD10, CD56, CK, CD30, CD1a, EBV, MPO, S-100 protein)

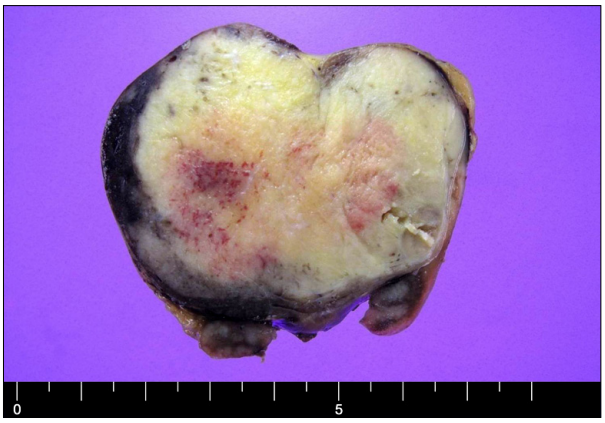

Fig. 2. Gross findings after surgical resection. The encapsulated mass measured 6.0×5.0×3.0 cm and showed a yellowish-to-brown color with hemorrhagic spots.

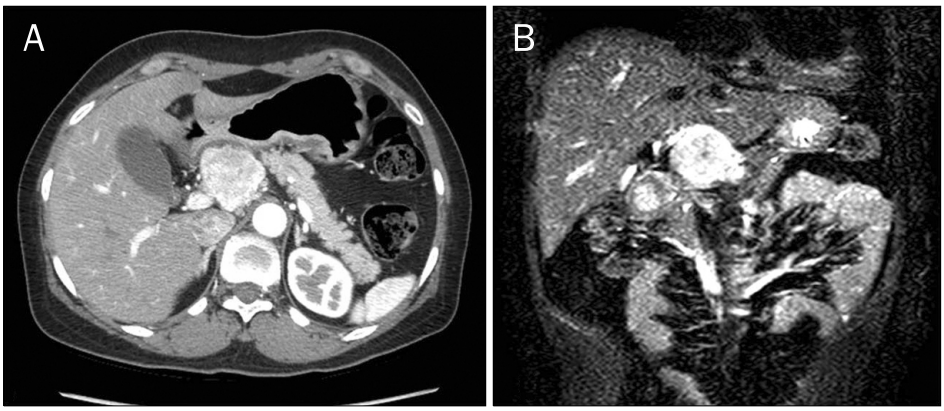

Fig. 1. Radiological findings. (A) A 4-cm well-enhancing mass was located around the liver, stomach, and pancreas (enhanced CT). (B) A 4.4-cm highly signal intensity mass lesion was noted in same lesion (MRCP, T2 weighted image).

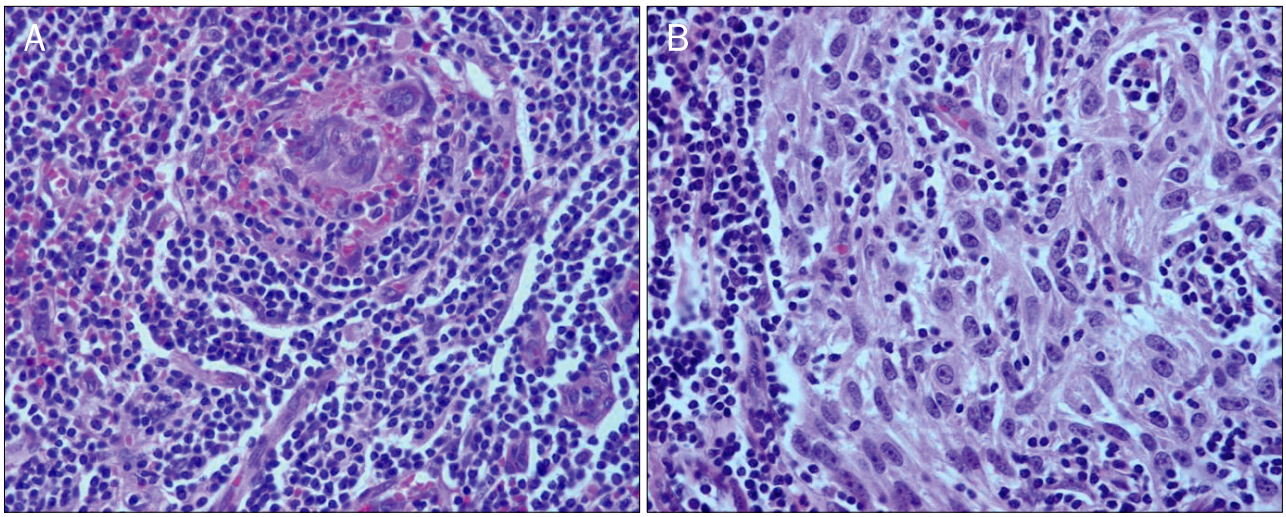

Fig. 3. Histological features of the mass (H&E, ×400). Microscopic findings indicated an atrophic germinal center with a penetrating vessel and follicular dendritic cell hyperplasia (A), as well as fascicles of spindle cells with atypical vesicular nuclei and eosinophilic cytoplasm, with admixed lymphocytes (B).

were negative. Pathological findings showed an FDC sarcoma, transformed in a background of focal residual Castleman's disease.

After surgery, the patient received radiation therapy due to the high risk of recurrence; the therapy consisted of a 4,500 cGY dose over 5 weeks. The patient is currently being monitored and has shown no signs of recurrence at 9 months postoperatively.

DISCUSSION

FDC sarcoma is an extremely rare malignant neoplasm arising from FDCs. It was first described in 1986 by Monda et al.[1] Since then, fewer than 80 cases have been reported in the English language literature.[1,8] FDC sarcoma affects both sexes equally. The median age of occurrence is 47 years, with a wide range from 14 to 77 years. It can involve both nodal and extranodal sites but has a higher incidence in nodal areas, especially in the head and neck area.[1,8-10] About 60% of the cases occur in lymph nodes such as the cervical, axillary, and mediastinal lymph nodes. Also, a wide variety of extranodal sites can be affected, including the tonsils, spleen, liver, gastrointestinal tract, mediastinum, and breast. Intra-abdominal tumor locations can involve the liver, spleen, or pancreas, in addition to the mesenteric or retroperitoneal lymph nodes.[11,12]

Clinical presentation varies according to the location of the primary tumor. Intra-abdominal FDC sarcomas usually have non-specific symptoms, and a diagnosis is made with a histopathological study.[13] Of the reported FDC sarcomas, 10-20% have been shown to be associated with Castleman's disease (usually HVCD), which can be concurrent with or precede the sarcoma. Castleman's disease is a lymphoproliferative disorder of B cells and is also known as angiofollicular lymph node hyperplasia.[2,6,14]

The etiology of Castleman's disease is unclear. Clinicohistologically, Castleman's disease is categorized into three types: a unicentric hyaline-vascular type, a unicentric plasma cell type, and a multicentric plasma cell type.[4] The clinical manifestations of Castleman's disease range from asymptomatic or localized lymphadenopathy to recurrent forms of generalized lymphadenopathy with severe systemic symptoms.[3,4] In the present case, Castleman's disease manifested as a single mass in the intra-abdominal cavity without systemic symptoms and was confirmed as a hyaline-vascular type by histology. Therefore, the patient was thought to represent a case of unicentric HVCD.

Castleman's disease has been found to be associated with FDC sarcoma, suggesting that it may represent a precursor lesion. Castleman's disease-related hyperplasia acts on the expression of the p53 gene, leading to FDC dysplasia in the germinal center of the affected lymphoid follicle.[2] However, firm evidence of a clonal relationship between Castleman's disease and FDC sarcoma is lacking.[2,11,14] In the English lan-

guage literature,[2] 13 examples of FDC sarcoma have been reported to be associated with Castleman's disease. They were mostly the hyaline-vascular type and rarely the plasma cell or mixed type. The most common occurrence was intra-abdominal lesions,[2] as was the case in our patient. Histopathological examination and immunostaining with antibodies against CD21, CD25, and CD35 which are specific for FDCs and not expressed by other cells of reticular dendritic origin, are essential to obtain a correct diagnosis.[2,15,16] In the Korean literature, Lee et al.[7] reported one case of paraneoplastic pemphigus associated with FDC sarcoma arising from Castleman's disease, which developed in the abdomen.

Although the optimal treatment for FDC sarcoma is unknown because of the small number of cases, the current approach is to apply therapeutic guidelines similar to those used for high-grade soft tissue sarcomas.[17] Complete surgical resection is the therapy of choice, and the roles of adjuvant chemotherapy and radiotherapy are controversial.[2,11,16,18] However, chemotherapy or radiotherapy should be considered in cases with adverse prognosis factors, such as large tumor size (> 6 cm), intra-abdominal location, presence of coagulative necrosis, high mitotic count (> 5 per 10 high-power fields), and moderate nuclear pleomorphism.[6,11,15,19] Adjuvant radiotherapy was found to have a role in prolonging disease-free survival.[2,11,17] However, adjuvant chemotherapy has not shown consistent results.[17] Local recurrence occurs in about 40% of cases, and metastases in 28%.[8,11,16] The mortality rate is about 20%.[6,11] In the present case, we decided to administer adjuvant radiation therapy after complete excision due to the high recurrence rate associated with large and intra-abdominal masses.

In summary, we report an unusual case of an FDC sarcoma arising from unicentric HVCD in the abdominal cavity. The case showed sequential pathological changes from Castleman's disease to FDC sarcoma. Although FDC sarcoma arising from Castleman's disease is a rare disorder, it should be considered when an intra-abdominal mass is detected in a patient.

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