Extranodal NK/T-cell lymphoma of nasal type primarily presenting with pericardial effusion

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Background: We report a case of Epstein-Barr virus-positive NK/T-cell lymphoma primarily presenting with pericardial effusion without nasal lesions.

Case: A 63-year-old man with dyspnea and 38°C fever was found in physical examination to have pericardial effusion of 1,000ml. Tumor cells in effusion showed marked nuclear pleomorphism and variable-sized basophilic cytoplasm with azurophilic granules. Flow cytometric and immunohistochemical analysis showed tumor cells to be positive for CD2, CD3ε, CD7, CD45RA, CD45RO, CD56, perforin, T-cell intracellular antigen 1, granzyme B, but negative for CD4, CD5, CD8, CD20, CD30, terminal deoxynucleotidyl transferase, and T-cell receptor β. An in situ hybridization study showed positive signals for Epstein-Barr virus encoding small ribonucleic acids on tumor cells. Despite chemotherapy, the patient died of respiratory failure due to disease progression 2 months after admission. No autopsy was done.

Conclusion: Based on the above data, we definitively diagnosed this case as extranodal NK/T-cell lymphoma of nasal type. It appeared to be unique in clinical manifestation, primarily affecting the pericardium.

I. Introduction

Primary effusion lymphoma commonly shows a B-cell lineage in addition to universal association with human herpes virus 8 (HHV-8), and many cases arise in human immunodeficiency virus (HIV) infection. Epstein-Barr virus (EBV) infection is rare1).

Extranodal NK/T-cell lymphoma of nasal type usually involves the upper respiratory tract, and is highly related to EBV infection. Most tumor cells are CD2+, cytoplasmic CD3ε+, surface CD3ε-, CD56+, and no rearrangement of T-cell receptor (TCR) genes. Only a few cases of this lymphoma manifesting a clinical presentation such as primary effusion lymphoma without detectable masses in extranodal sites have been documented1-3).

II. Case Report

A 63-year-old man treated 12 years for pulmonary tuberculosis and presenting with dyspnea and fever (38°C) was found in chest X-ray and computed tomography (CT) on admission to have marked pericardial effusion (Photo. 1). Positron-emission tomography (PET) showed strong signals in the heart, pericardium, and mediastinal and para-aortic lymph nodes (Photo. 2). Laboratory
Photo. 1  a: Chest X-ray showing cardiomegaly. b: Pericardial and pleural effusions observed in CT.

studies showed a white blood cell count of 1.8 × 10^9/L with a differential count of 58.3% neutrophils, 36.0% lymphocytes, 5.1% monocytes, 0.0% eosinophils, and 0.6% basophils. The patient’s hematocrit was 43.2%, platelet count of 118 × 10^9/L, serum lactate dehydrogenase of 1,432 IU/L, soluble interleukin 2-receptor of 6,670 U/ml, and serum β2-microglobulin of 18.5 mg/L. All other parameters were within normal limits. Serum IgG anti-EBV capsid antigen was 1: 80. Other EBV-related antibodies were negative. Pericardial effusion of 1,000ml was obtained by puncture. Systemic magnetic resonance tomography images (MRI) showed no tumorous lesions at extranodal sites after puncture (Photo. 3). Cytological examination showed an admixture of variable-sized tumor cells, ranging from medium to large, with nuclear pleomorphism and cytoplasmic azurophilic granules (Photo. 4). Flow cytometrical studies of pericardial effusion showed that tumor cells were positive for CD3ε, CD43, CD45RA, CD45RO, CD56, T-cell intracellular antigen 1 (TIA1), perforin, granzyme B, and CD56 (Photo. 5), but negative for CD5, terminal deoxynucleotidyl transferase (TdT), and TCRβ. Bone marrow aspiration cytology and histopathology showed no abnormalities. In situ hybridization (ISH) studies showed abundant positive signals of EBV encoding small ribonucleic acid (EBER) on tumor cells (Photo. 6). Chromosomal analysis showed 2 types of abnormalities: (A) 46, X, −Y, +8, −11, add (11) (q23), add (13) (q22), i (17) (q10), +mar1; and (B) 45, idem, −22, −22, +mar2 : 15/15 cells.

Deoxyribonucleic acid (DNA) analysis was not done for ethical reasons.

III. Discussion

Body-cavity-based presentation of extranodal NK/T-cell lymphoma of nasal type is rare, with few case reports of this type of lymphoma. Pullarkat, et al. described a 31-year-old woman who presented with abdominal pain and ascites involved with EBV-positive NK/T-cell lymphoma of nasal type without nasal lesions. The immunophenotype of lymphoma cells was as follows: CD2+, CD7+, CD45+, CD56+, CD71+, CD3−, CD4−, CD5−, CD8−, CD19−, and negative for surface immunoglobulin light chains. Ogata, et al. reported a 69-year-old woman who developed natural killer cell body cavity lymphoma following chronic active Epstein-Barr virus (CAEBV) infection. The patient presented with high fever and pericardial and pleural effusion. No clonal rearrangement of TCR B genes was detected in either case. Other types of lymphoma of conceivable NK/T-cell lineage affecting the mediastinum were reported as aggressive NK-cell lymphoma and blastic NK-cell lymphoma in the English literature. These lymphomas usually show mass lesions and aggressive NK-cell lymphoma is characterized by systemic involvement. Tao, et al. reported a case of aggressive NK-cell lymphoma presenting with a mediastinal mass and hepatosplenomegaly. The
patient was noted to have HIV\(^1\). The immunopheno-
type of lymphoma cells was as follows: CD2\(^+\), CD8\(^+\), CD16\(^+\), CD56\(^+\), CD3\(^-\), CD4\(^-\), CD7\(^-\), CD19\(^-\), CD20\(^-\), and TdT\(^-\). Isobe, et al. reported a case of blastic NK-cell lym-
phoma arising from the mediastinum\(^3\). Lymphoma cells were CD2\(^+\), CD56\(^+\), and TdT\(^+\), but negative for other T-
cell antigens. Our case appeared to be pathologically pro-
totypic with extranodal NK/T-cell lymphoma of nasal

type except for the unusual clinical presentation of pri-
mary effusion lymphoma and differed from these two cases.

EBV infection is believed to be closely related to the pathogenesis of NK/T-cell lymphoma and Burkitt

lymphoma\(^1\). Tomita, et al. described a case of extran-
odal NK/T-cell lymphoma of nasal type following mosquito bite allergy, which is a distinct disease in CAEBV
infection. They speculated that hypersensitivity to mos-
quitos bites caused lymphoproliferative disorders derived from EBV infected NK-cells\(^9\). Huang, et al. reported ag-
gressive extranodal NK-cell lymphoma arising from indol-
ent NK-cell lymphoproliferative disorder without evi-
dence of EBV infection\(^9\). Further study is thus

needed on the pathogenic function of EBV infection in NK-
cell lymphomas.

Cytologically, extranodal NK/T-cell lymphoma of nasal
type features nuclear pleomorphism, variable-sized tumor
cells, and cytoplasmic azurophilic granules\(^1,3,7,10\). Ne-
crosis, apoptotic debris, and tingible-body macrophages are commonly observed with lymphoma cells\(^1,7,10-13\).

Chromosomal abnormalities in extranodal NK/T-cell

lymphoma of nasal type are not constant\(^1,3\). Our case

showed 11q23, which is characteristic of acute myeloid

leukemia with MLL abnormalities.

IV. Conclusion

We report a rare case of extranodal NK/T-cell lym-
phoma of nasal type presenting with pericardial effusion,
but no upper respiratory tract lesions. This type of lym-
phoma is unique and may be regarded as a subtype of

NK/T-cell lymphoma.

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Photo 2  Strong signals detected in the mediastinum by PET.

Photo 3  No tumorous lesions detected on MRI at extranodal sites of the mediastinum.

Photo 4  Cytological findings showing variable-sized tumor cells with irregular nuclei and cytoplasmic azurophilic granules (a: Giemsa staining, ×100, b: Pap. staining, ×100).

Photo 5  Tumor cells positive for CD3ε and CD56 (Immunostaining, ×40).

Photo 6  Positive EBER signals on tumor cells (ISH, ×40).