Case Study

Lymph Node Infarction in Classical Hodgkin’s Lymphoma

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Among lymphoproliferative disorders, lymph node infarction appears to be most frequently seen in diffuse large B-cell lymphoma, followed by follicular lymphoma, with other types being rare. We experienced one such case, classical Hodgkin’s lymphoma (cHL) associated with lymph node infarction, in which Reed-Sternberg (RS) cells were positive for CD15, CD30, fascin, PAX-5, p53, latent membrane protein-1 (LMP-1), Bcl-2, and EBV-encoded small non-polyadenylated RNAs. Furthermore, RS cells in the infarcted area were still positive for CD30, fascin, p53, and Bcl-2. For definitive diagnosis of nodal lymphomas including Hodgkin’s lymphoma, identification of the effacement of normal nodal architecture is essential. Although this could not be evaluated in our case because of predominant reactive follicular hyperplasia with interfollicular distribution of RS cells, the presence of large cells with RS cell-related molecules together with the distorted distribution of cCD3-positive cells and CD20-positive cells led us to make a definitive diagnosis of cHL. It is, therefore, considered that immunohistochemical evaluation of the infarcted lymph node is, at least on some occasions, still informative for more accurate diagnosis of lymphoid neoplasia. Hodgkin’s lymphoma should also be considered when one encounters lymph node infarction. (J Clin Exp Hematopathol 52(1): 35-39, 2012)

Keywords: lymph node infarction, malignant lymphoma, Hodgkin’s lymphoma, immunohistochemistry

INTRODUCTION

Lymph node infarction is a rare pathologic process because of its abundant vascularity,1 but the process is frequently associated with concurrent or subsequent malignant lymphoma.2,3 Among malignant lymphoproliferative disorders, lymph node infarction appears to be most frequently seen in diffuse large B-cell lymphoma (DLBCL), followed by follicular lymphoma (FL),4,5 with other types being rare. To our knowledge, only a single case of classical Hodgkin’s lymphoma (cHL) has been reported as one of 10 cases of malignant lymphoma associated with lymph node infarction in the English literature, but the report focused on antigen preservation.7 Here we report a second such case including clinicopathologic features.
(LMP-1), CD10, Bcl-2, Bcl-6, MUM-1 (Dako, Glostrup, Denmark), fascin (Lab Vision, Fremont, CA, USA), and PAX-5 (Biocare Medical, Concord, CA, USA). The antigen retrieval step was performed using Bond Epitope Retrieval Solution 1 (citrate-based, pH6.0, Mitsubishi Chemical Medience, Tokyo, Japan).

In situ hybridization (ISH) was performed to detect Epstein-Barr virus (EBV)-encoded small non-polyadenylated RNAs (EBER) using EBER PNA probe and PNA ISH Detection Kit (Dako) according to the manufacturer’s instructions.

As shown in the frozen sections, one of the two lymph nodes was totally infarcted (7.5 × 6.5 mm) (Fig. 1A), and the other presented reactive follicular hyperplasia (Fig. 1B). Interfollicular area of the latter node was focally expanded with occasional mononuclear large to giant cells. In the non-frozen specimen, there were no infarcted areas and a process similar to non-infarcted frozen lymph node, with the exception of some multinucleated giant cells resembling classical/diagnostic Reed-Sternberg (RS) cells (Fig. 2A & 2B), was observed. Vascular wall thickening/luminal narrowing or thrombosis/embolism was not evident around infarcted lymph nodes.

Fig. 1. Histological findings of viable and infarcted areas. (IA) Whole mount view of the resected frozen lymph node. One of the lymph nodes (left) is totally infarcted. (IB & IC) Low power view of viable and infarcted areas. Expansion of interfollicular area is present at the subcapsular region in the former (IB), while nodal structure is not appreciable due to infarction with heterogeneous staining in the latter (IC). (IA) H&E stain, scale bar = 5 mm ; (IB&IC) H&E stain, scale bar = 1 mm
Fig. 2. Histological and immunohistochemical findings of viable and infarcted areas. (2A & 2B) Histological features of the viable area. Several diagnostic/classical Reed-Sternberg cells (one with emperipolesis) are present with small lymphocytes and plasma cells in the background. ([2A] H&E stain, scale bar = 200 µm; [2B] H&E stain, scale bar = 40 µm). (2C-2F) Immunohistochemical features of the viable area: Reed-Sternberg cells are CD15+ (2C), CD20+ (2D), CD30+ (2E), and LMP-1+ (2F). Immunohistochemical features of the infarcted area: Giant cells are CD30+ (2G) and LMP-1+ (2H). [Immunoperoxidase stain with hematoxylin counterstain: (2C) scale bar = 40 µm; (2D-2H) scale bar = 100 µm]
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Phenotypic features of the cells resembling RS cells in both viable and infarcted areas are shown in Table 1. RS cells in the viable area were positive for CD15, CD30 (Fig. 2), fascin, PAX-5, p53, and Bcl-2, but were negative for cCD3, CD20, CD79a, CD10, Bcl-6, and MUM-1. Moreover, CD30, fascin, p53, and Bcl-2-positive large cells were also found in the infarcted area of frozen specimen (Fig. 2). Effacement of normal nodal architecture in the area was confirmed by the distribution of CD20-positive cells and cCD3-positive cells in the background. Regarding EBV-related molecules, EBER was positive in cells resembling RS cells in the viable, but not infarcted, area. In contrast, LMP-1 was positive in the cells in both viable and infarcted areas (Fig. 2). On the basis of these features, a pathologic diagnosis of mixed cellularity cHL could be confirmed.

**DISCUSSION**

Pathologists should always take malignant lymphoma into consideration in differential diagnosis in cases when they encounter lymph node infarction because it is the most common cause of spontaneous lymph node infarction. However, malignant lymphoma with extensive necrosis is extremely difficult to diagnose on the basis of morphology. Although necrotic tissue is, in general, thought to be unsuitable for immunohistochemical analysis because of the loss of antigenicity and nonspecific staining, it is sometimes useful in elucidating the underlying processes in lymph node infarction. In addition, where a diffuse proliferation of necrotic large cells is evident, a definitive diagnosis of lymphoma may be made in selected situations, even in the absence of viable tumor tissue. We experienced a case of cHL associated with lymph node infarction, in which RS cells were positive for CD15, CD30, fascin, PAX-5, p53, LMP-1, Bcl-2, and EBV-encoded small non-polyadenylated RNAs. Furthermore, RS cells in the infarcted area were still positive for CD30, fascin, p53, and Bcl-2.

In patients with lymph node infarction, 32-89% have comorbid malignant lymphoma or develop malignant lymphoma within 2-24 months. Saito et al. reported the occurrence of lymph node infarction in 15 (25%) of 60 consecutive patients with non-Hodgkin’s lymphoma. Kojima et al. reported that, among 11 cases of CD20-positive B-cell lymphoma associated with lymph node infarction, they were classified as either DLBCL (seven cases) or FL (four cases). We could find only a single case of cHL associated with lymph node infarction in the literature. Biological differences between cHL and non-Hodgkin’s lymphoma (i.e., site of origin, property of vascular invasion, density of neoplastic cells, background structure/cytokine abnormalities, etc.) may account for the difference in incidence of lymph node infarction. Regarding the cause of infarction in our case, we could not find any histologic evidence of vascular abnormality. Because the clinical and pathologic features of cHL have been said to reflect an abnormal immune response that is thought to be due to the elaboration of a variety of cytokines by the malignant RS cells or surrounding tissues, cytokine abnormalities could be one of the causes of lymph node infarction of cHL. In addition, EBV might be involved in lymph node infarction of cHL as observed in this case, since EBV-positive DLBCL of the elderly may demonstrate large areas of geographical necrosis.

In this study, immunohistochemical examination could confirm that some of the molecules related to cHL were still detectable in non-viable RS cells present in infarcted lymph nodes. Among these, preservation of antigenicity of LMP-1, but no preservation of complementarity of EBER, is important because the presence or absence of EBV is occasionally crucial for the differential diagnosis of lymphoproliferative disorders and many of such EBV-related lesions show type II or type III latency.

For definitive diagnosis of nodal lymphomas including cHL, identification of the effacement of normal nodal architecture is essential because cytologic features useful for general surgical pathology, such as nuclear “atypia” and increased mitotic count, are not applicable to the first diagnostic step of lymphomas. Although this could not be evaluated in our case because of predominant reactive follicular hyperplasia with interfolicular distribution of RS cells in the viable lymph node, the presence of large cells with RS cell-related molecules together with the distorted distribution of cCD3-positive cells and CD20-positive cells in the infarcted lymph node led us to make a definitive diagnosis of Hodgkin’s lymphoma. It is, therefore, considered that immunohistochemical examination of the infarcted lymph node is, at least in some occasions, still informative for the more accurate

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<th>CD20</th>
<th>CD79a</th>
<th>cCD3</th>
<th>CD15</th>
<th>CD30</th>
<th>Fascin</th>
<th>PAX-5</th>
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<th>LMP-1</th>
<th>CD10</th>
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* Background small lymphocytes were positive.
diagnosis of lymphoid neoplasia. Hodgkin’s lymphoma should also be considered when one encounters lymph node infarction.

REFERENCES
9 Nasuti JF, Gupta PK, Baloch ZW: Clinical implications and value of immunohistochemical staining in the evaluation of lymph node infarction after fine-needle aspiration. Diagn Cytopathol 25:104-107, 2001

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