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Case Report Open Access

Natural Killer/T-cell Lymphoma, Nasal Type with Myocardial Involvement and Severe Heart Failure

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Abstract

We report a rare case of extranodal natural killer (NK)/T-cell lymphoma, nasal type (ENKL) with myocardial involvement and severe heart failure. A 50-year-old Japanese woman who presented with nasal obstruction feel and palpitation on exertion was introduced to our hospital. Computed tomography (CT) imaging showed a mass in the right nasopharynx. Echocardiography confirmed left ventricular hypertrophy and a moderate pericardial effusion without tamponade physiology. As the patient's left ventricular ejection fraction was depressed at 30%, heart failure was therefore diagnosed. Biopsy of the right nasopharyngeal mass revealed pathologic features diagnostic ENKL. Endomyocardial biopsy from the left ventricular posterior wall demonstrated myocardial involvement of ENKL.The patient received 3 cycle of systemic chemotherapy including of steroids, methotrexate, ifosfamide, L-aspaginase, and etoposide (SMILE). Myocardial function was improved with treatment of SMILE, but she died from progressive lymphoma within 2 months of completing 3 cycle of chemotherapy. Although, prognosis remains poor in disseminated ENKLs, the clinical course of the patient suggests that SMILE regimen is worth trying for ENKL patients with myocardial involvement.

Keywords: Extranodal NK/T-cell lymphoma; Nasal type (ENKL); Myocardial involvement; Endomyocardial biopsy

Introduction

Extranodal natural killer (NK)/T-cell lymphoma, nasal type (ENKL) is more prevalent in Asian and South American populations compared to people in Western countries and classified by the World Health Organization into aggressive lymphoma [1]. Although improved outcomes have been reported with concurrent chemoradiotherapy for localized nasal NK/T-cell lymphoma [2,3], outcomes remain poor for disseminated disease including of myocardial involvement and optimum treatment has not been established. We here discuss our case presented with myocardial involvement of ENKL, who has been free from severe heart failure by treating with SMILE regimen, compared with previously reported cases.

Case Report

A 50-year-old Japanese woman was admitted to our hospital due to nasal obstruction feel and palpitation on exertion. On presentation to the admission, no pyrexia (36.4^{0}C), hypotension (83/68 mmHg), and tachycardia (176/min) were noted. Physical examination revealed no lymphadenopathy or hepatosplenomegaly. Electrocardiography (ECG) showed a wide QRS tachycardia with left bundle branch block morphology, which was diagnosed as tachycardiac atrial fibrillation (Figure 1). The chest X-ray demonstrated cardiomegaly. Transthoracic echocardiography confirmed left ventricular hypertrophy and a moderate pericardial effusion without tamponade physiology. As the patient's left ventricular ejection fraction (LVEF) was depressed at 30%, severe heart failure was therefore diagnosed. She was prescribed antiarrhythmic drugs including amiodarone hydrochloride and digoxin.

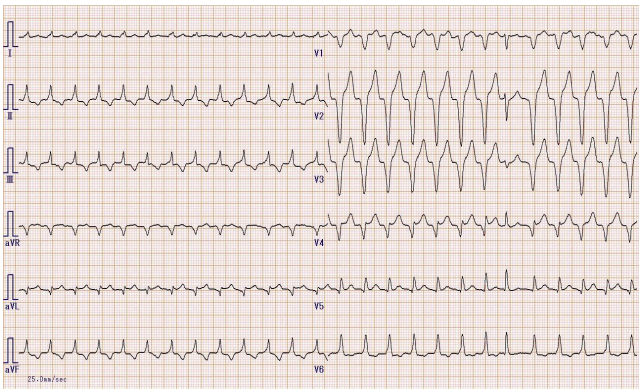

Figure 1: Baseline electrocardiography (ECG) shows wide QRS tachycardia, diagnosed as tachycardic atrial fibrillation and left bundle branch block.

Contrast-enhanced computed tomography (CT) showed a mass in the right nasopharynx, lymphadenopathy of mediastinum, diffuse enlarged pancreas, moderate pericardial effusion, and ascites (Figures 2A-2C).

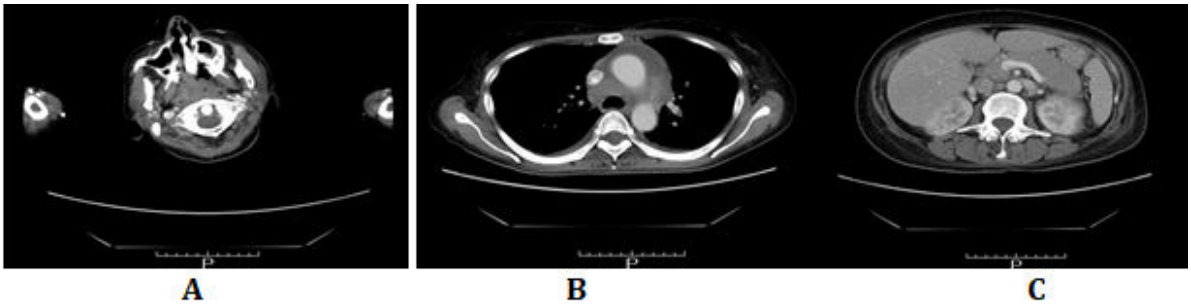

Figure 2: Contrast-enhanced computed tomography (CT) shows a mass in the right nasopharynx (A), lymphadenopathy of the mediastinum (B) and a diffusely enlarged pancreas (C).

Biopsy of the right nasopharyngeal mass showed that the tumor comprised atypical cells with medium size that were positive for CD3 ε, CD56, and *in situ* hybridization for Epstein-Barr virus-encoded RNA (EBER)-1, indicating Extranodal natural killer (NK)/T-cell lymphoma, nasal type (ENKL) (Figures 3A-3D).

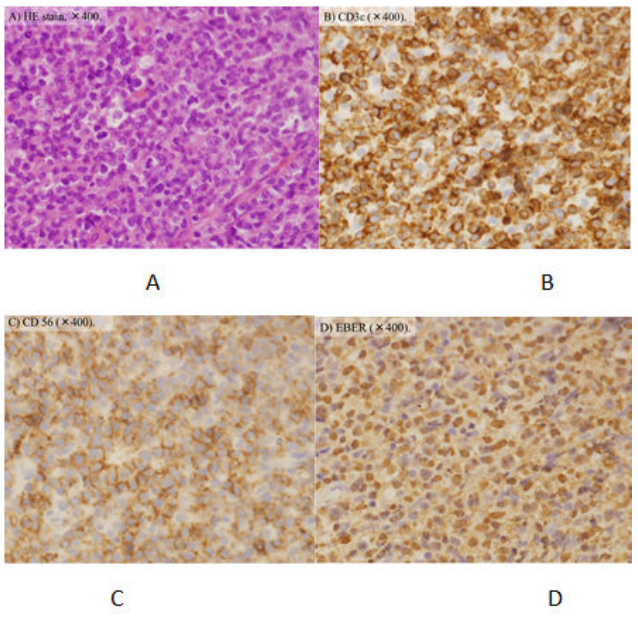

Figure 3: Biopsy of the right nasopharyngeal mass shows a tumor comprising atypical cells of medium size with positive results for immunoreactivity to CD3ε, CD56, and *in situ* hybridization for Epstein-Barr virus-encoded RNA (EBER)-1, indicating extranodal natural killer (NK)/T-cell lymphoma, nasal type (ENKL). A) HE stain (400X); B) CD3$_{\varepsilon}$(400X); C) CD56 (400X); and D) EBER (400X).

Hematological examination on admission showed a white blood cell count of 9,400/mm^3 with 80.0% neutrophilis, 8.0% lymphocytes, and 11.0% monocytes, hemoglobin level of 13.2 g/dl, hematocrit of 39.1%, and platelet count of 108,000/mm^3. Blood smear examination revealed that no abnormalities were seen in the differential white blood cell count. Blood biochemistry showed elevated lactate dehydrogenase (LDH) at 1564 IU/l (normal upper limit: 220 IU/l). Conjugated and unconjugated bilirubin was 0.6 mg/dl and 0.9 mg/dl (normal upper limit: 1.0 mg/dl). Asparate aminotransferase, alanine aminotransferase, and alkaline phosphate were 205 IU/l, 97 IU/l, and 446 IU/l respectively. The copy number of Epstein-Barr (EB) virus-DNA in peripheral blood mononuclear cells was 2.8×10^5 copy/10^6 cells.

The bone marrow was normocellular with abnormal lymphocyte. Analysis of the immunophenotype in bone marrow demonstrated the proliferation of lymphocytes expressing CD2, CD7, CD56, but not CD3, CD4, or CD8. Chromosomal analysis of the bone marrow showed a normal karyotype. Bone marrow biopsy from the posterior iliac spine revealed involvement of medium-sized atypical lymphocytes that expressed CD3$_{\varepsilon}$, indicating bone marrow involvement of ENKL. Endomyocardial biopsy from the left ventricular posterior wall showed proliferation of lymphocytes expressing CD3$_{\varepsilon}$ and EBER-1, myocardial involvement of ENKL was demonstrated (Figures 4A-4C).

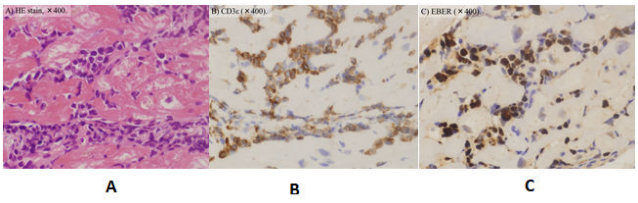

Figure 4: Endomyocardial biopsy from the left ventricular posterior wall shows proliferation of lymphocytes expressing CD3ε and EBER-1 and myocardial involvement of ENKL. A) HE stain (400X); B) CD3ε (400X); and D) EBER (400X).

The patient was treated with three cycles of systemic chemotherapy including of steroid (dexamethasone), methotrexate, ifosfamide, L-asparaginase and etoposide (SMILE) regimen [4,5]. As she had a moderate pericardial effusion, methotrexate was not used in first cycle of chemotherapy. The commencement of resolutions of a mass in the right nasopharynx, lymphadenopathy of mediastinum, diffuse enlarged pancreas, pericardial effusion, ascites and cardiomegaly were seen after one cycle of chemotherapy. After one cycle of SMILE, supraventricular arrhythmia was normalized and EB virus-DNA in peripheral blood mononuclear cells was decreased to 2.9×10^4 copy/10^6 cells. She was prescribed carvedilol only as a cardiac drug.

SMILE regimen was effective and she had an HLA-matched sister, we considered allogeneic hematopoietic stem cell transplantation (AHSCT) as treatment option for her. However, two cycles of SMILE was delayed due to severe liver dysfunction, the patient could not receive SMILE regimen every 28 days. Although EB virus-DNA in peripheral blood mononuclear cells was increased to 1.1×10^6 copy/10^6 cells before three cycles of SMILE, transthoracic echocardiography demonstrated recovery of left ventricular function (LVEF=56%). After completion of three cycles of SMILE, she had obvious progressive disease with jaundice and leukemic state of ENKL cells; however, there had been no recurrence of heart failure and supraventricular arrhythmia. Chromosomal analysis of peripheral blood cells revealed 47,XX,add(3)(p21),add(4)(q21),add(5)(p11),i(17)(q10),+21 [2] /46,idem,-X,-add (4),+add(4)(q21) [2] /46,idem,-X,add(6)(q13),del(11)(q?) [9] /46,X [1].

Lymphocytosis, anemia, and thrombocytopenia had been worsened. The patient expired on day 140 from initial systemic chemotherapy due to subarachnoid hemorrhage.

We obtained the consent of autopsy from the patient's family. The macroscopic examination demonstrated serous pericardial effusion to the amount of 50 ml. Pathological examination after death revealed systemic ENKL infiltration to multiple organ including heart, lung, liver, spleen, pancreas, and kidneys.

Discussion

Lymphomatous involvement of the heart has been detected in approximately 25% of lymphoma patients in autopsy studies [6]. However, extranodal natural killer/T-cell lymphoma, nasal type (ENKL) presenting with myocardial involvement is extremely rare. We found only 4 cases in the literature (Table 1).

Case	Publication	Age/Sex	Initial symptoms	Location	Type of arrhythmia	Management	Follow-up and outcome
1	Kanesvaran et al. [7]	65/M	Dysphagia and sore throat	Left tonsil and right atrium	Supraventricular tachycardia	4 cycles of ICE	Complete remission
2	Lepeak et al. [8]	54/M	Chest pain and dyspnea on exertion	Left pericardia and right atrium	No arrhythmia	2 cycles of CHOP and palliative radiotherapy	Death within 2 weeks of completing radiotherapy
3	Huang et al. [9]	25/M	Fever, palpitations,weakness, and left eyelid and lip swelling	Left ventricular posterolateral wall	Ventricular tachycardia	mPSL 2 mg/kg/day and 1 cycle of mPSL and CPA	Relapse 4 month after 1 cycle of mPSL and CPA; death
4	Baek et al. [10]	23/M	Abdominal pain	Pancreas and right ventricle	Ventricular tachycardia	IMVP-16/Pd and L-asparaginase	Death 2 days after starting chemotherapy

Table 1: Clinical data and results of myocardial involvement of ENKL.

Except for a case of achieving remission who was treated with 4 cycles of chemotherapy comprising of ifosfamide, carboplatin and etoposide (ICE) [7], whose long term outcome was unclear, so we selected SMILE which has been considered as the first line chemotherapy for ENKL [5]. Prognoses of other three cases were extremely poor [8-10]. Although our case has been free from severe heart failure by treating with SMILE regimen, fatal newly developed ventricular tachycardia during the early stages of chemotherapy has been reported [10], thus, outcome of chemotherapy for ENKL presenting with myocardial involvement is predictable.

The prognosis of disseminated ENKL is invariably poor despite the use of multi-agent chemotherapy [11]. Allogeneic haematopoietic stem cell transplantation (AHSCT) as a promising treatment for natural killer-cell neoplasms has been reported [12]. We considered AHSCT as a treatment option for our patient, but we had to abandon the procedure due to disease progression. AHSCT for ENKL presenting with myocardinal involvement may improve the prognosis if the disease is in remission.

Despite the progressive disease,there had been no recurrence of heart failure and supraventricular arrhythmia. The result of autopsy revealed myocardial involvement of ENKL. The commencement of resolutions of pericardial effusion was seen after one cycle of chemotherapy and maintained until death. Autopsy revealed only 50 ml of serous pericardial effusion. We considered that the small amount of pericardial effusion would not induce heart failure and tamponade. The reason for no recurrence of cardiac complication may be pericardial effusion; however, precise mechanism is unclear.

Prognosis remains poor in disseminated ENKLs, but at least the clinical course of the patient free from severe heart failure suggests that SMILE regimen is worth treatment option for ENKL patients with myocardial involvement in terms of quality of life, even though the disease progressed despite the therapy. Further accumulation of data for ENKL presenting with myocardial involvement is needed to improve the treatment and prognosis.

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