

Simultaneous occurrence of Kaposi's sarcoma and nodular lymphocyte predominant subtype of Hodgkin's lymphoma in the same lymph node

Aynı lenf nodülünde Kaposi sarkomu ve nodüler lenfosit predominant Hodgkin lenfoma birlikteliği

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Abstract

Many cases have been established with coexisting Kaposi's sarcoma (KS) and classical Hodgkin's Lymphoma (C-HL) in the same lymph node. But composite presentation of KS and Nodular Lymphocyte Predominant subtype of Hodgkin's lymphoma (NLPHL) in the same lymph node has not been described yet. KS is related to immunodeficiency most frequently due to human immunodeficiency virus (HIV) infection or immunosuppression by other reasons. Our case presented here was not related to any immunodeficiency status. Besides of being the first case of composite KS and NLPHL in the same lymph node, it was also unusual with the indolent behaviour of the NLPHL without any therapy for 8 years follow up and primary lymph node presentation of KS without cutaneous involvement. (*Turk J Hematol 2009; 26: 201-3*)

Key words: Hodgkin's disease, Kaposi's sarcoma, Lymph node

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Özet

Kaposi Sarkomu (KS) ve Klasik Hodgkin Lenfomanın (K-HL) aynı lenf nodülünde eş zamanlı infiltrasyon gösterdiği pek çok vaka bildirilmektedir. Fakat aynı lenf nodülünde KS ve Nodüler Lenfosit Predominant Hodgkin Lenfoma (NLPHL) birlikteliği henüz tanımlanmamıştır. KS sıklıkla "human immunodeficiency virus (HIV)" veya başka nedenlerle ortaya çıkan immünyetmezlik zemininde gelişim göstermektedir. Olgumu immünyetmezlik zemini bulunmaması açısından farklılık göstermekteydi. Ayrıca aynı lenf nodülünde KS ve NLPHL birlikteliğinin görüldüğü ilk olgu olmasının yanısıra, NLPHL'nin 8 yıllık tedavisiz takip sürecine rağmen çok yavaş seyir göstermesi ve KS'nun cilt tutulumu olmaksızın primer olarak lenf nodülü tutulumu şeklinde ortaya çıkması açısından önemliydi. (*Turk J Hematol 2009; 26: 201-3*)

Anahtar kelimeler: Hodgkin hastalığı, Kaposi Sarkomu, Lenf Nodülü

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Introduction

Kaposi's sarcoma (KS) is a neoplasm of endothelial cells, affecting mainly the skin but also involving regional lymph nodes and internal organs. It occurs in several clinical-epidemiologic forms, all associated with infection by the human herpesvirus-8 (HHV-8) [1]. An association between KS and lymphoreticular malignancies, especially B cell lymphomas, has been previously reported [2]. Coexistence of KS and Classical Hodgkin's Lymphoma (C-HL), even in the same lymph node has also been established [3-6]. But, this is the first case of nodular lymphocyte predominant (NLPHL) subtype of HL associated with KS, without cutaneous or any other involvement. It is also important that both of them were diagnosed simultaneously and there was no predisposition of human immunodeficiency virus (HIV) infection or immunosuppression due to any reason.

Material and Method

Fifty seven years old male patient was admitted to the hospital in 1999, with complaints of gradually enlarged inguinal lymphadenopathy, reaching a diameter of 6.5 cm within five years. He had a history of lymph node excision from the same site in 1985, which had been reported as reactive lymphoid hyperplasia. The serology for HIV was negative, but HBsAg was positive. Excisional biopsy of the inguinal lymph node was performed.

The surgical specimens were fixed in unbuffered formalin and embedded in paraffin. 4-5 μ m thick cut sections stained with hematoxylin and eosin (H&E). Immunohistochemistry was performed on tissue sections by using Ventana Automated Immunostainer. The antibodies used included CD20 (Novacastra, 1/200), CD45 (Neomarkers, 1/500), EMA (Neomarkers, 1/1000), EBV (LMP1) (Novacastra, 1/100), CD34 (Neomarkers, 1/200), CD31 (Neomarkers, 1/50), Factor VIII (Neomarkers, 1/150), HHV-8 (Novacastra, 1/30), CD30 (Neomarkers, 1/50), CD15 (Neomarkers, 1/50) antibodies. Appropriate positive tissue controls were used.

Written informed consent was obtained from the patient.

Results

Histopathological examination showed effacement of the inguinal lymph node architecture by a nodular infiltrate of small lymphocytes, admixed with histiocytes and scattered atypical multilobated Hodgkin's-like cells. Among these areas, nodules composed of fascicles of spindle shaped cells arranged between slit-like vascular spaces filled with red blood cells were detected. Immunophenotype of the Hodgkin's-like cells were CD20, CD45 and EMA positive B lymphoid nature and negative for EBV(LMP1), CD30 and CD15. The spindle cells showed positive reaction with CD34, CD31, Factor VIII and HHV-8 (Figs. 1,2). The findings were consistent with coexistence of NLPHL and KS in the same lymph node. There was no cutaneous involvement of KS and no malignant infiltration was detected in the bone marrow biopsy specimen. The

patient was staged as early favorable stage I-A NLPHL. The clinical follow up with short intervals was performed instead of chemotherapy. Multiple axillary lymphadenopathies with the largest diameter of 3 cm were detected within three months time. Biopsy again revealed NLPHL. Follow-up of the patient continued without any significant progression during the next four years. In 2004, left inguinal lymph node enlargement was detected again and rebiopsied. The diagnosis was relapse of both tumors, NLPHL and KS. Following year, NLPHL relaps was diagnosed in axillary lymph node. The patient is being followed with left axillary lymphadenopathies which remain stable in size and without any progression of disease.

Discussion

NLPHL is an infrequent (5%) form of HL and differs from C-HL both histologically and clinically. The presentation of the disease in our patient was consistent with the natural behavior of NLPHL which usually presents with early clinical stage and with cervical or inguinal involvement. The disease course is indolent and progresses slowly. NLPHL is reported to relapse frequently but the relapses are rarely fatal. Frequent local relapses occurred in our patient. However, the lymph nodes did not enlarge rapidly and usually were stable during the follow up. Establishing a standart treatment for NLPHL especially in the early favorable stages has been difficult. Involved field radiotherapy has been recommended as standart therapy for early favorable stage I-A disease. However, extended field radiotherapy, combined modality treatments and monoclonal antibodies have been tried [7].

Some pediatric groups reported that wait and watch strategy after initial lymph node surgery may be appropriate treatment for selected group of patients [8,9]. Our patient has survived for 8 years after the initial diagnosis without significant progression but frequent localized relapses.

KS is an indolent endothelial neoplasm for immunocompromised patients developed by the oncogenic effect of HHV-8 which is not restricted to endothelial cells. It also infects B lymphocytes and is associated with two B-cell lymphoproliferative diseases, primary effusion lymphoma [10] and multicentric Castleman's disease [11]. The most common lymphoproliferative malignancies associated with KS were documented as lymphoid neoplasms of B-cell origin including NHL, CLL/SLL and MM [2]. But, a great many cases have also been established with coexisting KS and C-HL, some of whom were in association with HIV [3-6]. An analysis of 65 KS cases associated with lymphoreticular malignancies showed that 29% of them had C-HL as a second malignancy [2]. It has been known that 30-50% of HL's were associated with Epstein-Barr virus (EBV) [12] and %95 of KS's were associated with HHV-8 [1]. EBV and HHV-8 are human γ herpesviruses that establish persistent latent infection and prevent apoptosis of infected cells which result in malignant transformation in the presence of immunosuppression. The concomitant occurrence of KS and C-HL in the same lymph node has led researchers to investigate a common ethiopathogenetic mechanism which could not be proved yet. Neither EBV nor HHV-8 were found in association with both of these malignancies by itself. HHV-8 was demonstrated in relation to KS in our case, but neither EBV nor HHV-8 were presented on the L&H cells of NLPHL. Role of

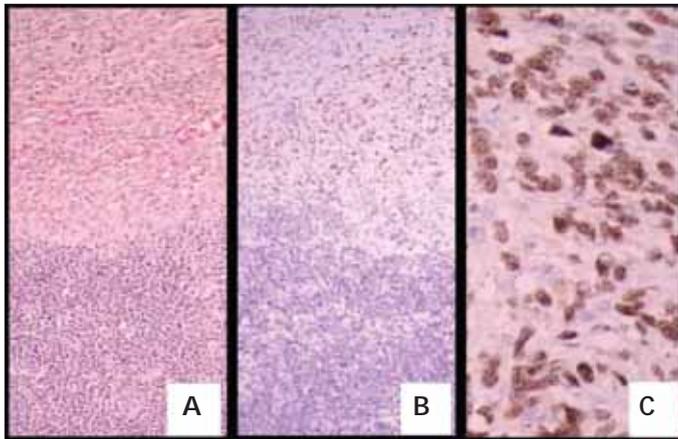


Figure 1. Neoplastic cells of KS and NLPHD (H&E x200). B,C: HHV8 positivity of KS's cells (x200, x400)

EBV on C-HL pathogenesis has been well documented in the previous studies, but no such relation with any agent has been demonstrated for NLPHL [13]. Somatic hypermutations in several transcription factor genes has been speculated to play a role on the development of NLPHL and C-HL. Bcl-6 mutations have been documented most frequently in NLPHL cases [14,15] and it reveals the germinal center origin of neoplastic cells [13]. Longstanding antigenic stimulus causes B cells to be vulnerable to chromosomal aberrations by inducing B cell proliferation. In relation to the pathogenesis of composite presentation of KS and NLPHL, it can be speculated that the chronic antigenic stimulus of HHV-8 and immune response mechanisms may be playing a role in the development of NLPHL.

Our case of composite neoplasia of KS and NLPHL has unique characteristics in several respects. It is the first case of NLPHL associated with KS. It is also important that both of the tumors were diagnosed simultaneously and there was no predisposition of HIV infection or immunosuppression due to any reason. KS presented only in the lymph node without cutaneous or any other involvement. The clinical follow up also revealed the indolent behaviour of both neoplasia without any therapy.

No author of this paper has a conflict of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included in this manuscript.

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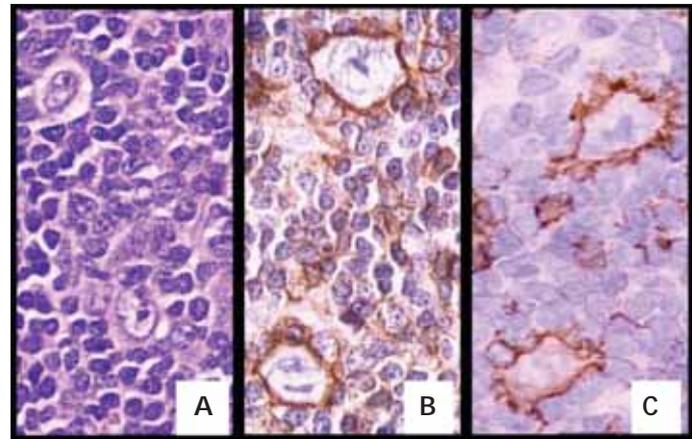


Figure 2. Popcorn cells of NLPHD (H&E x1000). B, C: CD45 and CD20 positivity of tumor cells (x1000)

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