Korean J Gastroenterol Vol. 59 No. 1, 53-57
http://dx.doi.org/10.4166/kjg.2012.59.1.53

CASE REPORT

간암으로 오인된 Castleman 병: 증례 보고 및 문헌 고찰

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A Case of Castleman's Disease Mimicking a Hepatocellular Carcinoma: A Case Report and Review of Literature

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Castleman's disease is a rare disease characterized by lymph node hyperplasia. Although Castleman's disease can occur wherever lymphoid tissue is found, it rarely appears in the abdominal cavity, and is especially rare adjacent to the liver. Here, we report a rare case of Castleman's disease in the portal area that mimicked a hepatocellular carcinoma (HCC) in a chronic hepatitis B patient. A 40 year-old woman with chronic hepatitis B presented with right upper quadrant discomfort. Computed tomography and magnetic resonance imaging results showed a 2.2 cm-sized, exophytic hypervascular mass in the portal area. HCC was suspected. However, histologic examination revealed Castleman's disease. We suggest that Castleman's disease should be included as a rare differential diagnosis of a hypervascular mass in the portal area, even in patients with chronic hepatitis B. **(Korean J Gastroenterol 2012;59:53-57)**

Key Words: Castleman's disease; Liver neoplasms

INTRODUCTION

Castleman's disease, also known as angiofollicular lymph node hyperplasia, is characterized by non-clonal lymph node proliferation, and was first described by Benjamin Castleman in 1954.[1] Pathologically, it is classified into three types: hyaline-vascular (HV), plasma-cell (PC) and mixed type.[2] Castleman's disease is also categorized into two clinical types: unicentric and multicentric forms.[3] When based on the clinical and pathological subtypes of Castleman's disease, clinical manifestation and management of the disease are distinct.[4,5]

Unicentric Castleman's disease is most commonly found in the mediastinum. However, it can develop anywhere lymphoid tissue is found, such as in cervical, axillary, or abdominal regions.[6,7] Herein we report a case of Castleman's disease that masqueraded as hepatocellular carcinoma (HCC) in a chronic hepatitis B patient who suffered from right upper quadrant pain for one month.

CASE REPORT

A 40 year-old woman presented to a primary clinic with pain in the right upper quadrant and right flank areas a month ago. She was diagnosed with chronic hepatitis B at that time, but she received no further evaluation. Subsequently, she continued to suffer from right upper quadrant discomfort, of-

Received August 30, 2011. **Revised** September 20, 2011. **Accepted** September 20, 2011.

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Financial support: None. Conflict of interest: None.

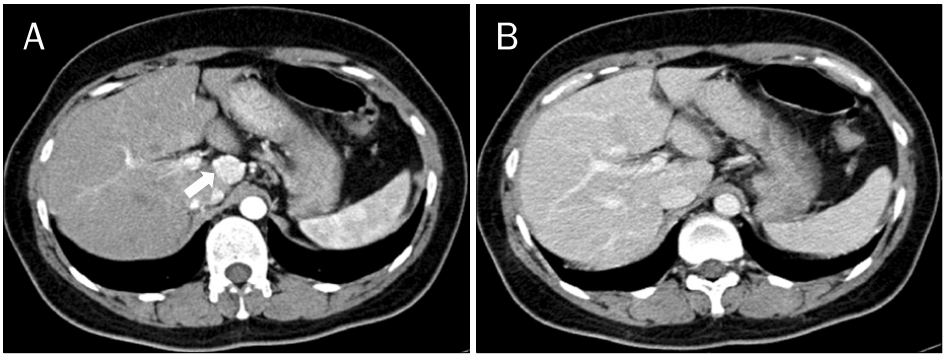

Fig. 1. Liver CT findings. (A) CT image on hepatic arterial phase showed a 2.1 cm diameter enhancing mass in the caudate lobe of the liver (arrow). (B) CT image on delayed phase showed that the nodule became isodense, compared with the liver parenchyma.

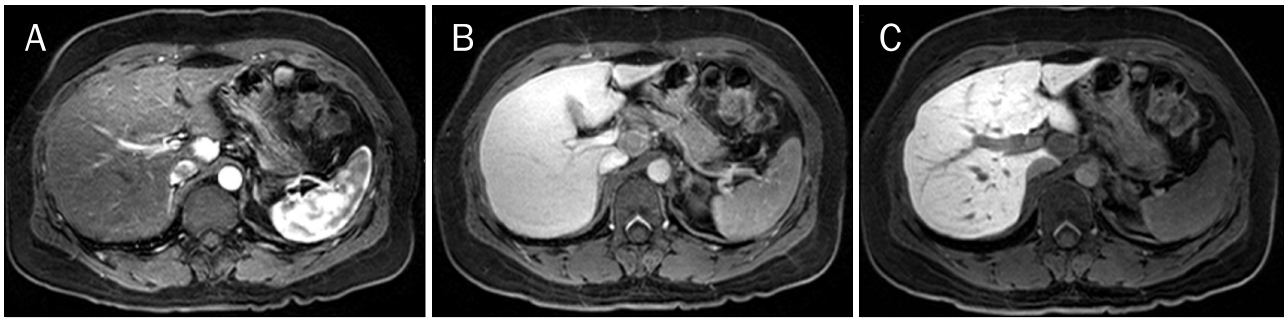

Fig. 2. Liver MRI findings. (A) Contrast-enhanced (gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid) T1-weighted MRI on hepatic arterial phase showed a 2.2 cm diameter, exophytic enhancing nodular lesion in the caudate lobe of the liver. (B, C) Contrast-enhanced T1-weighted MRI on delayed phase (at 3 minutes and 20 minutes) showed no contrast uptake in the hepatic nodule.

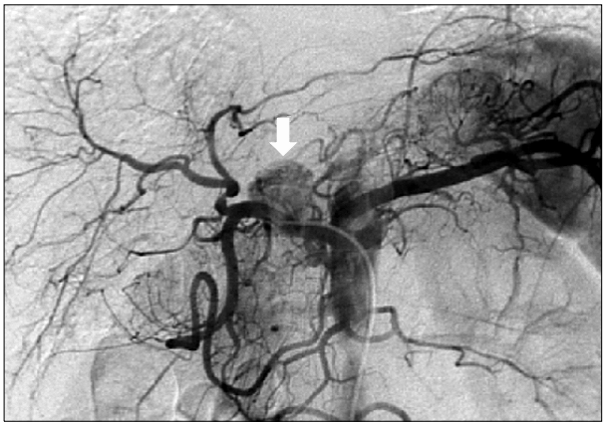

Fig. 3. Angiography findings. Celiac angiography showed a round extrahepatic hypervascular mass supplied by the common hepatic artery (arrow).

ten with a sense of fever and chills. She denied alcohol intake and smoking. She had undergone tonsillectomy 11 months ago.

On admission, her vital signs were: blood pressure, 117/66 mmHg; heart rate, 93 beats per minute; respiratory rate, 18 breaths per minute; and body temperature, 36.6°C. On physical examination, she presented right upper quadrant tenderness, but no rebound tenderness. Hepatosplenomegaly, ascites, and lymph node enlargement were not observed.

Laboratory blood analysis was performed and the following results were obtained: white blood cells, 8,000/mm^3; hemoglobin, 12.4 g/dL; hematocrit, 36.6%; platelets, 242,000/mm^3; AST, 20 IU/L; ALT, 26 IU/L; total bilirubin, 0.38 mg/dL; ALP, 228 IU/L; and GGT, 25 IU/L. Viral markers of HBV showed a positive HBsAg, a negative HBeAg, a positive antibody to HBeAg, and a serum HBV DNA level of 4,123 IU/mL. Tumor marker results were as follows (with reference ranges in parentheses): AFP, 1.46 ng/mL (0-7 ng/mL); carbohydrate CA 19-9, 12.66 U/mL (0.1-34 U/mL); and proteins induced by vitamin K antagonists (PIVKA-II), 16 mAU/mL (0.1-40 mAU/mL). CT and MRI revealed a 2.2 cm sized, exophytic hypervascular mass in the caudate lobe of the liver (Figs. 1, 2). Celiac angiography was performed because HCC was suspected. The celiac angiogram demonstrated a hypervascular mass with rapid wash-out supplied by the common hepatic artery; the mass was extrahepatic in location (Fig. 3). With these radiologic studies, we suspected an extrahepatic hypervascular mass rather than exophytic HCC.

The patient underwent laparoscopic resection of the extra-

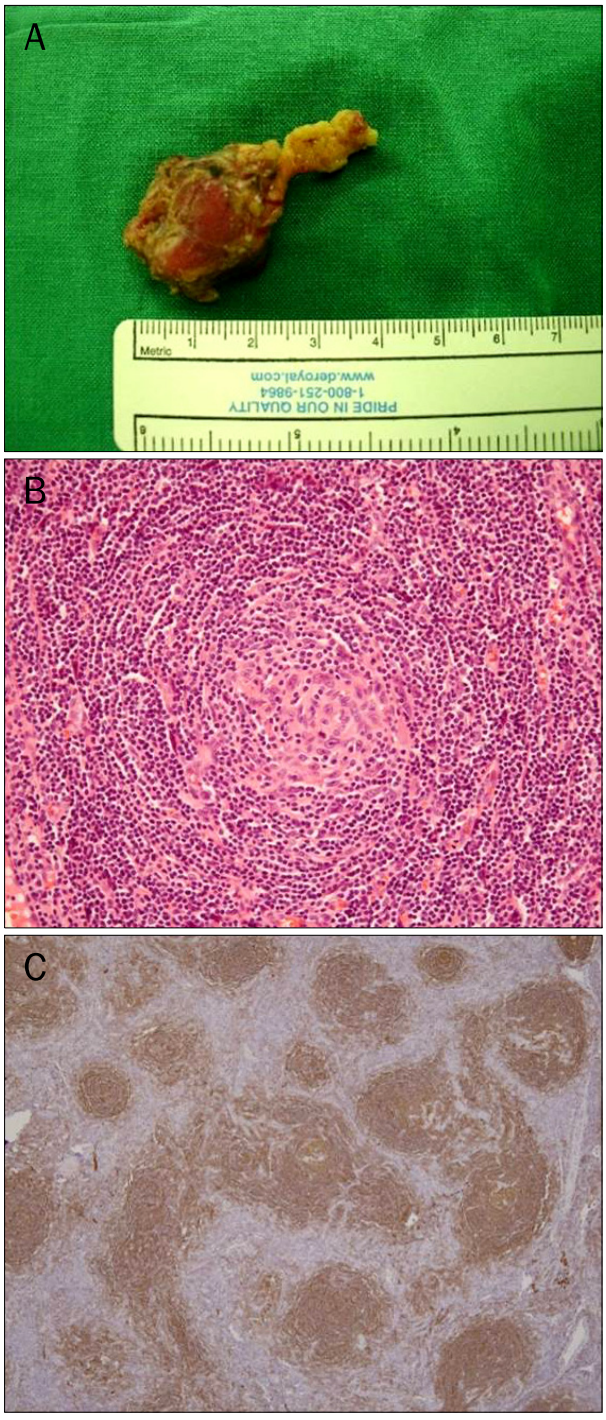

Fig. 4. Gross and histologic findings. (A) Photograph of the surgical specimen revealed a round mass with encapsulation. (B) Regressed germinal center replaced by hyalinized vessels and surrounded by concentrically arranged small lymphocytes (H&E, ×200). (C) Immunohistochemical stains for CD21 showing an expanded network of multiple tight collections of follicular dendritic cells (CD21, ×40).

hepatic mass. Gross examination disclosed an encapsulated 3×2×2 cm mass (Fig. 4A). Histopathological examination of the mass revealed hyperplastic lymph nodes characterized by evenly distributed numerous small involuted follicular centers. On high power examination, the regressed germinal centers showed a prominent central hyalinized vessel surrounded by concentric layers of small lymphocytes (Fig. 4B). The interfollicular areas showed a proliferation of small vessels admixed with many small lymphocytes along with a minor component consisting of plasma cells and immunoblasts. Immunohistochemical staining for the CD21 revealed an expanded network of follicular dendritic cells (Fig. 4C). These histological findings were compatible with the presence of HV type Castleman's disease. CT was performed 1 month after surgery, and there were no abnormal findings in the portocaval space.

DISCUSSION

Castleman's disease was first described by Benjamin Castleman in 1954. It is characterized by hyperplasia of lymphoid tissue.[1] Castleman's disease is rare and affects 100,000 to 200,000 people in the USA.[4,8] The distribution of localized Castleman's disease has been reported as 65% in the mediastinum, 16% in the neck, 12% in the abdomen, and 3% in the axilla.[7] The porta hepatis is an unusual site for Castleman's disease with only 5 porta hepatis cases reported among 73 with localized Castleman's disease in the abdominal cavity.[7] Five more cases of localized Castleman's disease adjacent to the liver have been reported.[9-17] According to the case reports for localized Castleman's disease in the portal area, most cases had abdominal pain of variable intensity and duration (as in our case), whereas patients of localized Castleman's disease are commonly asymptomatic (Table 1). In addition, most of them were HV type (Table 1).

Histopathologically, Castleman's disease is subdivided into HV, PC and mixed types.[2] The HV type displays lymphoid follicular hyperplasia with poorly formed germinal centers that are infiltrated by hyaline material and vessels. Germinal centers are concentrically arranged ("onion peel") by a mantle zone of small lymphocytes.[5,6] Dysplastic follicular dendritic cells are often seen in the interfollicular region.[5] The PC type shows a predominance of plasma cells in the interfollicular area,[2,6] while the mixed type demonstrates features of both HV and PC types.[6]

Clinically, there are two types of Castleman's disease; unicentric (localized) form and multicentric.[3-5] Within the uni-

Table 1. Cases of Localized Castleman's Disease Adjacent to the Liver

	Sex/age	Clinical presentation	Size	Imaging	Treatment	Pathology
Rahmouni et al[9]	F/48	Abdominal pain	5 cm	Hypervascular, calcifications	Surgery	HV
	M/28	Asymptomatic	3 cm	Hypervascular	Surgery	HV
Farkas et al[10]	F/40	-	4 cm	-	-	-
Peck and Lum[11]	F/29	Abdominal pain	7 cm	Hypervascular	Surgery	HV
Cirillo et al[12]	F/43	Abdominal pain	13 cm	Hypovascular, calcifications	Surgery	HV-PC
Uzunlar et al[13]	F/56	Abdominal pain	3.5 cm	Hypervascular, central low density	Surgery	HV
Al-Salamah et al[14]	M/48	Jaundice	-	-	Surgery	HV
Sato et al[15]	F/26	Asymptomatic	4.5 cm	Hypervascular	Surgery	HV
Karami et al[16]	F/5	Abdominal pain	3.7 cm	Hypervascular	Surgery	HV
User et al[17]	M/8	Sore throat, hepatosplenomegaly	4 cm	Hypovascular	Surgery	HV

F, female; M, male; HV, hyaline-vascular; PC, plasma-cell.

centric Castleman's disease, the HV type is most commonly reported (>80% of cases). The PC and mixed types are found in less than 20% of cases.[4-6] Patients with unicentric Castleman's disease usually present as asymptomatic and are diagnosed incidentally.[4,5] However, they sometimes have constitutional symptoms that are related to the involved organ.[4,5] Multicentric Castleman's disease affects more than one lymph node area, and the PC type is most common among multicentric cases.[4,5] In such cases, patients frequently have systemic symptoms such as fever, hepatosplenomegaly, ascites, night sweat, and anemia.[4,5] In some patients, the presence of multicentric Castleman's disease is associated with polyneuropathy, organomegaly, endocrine abnormality, M- protein, and sclerotic bone lesion (POEMS syndrome).[7,18]

Radiologic characteristics of Castleman's disease are quite non-specific. Ultrasonography usually reveals a hypoechogenic and homogenous mass.[7] CT shows a solid homogenous hypervascular mass when the tumor diameter is less than 5 cm, whereas larger tumors (>5 cm), because of necrosis or fibrosis, tend to have more heterogeneous enhancement with a central low-attenuation area.[8] Our review of the relevant literature also demonstrated hypervascular mass in almost all cases (Table 1). One case showed a 3.5 cm-sized well-enhanced mass with central low density. Another revealed a 4 cm-sized low-attenuated mass.[13,17] A 43 year-old female patient had a 13 cm diameter non-enhanced mass with calcification.[12] MRI of Castleman's diseases masses displays a hypodense mass in a T1-weighted image, and a hyperdense lesion in a T2-weighted image.[7,8] Images from 18-fluorodexyglucose PET demonstrates high standardized uptake values in Castleman's disease, but not as high as in active lymphoma.[8] Angiography also reveals a hypervascular lesion in Castleman's disease.[7] It is difficult to distinguish Castleman's disease from other malignancies by using radiologic methods.[12] However, needle biopsy is not recommended because an adequate tissue amount cannot be obtained, and biopsy increases the risk of bleeding or tumor seeding.[7,8]

For hypervascular lesions in the liver, differential diagnosis may include focal nodular hyperplasia, adenoma, angiosarcoma, and HCC.[11] Cholangiocarcinoma can also form a hypervascular mass, but is generally associated with biliary dilatation.[19] Malignant lesions such as lymphoma, metastasis, sarcoma, or malignant fibrous histiocytoma can be related to extrahepatic masses in the porta hepatis. However, while Castleman's disease frequently presents as a vascular mass, Castleman's disease masses usually show a lack of vascularity.[11]

Treatment of Castleman's disease is dependent upon whether it is unicentric or multicentric. In unicentric Castleman's disease, surgical extirpation is the most effective treatment for both HV and PC types. Constitutional symptoms can also be relieved by surgical resection.[5,6] Radiotherapy has been applied to inoperable unicentric Castleman's disease, but the effect of radiotherapy is controversial.[3-5,20] Preoperative embolization is an option that can make unicentric Castleman's disease surgery easier.[5,6] There is no established treatment for multicentric Castleman's disease. Surgical removal has no role for the treatment or symptom control of multicentric Castleman's disease.[4,6] Corticosteroids can be used for symptom control but may increase the risk of bacterial infection.[4,5] Chemotherapy for non-Hodgkin

lymphoma: cyclophosphamide, vincristine, doxorubicin and prednisone (CHOP) or dexamethasone (CVAD) can be used to multicentric Castleman's disease.[4,5]

Castleman's disease is a rare lymphoid disorder that occurs predominantly in the mediastinum. Here, we report an unusual case of Castleman's disease located near the caudate lobe of the liver with review of the literature. A hypervascular mass in a patient with chronic hepatitis B was presumed to be a HCC. However, pathological examination revealed a Castleman's disease mass of the HV type. On the basis of this result, Castleman's disease should be considered as a rare differential diagnosis in patients with a hypervascular perihepatic mass, even if the patients are infected with HBV.

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