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Case Report

A Case of Aggressive Natural Killer Cell Lymphoma

Shigeo NAKAMURA[1],

Takashi KOSHIKAWA[1], Masaru KOJIMA[2], Tadashi MOTOORI[3]

and Taizan SUCHI[1]

[1]Department of Pathology and Clinical Laboratories, Aichi Cancer Center Hospital, Nagoya, Japan
[2]Department of Pathology and Clinical Laboratories, Ashikaga Red Cross Hospital, Ashikaga, Japan
[3]Department of Pathology, Kitasato Institute Medical Center Hospital, Saitama, Japan

Abstract

We report a case of CD56-positive aggressive angiocentric lymphoma arising in the skin of the left lower leg. This tumor was characterized by the angiocentric and angioinvasive infiltrate, and showed the monotonous proliferation of medium-sized cells with "lymphoblastoid" appearance and cytoplasmic azurophilc granules. Phenotypic analysis showed $CD1^-$, $CD2^-$, $CD3^-$, $CD4^+$, $CD5^-$, $CD7^-$, $CD8^-$, $CD16^-$, $CD56^+$, $CD57^-$, and T-cell receptor (TCR) $antigens^-$ phenotype. Neither rearrangement of TCR beta and gamma chain genes or of immunoglobulin heavy chain gene was detected in DNA extract from fresh material. Epstein-Barr virus-encoded small RNAs were undetected in lymphoma cells by in situ hybridization. These data indicated that the present case might represent natural killer cell neoplasm.

Key words: Angiocentvic lymphoma, natural Killer cell, CD56, NCAM

Introduction

Angiocentric lymphoma is a rare disorder in the Western countries, but is more common in Oriental populations. Extranodal sites are invariably involved, including nose, palate, and skin.[1)] Many of the cases express CD56 and some T-cell makers with CD3 negativity and could conceivably represent true natural killer cell neoplasms because T-cell receptor (TCR) genes are rarely demonstrated in these tumors.[2-5)]

In this report we describe a case of CD56-positive aggressive angiocentric lymphoma (AAL) arising in the skin of the left lower limb.

Address for Correspondence: Shigeo NAKAMURA, Department of Pathology and Clinical Laboratories, Aichi Cancer Center Hospital , Kanokoden, Chikusa-ku, Nagoya 464, Japan

Case report

A 57 year-old Japanese man presented with a tumor of the skin of the left lower leg in December 1990, and was diagnosed as non-Hodgkin's lymphoma. The other work-up failed to reveal any additional ecidence of disease. He received no further therapy. In October 1991, he developed multiple cutaneous lesions, partially ulcerated at the left lower limb, thigh and inguinal area, but no superficial lymphadenopathy. He was treated with chemotherapy, but later had another recurrence and treated again. He is currently in a partial remission.

Materials and Methods

The present case has been reported as case no. 2 of 10 cases of CD56-positive angiocentric lymphoma occurring in sites other than upper and lower respiratory tract,[6)] and also has been discussed at T-cell lymphoma workshop, Hong-Kong, on October 1994.

Tissue samples were fixed in 10% formalin and embedded in paraffin. Sections (5-μm thich) were stained with hematoxylin and eosin, Elastica-van Gieson, silver impregnation, periodic acid-Schiff, May Grünwald-Giemsa, and methyl green-pyronine. Imprint smears of the surgically resected specimen were stained with May-Grünwald-Giemsa.

Surface immunophenotyping of the lymphoma cells was performed by flow cytometry with use of a broad panel of lymphoid-associated monoclonal antibodies (MAbs). The samples studied were received within one-half hour of the surgical biopsy, immediately made into single sell suspensions, and analyzed on a FACS Analyzer (Becton Dickinson) for fluorescent intensity with use of a panel of fluorescein isothiocyanate (FITC)-conjugated antibodies. Multiparameter analysis of gated cell populations on cell suspension studies were used in providing more definitive immunopheno-

typing information (Consort 30 computer software, Becton Dickinson).

The DNA used for gene rearrangement studies was extracted from frozen tumor tissue. It was digested with restriction enzymes: BamHI, EcoRI, and XbaI. Genotypic blot hybridization was done as previously described.[7)]

Presence or absence of EBV-encoded small RNAs (EBERs) by in situ hybridization using EBER oligonucleotides was performed on formalin-fixed paraffin embedded sections as previously described.[8)]

Results

Histolgic Findings

The excised specimen histologically showed prominent diffuse infiltration of the cells in entire layers of skin and subcutis. Angiocentric growth pattern involving the arteries and veins were occasionally observed (Photo 1). The infiltration of the cells often show a stream-like pattern (Photo 2). The neoplastic cells were distinctly uniform and monotonous, medium to large in size, and in a way "lymphoblastoid" in appearance with fine chromatin (Photo 3).

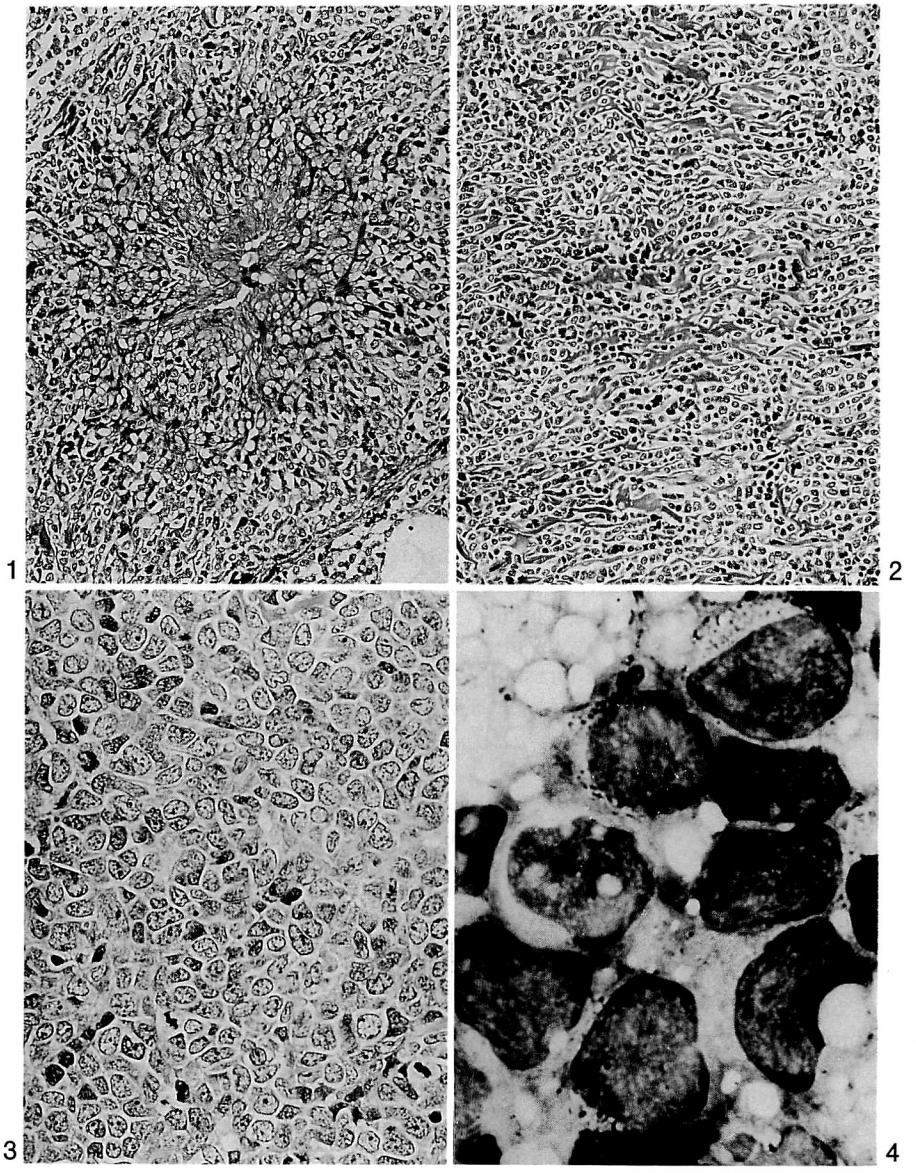

Fig. 1, Photo 1. Angiocentric growth pattern with lymphoma cells infiltrating the wall of artery.
Fig. 2, Photo 2. The interstitial infiltration showing stream-like pattern.
Fig. 3, Photo 3. The lymphoma cells consisting predominantly of medium-sized cells with "lymphoblastoid" appearance.
Fig. 4, Photo 4. Cytologic appearance of touch imprint of the tumor. Note the azurophilic granules in the cytoplasm. (Giemsa stain).

Imprint cytology showed azurophilic granules in the cytoplasm of the tumor cells (Photo 4).

Phenotypic Findings

The neoplastic cells reacted with the antibodies CD4 and CD56, but not CD1, CD2, CD3, CD5, CD7, CD8,CD16, CD20, CD57, TCR antigens, nor the other B-cell antibodies.

Genotypic Findings

Southern blot hybridization studies showed germline configuration for the TCR beta and gamma chain genes and immunoglobulin (Ig) heavy chain gene.

In Situ Hybridization Findings

The lymphoma cells showed no signal for the EBERs.

Discussion

The present case was featured by extranasal site of involvement, CD56-positivity with CD3 negativity, monomorphic, high-grade histology with angiocentric growth pattern and high infiltrative tendency, and azurophilic granules in the cytoplasm.

CD56-positive lymphoma oocupys a small proportion of non-Hodgkin's lymphomas, [9,10] and many of them occur in the upper aerodigestive tract, having been various labels, such as "lethal midline granuloma," "polymorphic reticulosis," "angiocentric immunoproliferative lesion," and "nasal T-cell lymphoma."[2-6] Recent studies have shown that the "T-cell" lymphoma of the upper aerodigestive tract are strongly associated with EBV.[3] They are also considered to be of putative natural killer (NK) cell lineage on the basis of CD3-negativity and no rearrangement of TCR genes, but which is insufficient in ditinguishing between T-and NK-cell lymphoma. Indeed, NK-cells and T-cells share a common developmental pathway, and are remarkably similar with respect to expression of other membrane receptors and immune effector cell functions, although TCR gene rearrangement clearly discriminates beteen these cell types.[11]

The preferred diagnosis in the present case was "aggressive natural killer cell lymphoma", and was unique in the originating site, monomorphic "lymphoblastoid" appearance, and lack of CD2 and EBV in contrast to nasal/nasopharyngeal T/NK-cell lymphoma.

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