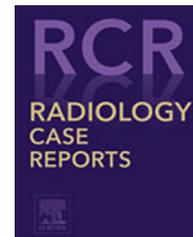


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Case Report

Hepatic Hodgkin lymphoma with delayed enhancement on CT and MRI

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ABSTRACT

Hepatic Hodgkin lymphoma is a rare disease, characterized by the presence of abundant granulofibrous stroma, and its radiological features have rarely been described. We report a 67-year-old man, who presented with liver masses that showed apparent delayed enhancement, along with systemic lymphadenopathy and musculoskeletal lesions. Repeated percutaneous needle biopsy, however, failed to confirm the diagnosis, and surgical biopsy finally revealed small amount of Hodgkin cells and Reed-Sternberg cells. In this report, the radiological features of hepatic Hodgkin lymphoma will be presented and discussed, in correlation with its histological findings.

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Case report

A 67-year-old man, who had been suffering from persistent fever for more than a month, was admitted to our institution to scrutinize liver mass and multiple lymphadenopathy in the

neck and abdomen. Abnormal laboratory test data on admission included mild leukocytosis, mildly elevated liver function tests, and moderately to markedly elevated C-reactive protein and soluble interleukin-2 receptor. Neither hepatitis B virus surface antigen nor hepatitis C virus antibody was positive. Other tumor

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Declaration: All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This case report has never been published or is not under consideration for publication elsewhere in English or other language. Informed consent was waived by our institutional review board in this case report. This study was not funded by any company.

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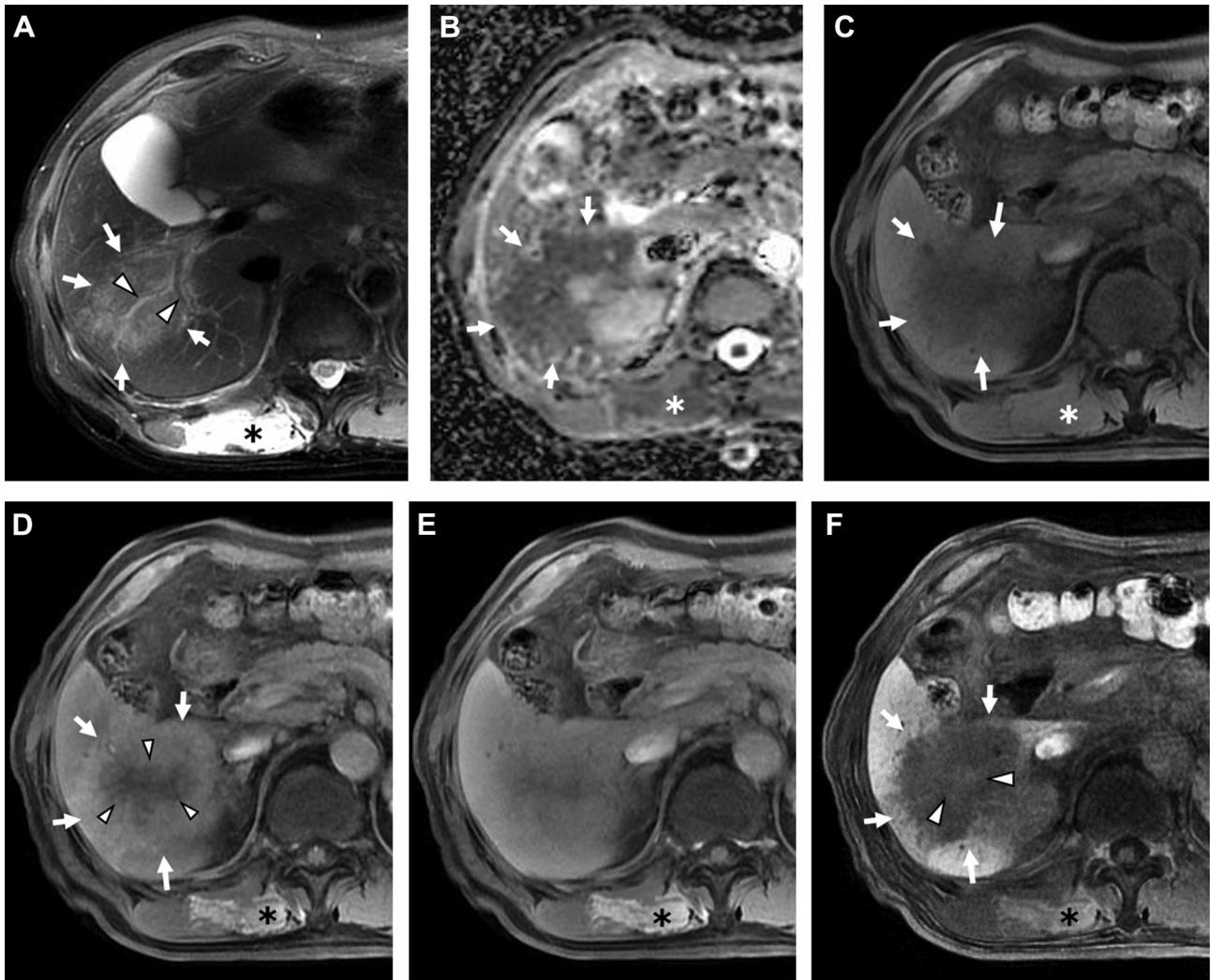


Fig. 1 – Magnetic resonance (MR) imaging of the liver. (A) T2-weighted image with fat suppression (repetition time [TR]/echo time [TE] = 8000/85.9 ms). A slightly hyperintense mass of 7 cm in its largest dimension is seen (arrows). Note branches of portal vein are penetrating the mass without occlusion (arrowheads). There is another hyperintense mass involving the right paraspinal muscle (asterisk). (B) Apparent diffusion coefficient (ADC) map 2 cm caudad to panel A, calculated from echo-planar diffusion-weighted image (TR/TE = 7000/64.5 ms, b factors 0 and 800 s⁻¹). ADC value of the hepatic mass (arrows) was 0.99×10^{-3} mm²/s. The lesion in the right paraspinal muscle also shows similar ADC value (asterisk). (C) Precontrast 3D T1-weighted image (TR/TE/flip angle [FA] = 6.3/2.2 ms/15°) through the same slice as panel B. The mass is shown as a faintly hypointense area (arrows). The lesion in the right paraspinal muscle shows almost similar signal intensity as the surrounding tissue (asterisk). (D) Arterial phase of the dynamic scan obtained using bolus tracking method through the same slice as panel B. Note faint enhancement of the mass (arrows) with central part sparing (arrowheads). The lesion in the right paraspinal muscle also shows apparent enhancement (asterisk). (E) Transitional phase (180 seconds) of the dynamic scan through the same slice as panel B. The mass exhibits mostly homogeneous enhancement, suggesting delayed enhancement of the central part. No necrosis is evident. The lesion in the right paraspinal muscle also shows persistent enhancement (asterisk). (F) Hepatobiliary phase of gadoxetate enhancement obtained 15 minutes after gadoxetate enhancement through the same slice as panel B. Note fuzzy margin of the mass, suggesting the infiltrative nature of the lesion (arrows). There is a faint uptake of contrast in the central part of the mass (arrowheads), corresponding to the spared area in the early enhancement in panel D. The lesion in the right paraspinal muscle shows apparent persistent enhancement (asterisk).

markers including carcinoembryonic antigen, carbohydrate antigen 19-9, alphafetoprotein, and protein induced by vitamin K absence or antagonist-II, were all negative.

Magnetic resonance imaging (MRI) using gadoxetate (Primovist; Bayer, Osaka, Japan) enhancement was performed

for the liver lesion; an ill-defined, irregularly shaped mass of 7 cm in diameter was found in the right hepatic lobe, showing slight T1 and T2 prolongation, diffusion restriction, and vessel penetration sign, along with several satellite lesions. The central part of the mass showed delayed enhancement on the

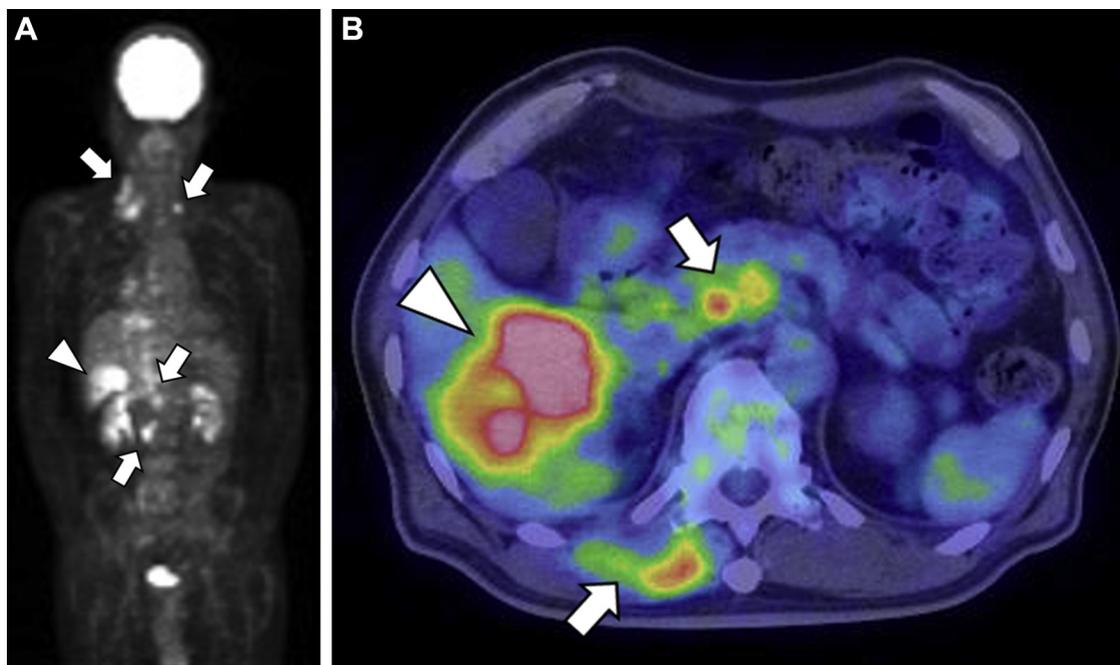


Fig. 2 – Fluorine 18 fluorodeoxyglucose (^{18}F FDG) positron emission tomography-computed tomography (PET-CT). (A) Coronal maximum intensity projection image. There are uptakes of radioisotope in the cervical, mediastinal, and abdominal lymph nodes (arrows), and in the liver mass (arrowhead), as well. (B) Transaxial image through the level of the liver mass. ^{18}F FDG uptake is evident in the liver mass (arrowhead), right paraspinal muscle, and porta hepatis lymph nodes (arrows). The maximum standardized uptake value of the liver mass was 8.59.

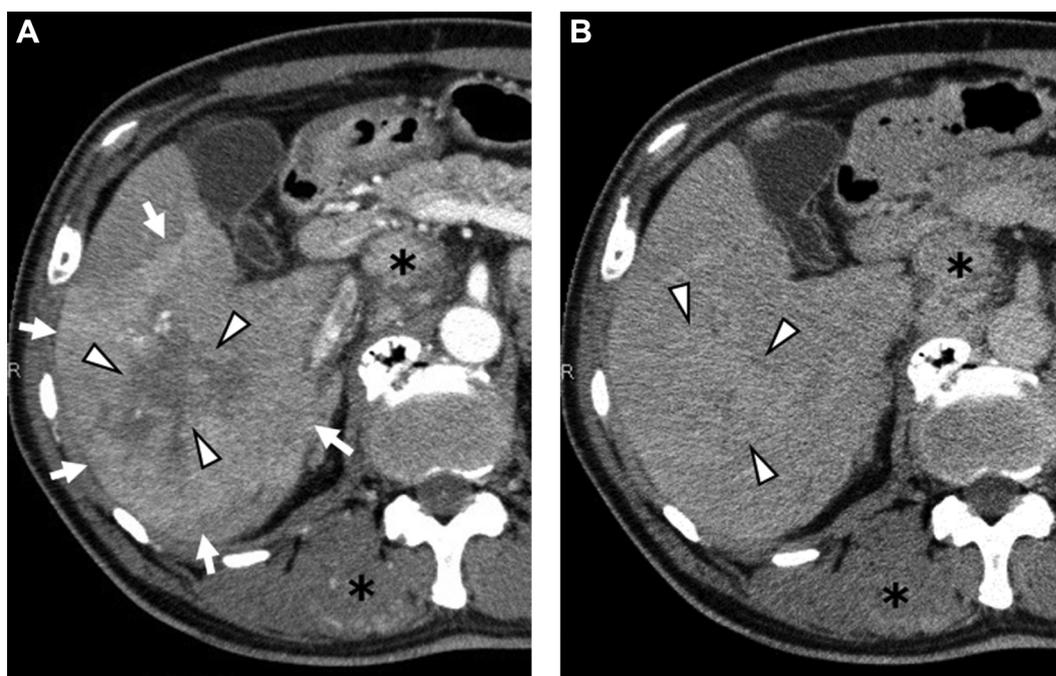


Fig. 3 – Dynamic CT obtained 3 months after MR imaging using total volume of 600 mgI/kg iodine contrast medium, injected in 30 seconds. (A) Arterial phase obtained 40 seconds after the commencement of contrast medium injection. The mass showed enhancement (arrows) with central part sparing (arrowheads). The porta hepatis lymph nodes and right paraspinal muscle are also involved by the disease (asterisks). (B) Equilibrium phase obtained 240 seconds after the commencement of contrast medium injection. The whole lesion showed persistent enhancement, with the central part showing more prominent enhancement as compared with the periphery (arrowheads). No necrosis is evident. The lesions in the porta hepatis lymph nodes and right paraspinal muscle also show faint persistent enhancement (asterisks).

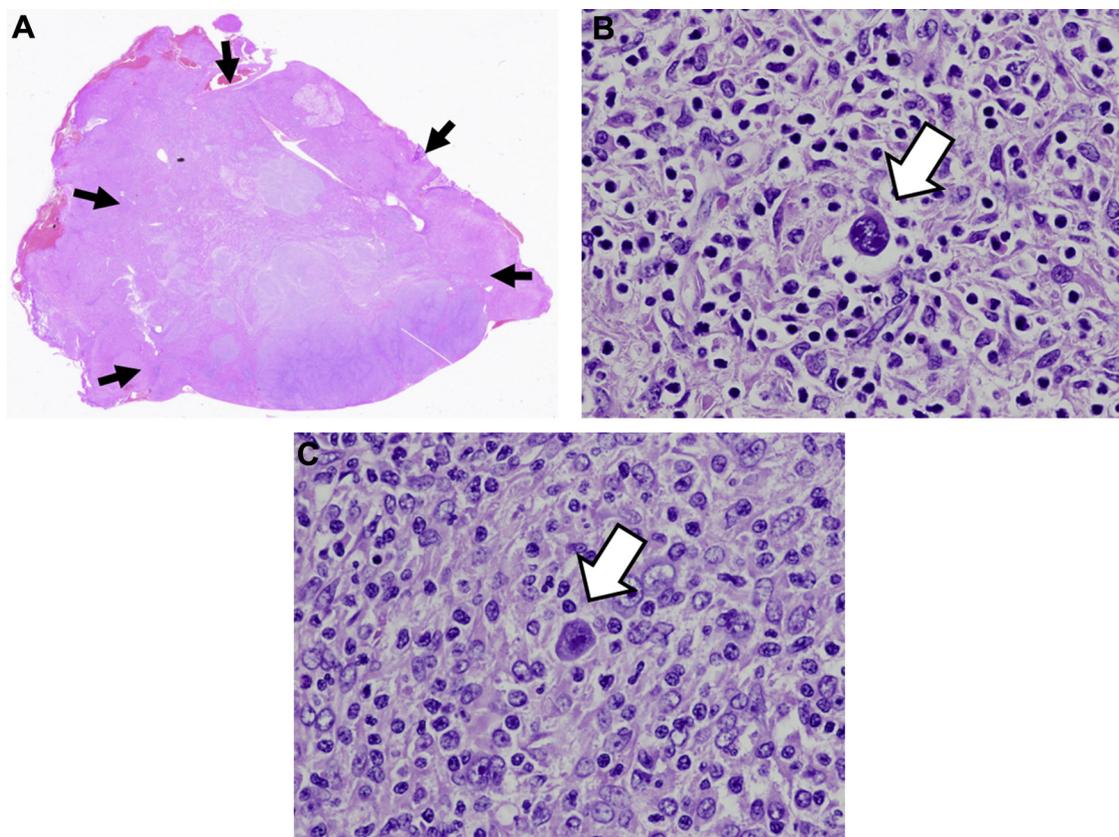


Fig. 4 – Surgically resected specimen of the liver. (A) Low magnification view with hematoxylin and eosin staining. The mass is shown with arrows, measuring about 2 cm in its largest dimension. (B) High magnification view revealed a Reed-Steinberg cell (arrow) in the abundant granulomatous background. (C) High magnification view at other site of the specimen revealed a Hodgkin cell (arrow) in the abundant granulomatous background.

dynamic phase, and also faint uptake of gadoxetate on the hepatobiliary phase (Fig. 1). Fluorine 18 fluorodeoxyglucose (^{18}F FDG) positron emission tomography-computed tomography (CT) showed strong uptake of the radioisotope at the liver mass, with the maximum standardized uptake value of 8.59 (Fig. 2). Multiple lesions of similar ^{18}F FDG uptake were found in the cervical and abdominal lymph nodes and musculoskeletal system (Fig. 2). Clinicoradiologically, malignant lymphoma was strongly suspected, and percutaneous needle biopsies were performed for the cervical lymphadenopathy once, and for the multiple liver masses twice; however, only inflammatory to fibrogranulomatous tissues, or epithelioid cell granulomas were found, with no evidence of malignant cells. A possibility of sarcoidosis was considered, which was denied by the absence of uveitis, typical pulmonary or myocardial lesions, and negative angiotensin converting enzyme. A conservative therapy using 30 mg prednisolone per day was given, but follow-up dynamic CT using iodine contrast medium (Iomeron 350, Eisai Co Ltd, Tokyo) obtained 3 months after admission revealed apparent disease progression: the liver mass increased in size, showing prominent delayed central enhancement that suggested presence of abundant fibrous stroma, without evident necrosis (Fig. 3). To make a definitive diagnosis, surgical biopsy was performed for one of the liver nodules located at the edge of the lateral segment and intra-peritoneal enlarged lymph nodes. Microscopically, the

specimens revealed a small number of Hodgkin cells and Reed-Sternberg cells scattered in the abundant fibrogranulomatous background tissue (Fig. 4). A final diagnosis of secondary hepatic Hodgkin lymphoma (HL), mixed cellularity type, was made. The patient was given twelve courses of chemotherapy using adriamycin, bleomycin, vinblastine, and dacarbazine, and showed complete response 10 months later.

Discussion

Hodgkin disease, or HL, is a relatively rare entity, accounting for less than 10% of all malignant lymphoma [1–4]. Hepatic lymphoma is usually non-Hodgkin diffuse large B-cell lymphoma [1], and its radiological features have been well described [2,3,5]. They may exhibit various imaging findings; however, typically show relatively homogeneous mass with mild T1 and T2 prolongation, strong diffusion restriction, mild enhancement, and vessel penetration sign [2,3,5]. On the other hand, primary hepatic HL is extremely rare, whereas secondary hepatic involvement by HL is relatively commonly encountered, with an incidence of around 20% of all HL [1–4], and little has been reported on its radiological features [6]. Because HL is very chemo- and radio-sensitive, early precise diagnosis benefits patients' prognosis [1,4]. In our case, several imaging features were similar to those of non-Hodgkin

lymphoma (NHL), as previously reported. However, one peculiar finding was a delayed enhancement without evident necrosis, which was observed in the central part of the main liver mass both on MR imaging and dynamic CT (Figs 1, 3), which has never been described in the literature in hepatic HL.

Histologically, HL is characterized by the presence of Hodgkin cell and Reed-Sternberg cell within abundant fibrogranulomatous background tissue [1–6]. It has been well known that presence of fibrous stroma results in delayed enhancement when extracellular contrast medium is given [7,8]. Because iodine contrast medium for CT is a purely extracellular agent, whereas gadoxetate is half extracellular and half tissue-specific agent [9], it is reasonable that this delayed enhancement was more prominent on CT rather than on MRI in our case. According to the previous study in which HL and NHL were compared in the cervical lymphomatous nodal lesions, HL showed significantly higher density than NHL on the delayed phase of CT after iodine contrast medium administration [10]. Findings in our case is consistent with this observation, and we consider that this delayed enhancement without evident necrosis could be a sign to distinguish HL from NHL in the liver as well.

As for the definitive diagnosis of HL, verifying the presence of Hodgkin cell and Reed-Sternberg cell is essential, but it has been known that it is occasionally difficult to obtain sufficient amount of tissue with percutaneous needle biopsy, because the number of Hodgkin cells and Reed-Sternberg cells can be so small, being scattered within the abundant fibrogranulomatous background tissue [1,4]. Similarly, in our case, despite clinicoradiological data strongly suggesting the diagnosis of malignant lymphoma, percutaneous needle biopsy performed 3 times in total for the cervical nodal lesion and hepatic masses, failed to provide the correct diagnosis of HL. In mediastinal HL, therefore, surgical open biopsy is recommended rather than percutaneous needle biopsy when the disease is suspected [4].

In conclusion, in patients with liver mass along with clinicoradiological features strongly suggesting malignant lymphoma, diagnosis of HL should be considered when

delayed enhancement is evident on CT or MRI, or percutaneous needle biopsy reveals only inflammatory to granulomatous tissues with no malignant cells. Then, larger specimens should be obtained with surgical biopsy to confirm the diagnosis.

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