Extranodal NK/T-cell lymphoma presenting with primary cardiac involvement

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Abstract

Primary cardiac lymphoma is extremely uncommon. We report a case of a 54 year old Caucasian male with a history of non-small cell lung cancer treated by surgical resection who presented with chest pain and dyspnea on exertion. Computerized tomography (CT) imaging confirmed a 7.8×3.8 cm right atrial soft tissue mass infiltrating the lateral wall of the right atrium, and a 5 cm pericardiophrenic mass. Echocardiography confirmed a moderate pericardial effusion without tamponade physiology. Percutaneous biopsy of the pericardiophrenic mass revealed pathologic features diagnostic of NK/T-cell lymphoma. He received CHOP chemotherapy with some improvement in symptoms, but experienced radiographic progression after 2 cycles. He received palliative involved field radiotherapy but developed new sites of progressive disease within the abdomen and died shortly after completing radiotherapy. NK/T-cell lymphomas are aggressive tumors that may present with unusual extranodal disease sites. Prompt diagnosis with consideration for referral to a specialty center with experience in treatment of these rare tumors may offer the greatest potential for improving treatment outcomes.

Introduction

NK/T-cell lymphomas (NKTCLs) represent an uncommon subtype of non-Hodgkin's lymphoma (NHL), comprising only 5% of NHL cases in Western countries.[1-2] NKTCLs are highly aggressive, accounting for their previous description as *lethal midline granulomas*. NKTCLs generally have poor outcomes, with high rates of relapse and progression even in the setting of limited stage disease.[1,3] At least 80% of NKTCLs are localized at presentation, most commonly to the nasal cavity with extension to the nasopharynx and paranasal sinuses.[3] However, distant sites of involvement may be observed, most commonly involving the skin, liver, lung, gastrointestinal tract, or testis.[1] In cases of extranodal NKTCLs, only rare reports exist of primary cardiac involvement.[4-6] We report a rare case of a patient with extranodal NKTCL presenting with primary cardiac involvement.

Case Report

A 54 year old Caucasian male with a history of polysubstance abuse and stage IA squamous cell lung carcinoma resected 2 years previously, presented to clinic with a 3 month history of progressive chest pain and dyspnea on exertion. Physical examination revealed normal vital signs and no abnormalities on cardiopulmonary examination. Chest x-ray revealed a new mass in the anterior left lower mediastinum. Computerized tomography (CT) imaging of the chest showed a 7.8×3.8 cm right atrial soft tissue mass infiltrating the lateral wall of the right atrium with associated pericardial effusion, and a 5 cm pericardiophrenic mass, both new when compared to CT imaging performed 6 months previously (Figure 1). Transthoracic echocardiography showed a large irregular, mural right atrial mass in the area of the tricuspid annulus with extensive infiltration of both ventricles and the posterior wall of the left atrium. In addition, he was noted to have a pericardial effusion with early tamponade physiology. A percutaneous core needle biopsy of the pericardiophrenic mass was performed (Figure 2). Hematoxylin and eosin stained sections of the mediastinal mass revealed a dense infiltrate of primarily small lymphocytes with irregular nuclear contours in a background of focal fibrosis and scattered histiocytes. Immunohistochemistry and *in situ hybridization* demonstrated that the neoplastic cells co-expressed CD3ε, CD56, Epstein-Barr virus encoded RNA, granzyme-B, and TIA-1. Mitotic figures were easily found, but angiodestruction was not present. The final pathologic diagnosis was extranodal NK/T-cell lymphoma, nasal-type.

A unilateral bone marrow biopsy did not show any morphologic evidence of involvement by lymphoma. Flow cytometry on the bone marrow biopsy was negative and immunostaining for EBER was negative. Retrospective review of his non-small cell lung cancer biopsy confirmed squamous carcinoma with no atypical findings, and EBER immunostaining was negative. His blood counts at diagnosis were normal, including a normal LDH of 160 U/L. HIV testing was negative. Nasal endoscopy with biopsies and CT/PET imaging were recommended in order to complete the staging evaluation. Multiple attempts were made to schedule and perform these procedures, but the patient was unwilling and/or unable to comply due to his chaotic psychosocial circumstances and his concerns about costs due to lack of medical insurance.

Although a more dose-intensive regimen would have been preferred, CHOP chemotherapy was administered for palliative treatment in this case due to issues with poor patient compliance and continued polysubstance abuse. Two attempts had been made to administer the more dose-intensive SMILE (steroids, methotrexate, ifosfamide, L-asaparaginase, and etoposide) regimen as an inpatient, but the patient left within several hours of admission against medical advice. There were several intervening emergency department visits with tachyarrhythmias and cocaine intoxiciation. Based on these limiting factors, the patient received 2 cycles of CHOP chemothera-

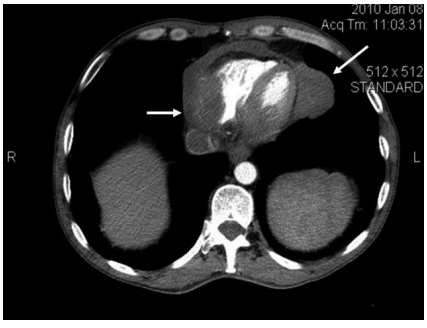

Figure 1. Computerized tomography imaging confirms a large left pericardiac mass (top right arrow) and infiltrative mass arising from the right atrium (left arrow).

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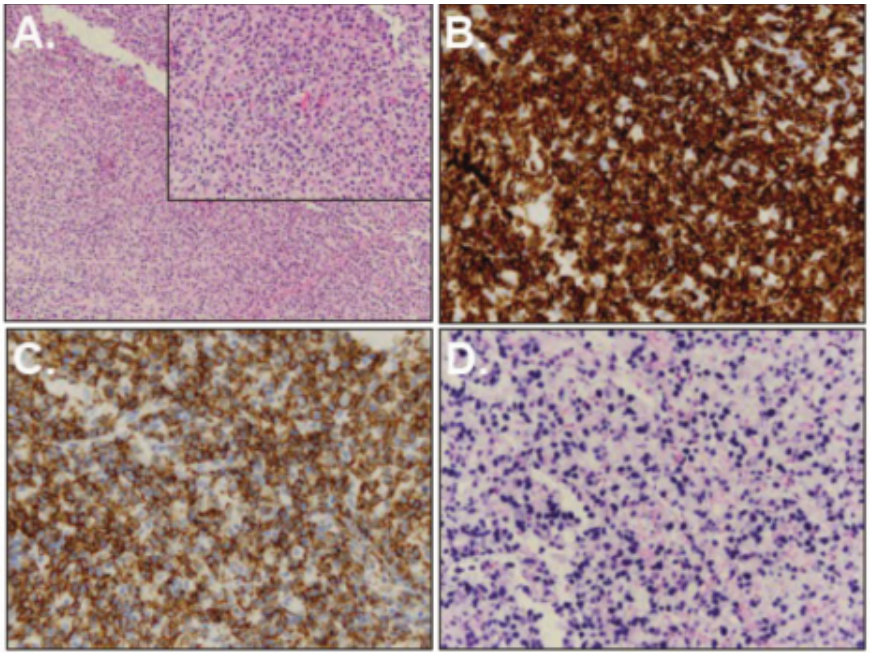

Figure 2. Extranodal NK/T-cell lymphoma, nasal type. Hematoxylin and eosin stained sections of the mediastinal mass reveals a dense infiltrate of primarily small lymphocytes with irregular nuclear contours (A) and immunohistochemistry shows the neoplastic cell co-express CD3ε (B) and CD56 (C). Almost all of the neoplastic cells contained EBV-encoded RNA (EBER) when assessed by *in situ hybridization*.

py as an outpatient, but demonstrated disease progression on follow up CT imaging. The patient was then referred for palliative radiotherapy which he tolerated well with improved symptoms of chest pain and dyspnea. He developed acute abdominal pain approximately 1 week after completing radiotherapy, and repeat CT imaging showing a new confluent soft tissue mass encasing the duodenum, pancreatic head, and inferior vena cava. He died from progressive lymphoma within 2 weeks of completing palliative radiotherapy.

Discussion

Although improved outcomes have been reported with combined chemoradiation for treatment of limited stage nasal NK/T-cell lymphoma,[7-8] outcomes remain poor for disseminated disease and extranasal NKTCLs. Given the rarity of primary cardiac lymphomas, most clinical management decisions of this entity are extrapolated from experience with other aggressive lymphoma subtypes presenting with advanced stage disease and extranodal involvement.[9]

Chemotherapy resistance of NKTCLs may be related to high rates of expression of P-glycoprotein, which is the product of the multidrug resistance (MDR) 1 gene.[10] High-intensive chemotherapy regimens combined with radiotherapy may be a rationale means for bypassing the innate MDR of NKTCLs, with some limited data to support improved outcomes with such an approach.[1,11]

L-asparaginase has shown impressive single-agent activity in NKTCLs.[12] More recent reports have focused on combining L-asparaginase with chemotherapy agents known to be independent of MDR. For example, outcomes with the SMILE regimen, have reported rates of response exceeding 50% in a phase I study of relapsed, refractory NKTCLs.[13] These promising results have led to on ongoing phase II study of SMILE chemotherapy in Asia.

Although prognosis remains poor in disseminated NKTCLs, prompt diagnosis and possible referral to a specialty center with experience in treatment of NKTCLs may offer patients the best opportunity for longer-term disease outcomes.

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