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Classical Hodgkin lymphoma concurrently evolving in a patient with marginal zone B-cell lymphoma of the spleen

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Abstract Combination of the splenic marginal zone B-cell lymphoma (SMZL) and classical Hodgkin lymphoma (cHL) is extremely rare. We report a unique case with concurrent SMZL and cHL. The patient was a 63-year-old man who presented with fatigue and anemia, showing a splenomegaly and retroperitoneal lymphadenopathy. A splenectomy revealed monotonous marginal zone lymphocytic infiltrates and numerous large Reed-Sternberg–like cells. Flow cytometry revealed a κ light-chain–restricted CD5 (−), CD23 (−) B-cell population. DNA polymerase chain reaction analysis confirmed the presence of clonal rearrangement of the immunoglobulin heavy-chain gene. Immunohistochemical studies revealed that the large atypical cells were CD30 (+), CD15 (weakly +), CD20 (−), CD45 (−), Pax5 (weakly +), BOB.1 (−), and Oct2 (−), indicating the coexistence of SMZL with cHL. After the chemotherapy, the patient achieved a clinical/radiologic remission, whereas cHL was detected in liver and bone marrow subsequently. The case indicates that both components of lymphoma can present concurrently as a composite form of lymphoma and both need to be treated adequately.

Keywords: Composite lymphoma; Splenic marginal zone lymphoma; Hodgkin lymphoma; Reed-Sternberg cells; Non-Hodgkin lymphoma; Spleen

1. Introduction

Lymphomas are divided into Hodgkin lymphomas and non-Hodgkin lymphomas. However, a lymphoma with features of both Hodgkin lymphoma and non-Hodgkin lymphoma in the same organ or mass has been reported. When 2 histologically distinct architectural and cytologic subtypes of lymphoma occur simultaneously in the same anatomic site or tissue, it is called “composite lymphoma” [1]. In contrast, non-Hodgkin lymphoma may contain large cells with the morphologic features of Hodgkin Reed-Sternberg (RS) cells. In these cases, RS cells or its variants are present in the background of non-Hodgkin lymphoma. This type of presentation is considered Hodgkin-like transformation. Although substantial cases of composite lymphoma of classical Hodgkin lymphoma (cHL) and B-cell lymphoma have been reported, combination of the splenic marginal zone B-cell lymphoma (SMZL) and cHL is extremely rare.

In this article, we report a case with concurrent SMZL with scattered cHL cells, diagnosed after splenectomy. The patient was treated with a regimen predominantly for low-grade B-cell lymphoma and achieved a clinical/radiologic remission. However, several months later, cHL was detected in the liver and bone marrow and caused liver failure. This case suggests the presence of both Hodgkin and non-Hodgkin components of lymphoma and both need to be treated adequately.

2. Case report

A 63-year-old man presented with 3 weeks of fatigue. Peripheral blood evaluation revealed a hemoglobin level of 8.9 g/dL, a platelet count of 224×10^9/L, a white blood cell count of $6.5 \times 10^3/\mu$L with a normal differential, a normal

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lactate dehydrogenase level, a direct antiglobulin test positive for both anti-IgG and anti-C3d, and a cold agglutinin titer of 1:128 (normal range, <1:4). Bone marrow review showed hypercellularity with erythroid hyperplasia. Iron stores are absent. The marrow contains a single lymphoid infiltrate composed of small lymphoid cells with slightly open nucleus and clear cytoplasm, suspicious but not diagnostic of a low-grade B-cell lymphoma. Computerized tomography imaging of the abdomen and pelvis showed marked splenomegaly and retroperitoneal lymphadenopathy. Histologic findings of the retroperitoneal lymph node are suspicious, but not diagnostic for a non-Hodgkin lymphoma mainly because of crush artifact and fibrosis.

Two months later, a splenectomy was performed because progressive splenomegaly was developed despite the treatment with cyclophosphamide and prednisone. A diagnosis of splenic marginal zone lymphoma (SMZL) with atypical RS-like cells was rendered. Subsequently, treatment with 3 cycles of cyclophosphamide, vincristine, and prednisone (COP) was initiated. Two months after the completion of the treatment, the patient developed a nonobstructive jaundice and hepatic failure. At this time, the patient had resolution of his previously positive direct antiglobulin test for anti-IgG and anti-C3d. Despite near resolution of hepatic failure with salvage chemotherapy with etoposide, vincristine, Adriamycin, cyclophosphamide, and prednisone, the patient died of neutropenic sepsis.

3. Materials and methods

Lymph node, liver biopsy specimens, and representative sections of spleen were submitted for histologic study. The tissues were fixed in 10% neutral-buffered formalin and paraffin-embedded. The bone marrow biopsies were also submitted for routine histology after fixation and light decalcification. Tissue sections were stained with hematoxylin and eosin (H&E). Immunohistochemical staining was performed on paraffin-embedded sections using a standard avidin-biotin-peroxidase method with heat-induced epitope retrieval. Antibodies used were CD3, CD20, CD30, CD45 (DAKO, Carpinteria, Calif), CD15 (Becton Dickinson [BD], San Jose, Calif), CD5 (Novocastra Labs, Newcastle upon Tyne, UK), Pax5 (Zymed Laboratories, South San Francisco, Calif), BOB.1 (Santa Cruz Biotechnology, Santa Cruz, Calif) and Oct2 (Lab Vision Corp, Fremont, Calif). The sensitivity and specificity of the stains were confirmed by parallel staining of appropriate control tissue.

Flow cytometric studies were performed with fresh tissue of spleen and bone marrow aspirate by using a FACS Calibur flow cytometer (BD). Antigen expression on abnormal populations was compared with appropriate isotopic controls to determine positive and negative cutoff values. Antibodies used were CD2, CD3, CD4, CD5, CD10, CD20, CD23, HLA-DR (BD), κ and λ (Biosource, Camarillo, Calif). The analysis gates for lymph node and bone marrow were based on forward and side-scatter parameters.

Polymerase chain reaction (PCR) analysis for immunoglobulin heavy-chain (IgH) gene rearrangement was performed on paraffin-embedded spleen tissue using primers complementary to the FRIII and JH regions. Post-PCR analysis was performed by capillary electrophoresis. Integrity of DNA is assessed by amplification of a segment of the beta-globin gene.

Epstein-Barr virus (EBV) RNA in situ hybridization studies for EBER (latency marker) and Not 1 (lytic marker) were performed on paraffin sections using a 30-base oligonucleotide complementary to a portion of the EBER-1 gene as described previously [2].

4. Pathologic findings

The removed spleen weighed 980 g with a smooth capsule, a red-tan cutting surface with multiple small, well-

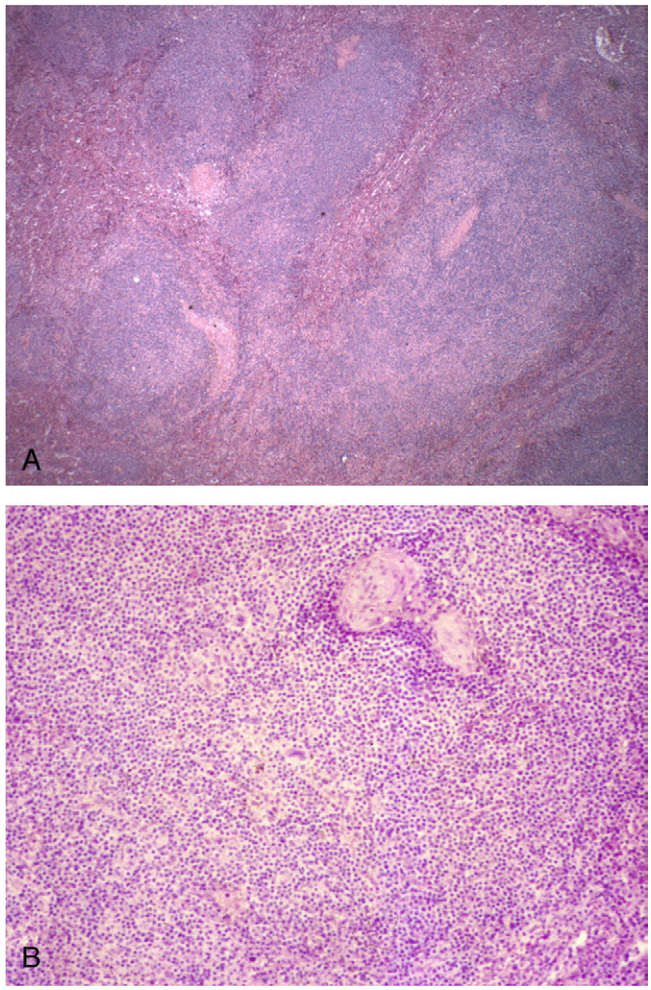

Fig. 1. Histologic examination of the spleen. (A). Expansion of white pulps with lymphoid cells in a marginal zone pattern (H&E, scanning magnification ×4). (B). Higher magnification of white pulp showing small to medium-sized cells with abundant pale cytoplasm (H&E, medium-power magnification ×10).