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Letters to the Editor

Mantle Cell Lymphoma Superimposed on Multicentric Castleman's Disease

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TO THE EDITOR

In August 2010, a 51-year-old man was transferred to our Hematology & Oncology Department from another hospital with a 1-month history of unknown fever, anasarca, and lymphadenopathy of bilateral neck, bilateral axilla, and bilateral inguen. Chest X-ray showed bilateral pleural effusion and swellings in the lymph nodes of the neck, axilla, mediastinum, paraaorta, and inguen ; furthermore, ascites and pleural effusion were detected on computed tomography. Positron emission tomography indicated the abnormal uptake in these lymph nodes. Laboratory tests indicated the presence of neutrophilia (white blood cells 13900/μL : band 4.0%, segmented 71.8%, eosinophils 1.0%, lymphocytes 19.2%, monocytes 3.0%, atypical lymphocytes 1.0%), and the increase of lactate dehydrogenase (286 IU/L), serum immunoglobulin (IgG 2,527 mg/dL, IgA 203 mg/dL, IgM 178 mg/dL), soluble interleukin-2 receptor (2,320 U/mL), and interleukin-6 (14.9 pg/mL). Viral tests for HBsAg, HCV antibody, and HIV antibody were negative.

The patient underwent biopsy via the right inguinal lymph node. Numerous follicles with atrophic germinal centers were scattered throughout the cortex and medulla in the lymph node, and the small vessel network in the interfollicular area and proliferation of small vessels in follicles were consistent with hyaline-vascular variant Castleman's disease (Figs. 1 & 2).

The cytology of pleural effusion and bone marrow (BM) indicated an increase in plasma cells. Two-color flow cytometry using anti-κ and-λ antibody did not confirm the clonality of B cells in the inguinal lymph node, pleural effusion, and BM. However, rearrangement of the *IgH* gene was detected in these samples by polymerase chain reaction (data not shown). On the other hand, chromosomal analysis using G-banding showed the translocation t(11;14)(q13;q32) in one of 20 cells with metaphase cells in pleural effusion; however, *Bcl1/IgH* gene was not detected in these samples. Lymphocytes from lymph node were found to be negative for human herpes virus-8 by polymerase chain reaction. Subsequently, immunohistochemical staining performed on sections of lymph node sample revealed that some broad mantle zones consisted of cells positive for CD20, CD5, and cyclin D1 (Figs. 3 & 4). Epstein-Barr virus-encoded RNA (EBER)-positive cells were not detected in lymph node or BM (data not shown). These findings were consistent with mantle cell lymphoma (MCL) superimposed on multicentric Castleman's disease (MCD). After one cycle of hyper-CVAD/high-dose MTX + Ara-C therapy (hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone combined with high-dose methotrexate and cytarabine), the pleural effusion and ascites diminished, and the enlarged lymph nodes were reduced in size. With regard to the occurrence of non-Hodgkin's lymphoma (NHL) and Castleman's disease (CD) in the same patient, diagnosis of NHL is concurrent with CD or follows the diagnosis of CD. In these cases, various histological features of NHL have been reported.[1] According to the study reported by Larroche *et al*.,[1] the histology of NHL in 3 of 6 CD patients with NHL was MCL, and all three patients died after treatment. Furthermore, the type of CD in 5 of the 6 patients was MCD. On the other hand, we had to differentiate this case from MCL resembling the plas-

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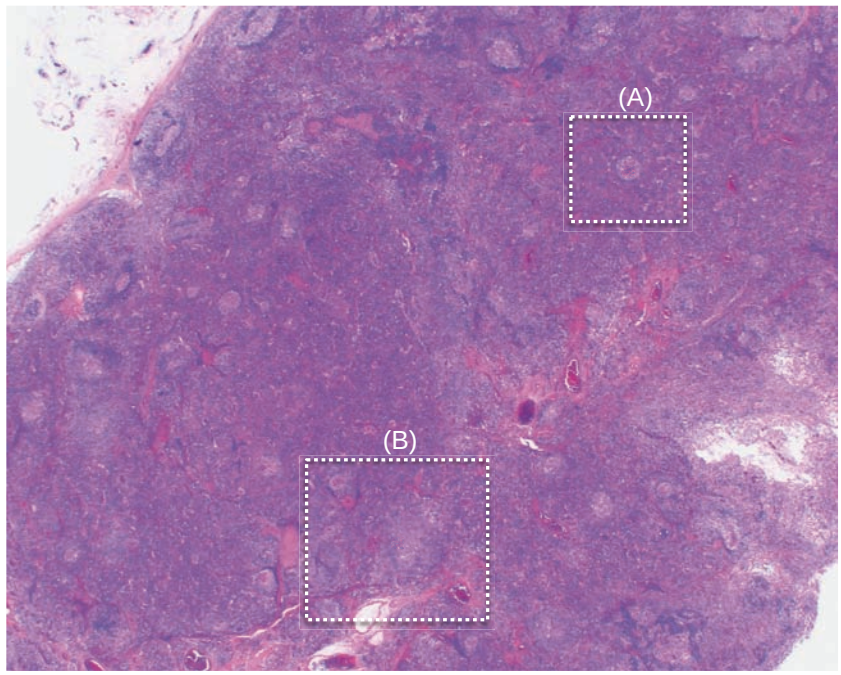

Fig. 1. Hyaline-vascular variant Castleman's disease with mantle cell lymphoma. (*A*) The white dotted line indicates a representative follicle. (*B*) This area contains a large follicle compared with others. Interfollicular areas contain a network of small vessels.

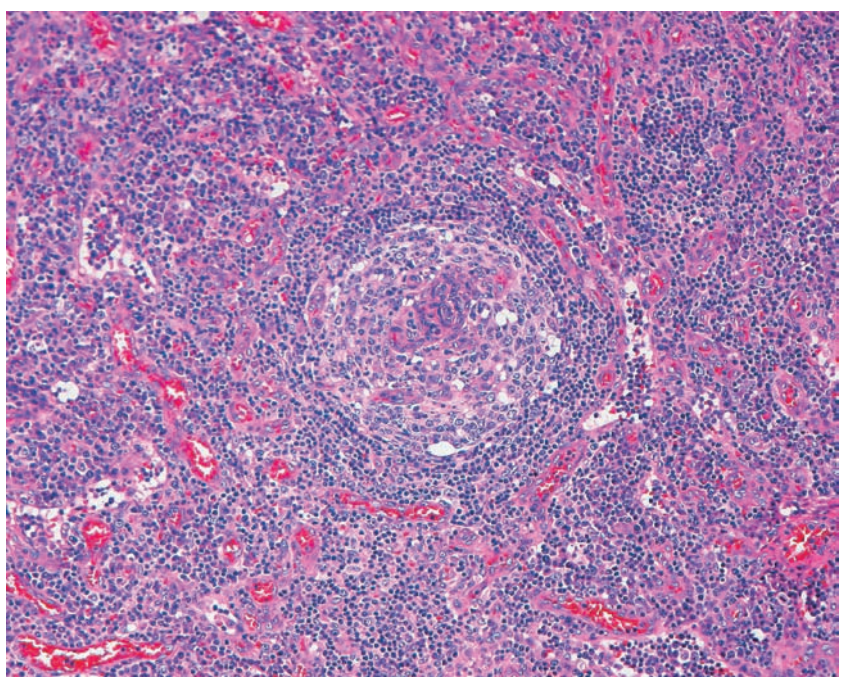

Fig. 2. Follicle in hyaline-vascular variant Castleman's disease. The atrophic germinal center of this follicle, which is indicated in area (*A*) of Fig. 1, showed proliferation of small vessels, and some follicular dendritic cells were mildly atypical.

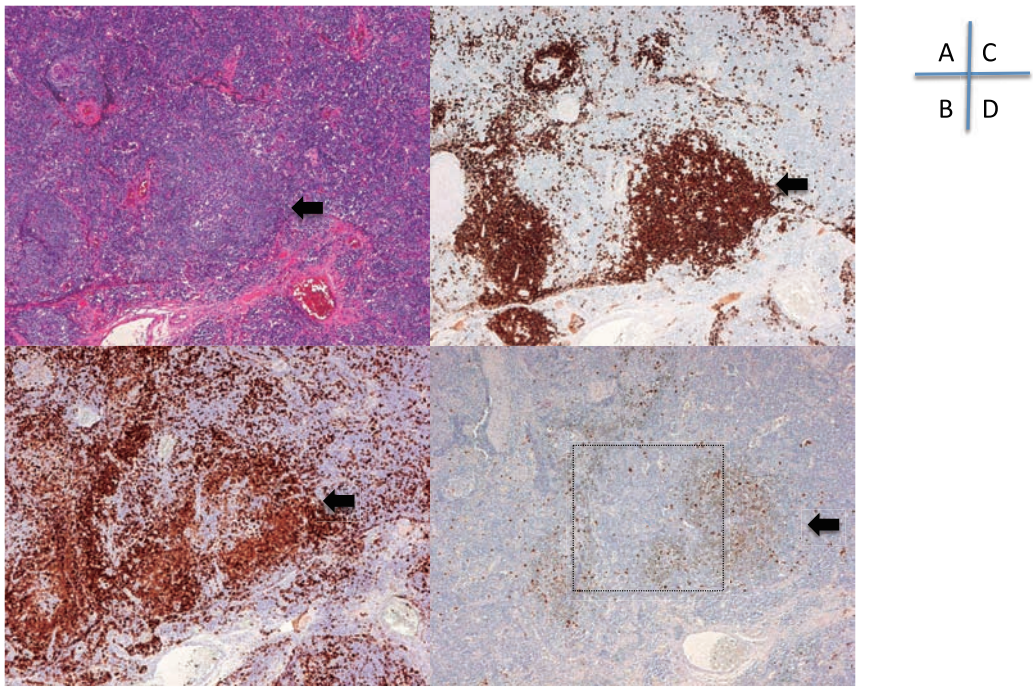

Fig. 3. Immunohistochemical staining of the large follicle in area (*B*) of Fig. 1. (**3A**) Attenuated germinal center surrounded by a broad mantle zone (indicated by *arrow*). (***3B***) Broad mantle zone consists of CD5-positive cells. (***3C***) Both the germinal center and the broad mantle zone consist of CD20-positive cells. (***3D***) The broad mantle zone contains numerous cyclin D1-positive cells.

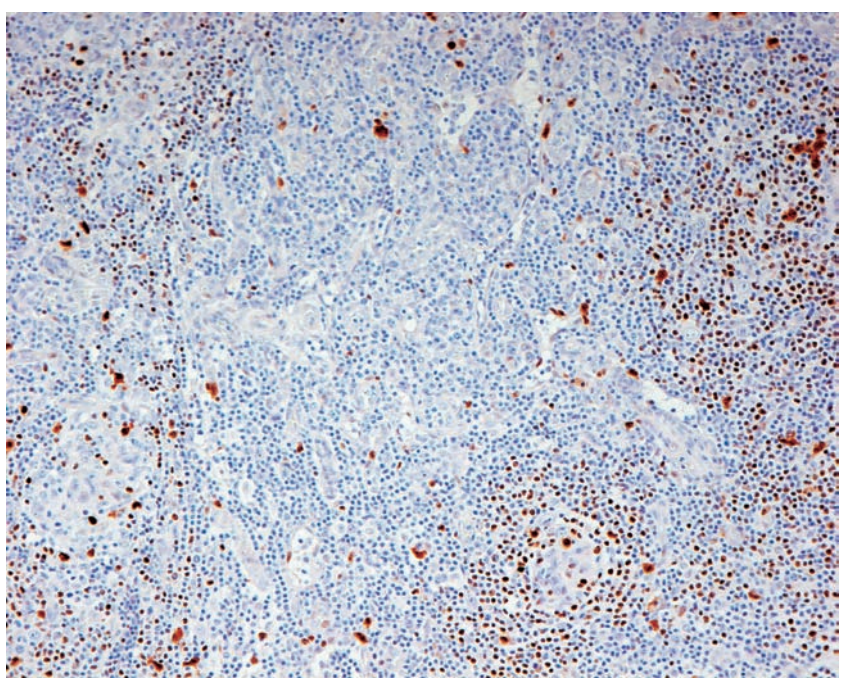

Fig. 4. Magnification of the area indicated by the dotted line in area (*D*) in Fig. 3. Nuclei of lymphocytes in the mantle zone surrounding the atrophic germinal center were positive for cyclin D1.

ma cell type of CD, as reported by Yatabe *et al*.[2] However, hyper-γ-globulinemia and the increase of interleukin-6 in serum and plasma cells in BM and pleural effusion were compatible with the characteristics of CD, as Levine reported that NHL associated with CD shares common features with the lymphoma seen in various types of immune deficiency, which is characterized by aggressive clinical course and short survival.[3] Although the propensity for CD patients to develop NHL might be explained by the underlying immune defects that characterize CD, our patient was negative for HIV and human herpes virus-8. Therefore, we hypothesize that cytokine stimulation in CD may expand clonal B cells with genetic abnormalities, such as *IgH* gene translocation.

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