Random Skin Biopsy of Intravascular Large B-cell Lymphoma: A Case Report

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A 72-year-old woman visited our clinic with fever of unknown origin above 38°C and arthralgia from 7 months before. Her symptoms recurred as oral steroid was reduced. Random skin biopsy was carried out from five points. One of the five specimens taken from abdomen revealed large atypical lymphoid cells in the vascular space of subcutaneous fat. Immunohistochemical analysis showed that these cells were positive for CD20, CD79a, bcl-2, bcl-6 and MUM-1. From these findings, a diagnosis of intravascular large B cell lymphoma was made.

Key words: Intravascular large B-cell lymphoma, Random skin biopsy

INTRODUCTION

Intravascular large B-cell lymphoma (IVLBCL) is a rare variant of non-Hodgkin's lymphomas, characterized by non-specific clinical presentation, lack of lymphadenopathy or mass formation, and the rapid and fatal clinical course. The non-specific presentation includes fever, general fatigue, anemia, elevated lactate dehydrogenase (LDH) and C-reactive protein (CRP) levels [1]. Because of difficulty in diagnosis of IVLBCL, prognosis is poor. Three-year survival is 56% in patients with only cutaneous involvement and 22% in patients with involvement of the organs other than the skin [2]. Thus, it is not rare that IVLBCL is diagnosed at autopsy [3].

The diagnosis is usually confirmed by biopsy of the affected organs, which should exhibit exclusive or predominant proliferation of malignant lymphoid cells within the vascular lumen. Chemokine-chemokine receptor engagement is expected for the pathogenesis of IVLBCL [4, 5]. The skin is useful because of easy accessibility in obtaining multiple biopsy specimens. In the suspected patients without apparent organ involvement, random skin biopsy (RSB) often demonstrates lymphoma cells of deep dermis vessel in normal appearing skin [1, 3, 6, 7]. Furthermore, some report that lymphoma cells are accepted inside of the senile hemangioma [8, 9].

CASE REPORT

A 72-year-old woman visited our clinic with fever of unknown origin (FUO) above 38°C and arthralgia from 7 months earlier. She consulted a doctor of internal medicine five months earlier and received blood test, abdominal ultrasonography and computerized tomography (CT), and there was no dominant inspection from these tests that proved malignant lymphoma. She was diagnosed as polymyalgia rheumatica, and was given oral steroid, however, the symptoms recurred as the steroid doze was tapered. For further examination, RSB was carried out from one lesion of seborrheic keratosis on the abdomen and two lesions of senile hemangiomas from abdomen and thigh, along with two normal appearing skin lesions from the forearm and the thigh. One of the five specimens taken from abdomen seborrheic keratosis revealed large atypical lymphoid cells in the vascular space of subcutaneous fat (Fig. 1). Immunohistochemical analyses showed that these cells were positive for CD20 (Fig. 2), CD79a, bcl-2, bcl-6 and MUM-1, and negative for AE1/3, CD3, CD5, CD10, p53 and EBV-ISH. High Ki-67-positive views suggested a high proliferating profile. Based on these findings of the skin, as well as bone marrow findings which showed large atypical CD20 positive cells, hepatosplenomegaly from CT taken 5 months ago, and gallium scintigraphy that showed accumulation in the spleen, a diagnosis of IVLBCL was made. This patient's treatment was started with R-CHOP (rituximab, cyclophosphamide, adriamycin, vincristine and prednisolone).

DISCUSSION

Japanese IVLBCL cases featured skin lesions in 24% [10]. The cutaneous manifestation is variable, presenting as erythema, purpura, telangiectasia with or without swelling, tenderness or hotness, which all wax and wane. The mechanism for eliciting cutaneous lesions is thought to be relatively simple [11]. Proliferated lymphoma cells occlude capillary vessels that activate coagulation cascade and thrombi are formed within the vessel lumina. If the invasion is not sufficient to cause occlusion of the vessels, skin lesion does not occur. Therefore, the lack of a skin lesion does not necessarily mean the absence of invasion of lymphoma cells in the skin.

In general, specimens are obtained from several

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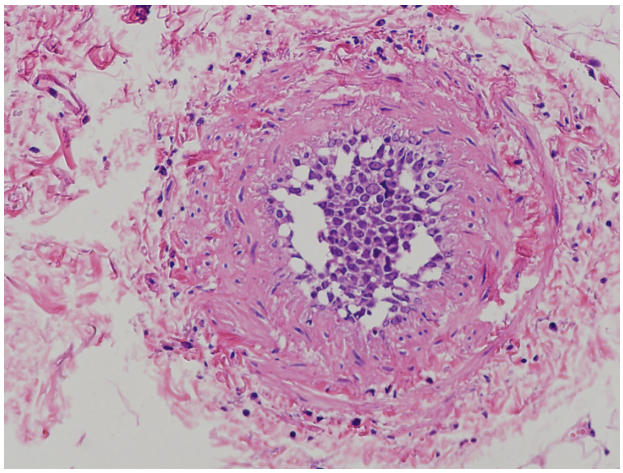

Fig. 1 Photomicrograph showing a vessel filled with lymphoma cells

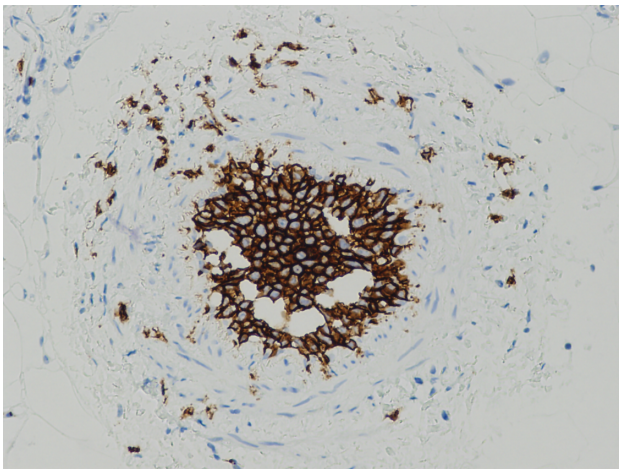

Fig. 2 Lymphoma cells were positive for CD20

body parts, usually abdomen and limbs, to the depth of the cutaneous and subcutaneous tissues, to increase precision of this examination [12] or if any, senile hemangioma [8, 9]. In our case, intravascular proliferation of lymphoma cells of B-cell origin shown by RSB suggested to us the diagnosis of IVLBCL. We were able to confirm atypical cells in a specimen from seborrheic keratosis. However, because the seborrheic keratosis was located in the dermis and atypical cells were located in the subcutaneous tissue, they are considered to be isolated events, without any association. As for senile hemangioma, we could not find any atypical cells. One of the reasons that the biopsy of senile hemangioma turned out negative could be that she had been administered oral steroid which might complicate confirmation of atypical cells.

Due to difficulty in early diagnosis and rapid progression, the prognosis of IVLBCL is poor. RSB from normal appearing skin led us to the early diagnosis of IVLBCL, contributing to the constitution of appropriate chemotherapy before extensive expansion of malignant cells. However, to avoid abuse, random skin biopsy should be considered only when IVLBCL is highly suspected. Furthermore, the accumulation of the cases is necessary to establish the standardized technique to bring higher probability of finding atypical cells.

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