A unique atrial primary cardiac lymphoma mimicking myxoma presenting with embolic stroke: a case report

Michael M. Quigley, Eric Schwartzman, Pamela D. Boswell, Rebecca L. Christensen, Lisa A. Gleason, Robert W. Sharpe, and Thomas A. d’Amato

An immunocompetent 29-year-old male presented with an embolic stroke from an unusual primary cardiac lymphoma. The cardiac lesion consisted of a polypoid, left atrial, mural fibrin thrombus with anaplastic tumor cells lining the surface of the clot. Histologic, immunophenotypic, and molecular characterizations were consistent with a diagnosis of CD30⁺ B-cell lymphoma with anaplastic cytology. While tumor emboli from invasive primary cardiac lymphomas have been reported, this noninvasive fibrin thrombus-associated lymphoma appears to be unique and previously unreported. (Blood. 2003;101:4708-4710)

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Introduction

Primary cardiac neoplasms are rare.¹ A wide range of presenting symptoms can be manifested depending on the tumor location, pattern of growth, and histologic type. Occasionally, patients present with embolic stroke. This manner of presentation is usually associated with tumors growing into the heart chambers. Lesions most commonly presenting as cardiac mural masses include myxoma, sarcoma, metastatic lesions, and mural thrombus.¹⁻³

Primary cardiac lymphomas (PCLs) compose a small fraction of primary cardiac malignancies.² The most common presenting symptoms are congestive heart failure, pericardial effusion, superior vena cava syndrome, and arrhythmia.¹⁻²⁻⁴⁻⁶ Reported tumors have always been invasive, with nodular or diffusely infiltrative patterns of growth.¹⁻⁴

Study design

A previously healthy 29-year-old man presented to the emergency department after being found unresponsive. On initial evaluation, he appeared alert, was aphasic, but nodded appropriately to questions. The remainder of the neurological exam was nonfocal. Cardiac examination revealed a II/VI holosystolic murmur. Laboratory findings were significant only for mild thrombocytopenia and an elevated serum lactate dehydrogenase level. A head computed tomography (CT) failed to reveal intracranial hemorrhage. Aphasía slowly improved over several days. The patient was able to recount that his symptoms began with right upper-extremity weakness that progressed to right hemiparesis and inability to verbalize.

On the third hospital day, the patient developed right-sided neurologic findings. Magnetic resonance imaging was consistent with a left middle cerebral artery infarction. A transesophageal echocardiogram demonstrated a mass attached to the left atrial appendage that prolapsed through the mitral valve during diastole (Figure 1). Cardiac catheterization revealed normal coronary arteries with no angiographic evidence of vascular extension into the mass.

Surgical resection was performed on cardiopulmonary bypass with moderate hypothermia via a transatrial approach. A calcified stalk arising from the posterior left atrium was resected with a small margin of normal atrial tissue.

The specimen was pedunculated and had a partially fimbriated surface (Figure 2A). Histologic sections revealed a fibrin thrombus with a predominantly polypoid architecture and numerous dense foci of malignant cells arrayed at the surface of the clot (Figure 2B⁻C). Cytologically, the infiltrate was composed of cells with high nuclear-cytoplasmic ratios and round to lobulated vesicular nuclei, containing multiple prominent nucleoli (Figure 2D). Occasional wreathlike nuclei and nuclei with cytoplasmic pseudoinclusions were observed (Figure 2E). Apoptotic cells and mitotic figures were numerous. Invasion into the myocardium was not identified in sections of the tumor mass or in the surgical margin from the base of the lesion.

Immunohistochemical studies revealed that the malignant cells stained positively with antibodies directed against CD45, CD20 (Figure 2F), CD79α, CD43, CD30 (Figure 2G), and embryonic membrane antigen. The cells were negative for CD3, Epstein-Barr virus (EBV), latent membrane protein, and human herpesvirus 8 antigen. Polymerase chain reaction (PCR) amplification of DNA extracted from paraffin tissue blocks with primers for immunoglobulin heavy chain genes, and gamma and beta T-cell-receptor genes, showed no evidence of clonal rearrangements. However, clonal kappa light chain rearrangement was detected by PCR. In situ hybridization performed on paraffin tissue sections with an oligonucleotide probe specific for EBER-1 RNA of EBV was positive in the malignant cells.

Further staging workup by physical exam, imaging studies, and bone marrow biopsy showed no other sites of disease. There was no clinical history of recurrent infections or autoimmune disorders. Additional laboratory studies, including serum protein electrophoresis, serologic and PCR-based tests for human immunodeficiency virus infection, and flow cytometry of peripheral blood, failed to demonstrate any indication of immune system abnormality.
The patient was diagnosed with primary cardiac CD30+ anaplastic large B-cell lymphoma and received 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone chemotherapy. Prophylactic cranial irradiation was not administered in the absence of identifiable disease. The patient is without evidence of disease 2 years after presentation.

Results and discussion

The definition of PCL has varied among authors. McAllister and Fenoglio2 excluded cases with any involvement outside the heart or pericardium. Others have allowed variable amounts of tumor outside the heart to be classified as PCL.1,4,6 By any criteria, it remains an extremely rare diagnosis.

This case demonstrates a number of unusual features that are important and challenging from clinical, diagnostic, and pathophysiologic perspectives. First is the consideration of the differential diagnosis of cardiac mural wall masses that present with embolic stroke. The most common primary cardiac tumor associated with stroke is myxoma.3 The age of the patient, the echocardiographic findings, and the mildly decreased platelet count suggested this as the most likely diagnosis; however, the location was noted to be somewhat unusual for myxoma. The preoperative differential diagnosis also includes primary cardiac sarcoma, metastatic disease, and mural thrombus. While rare, cardiac lymphoma should be considered in the differential diagnosis of cardiac mural masses.

In contrast to this case, PCL most commonly diffusely invades the pericardium, epicardium, or myocardium or presents as invasive nodular masses.1,4 A number of examples of intracavitary lymphomatous masses associated with an invasive component have been reported. Proctor et al7 describe a case of an intracavitary lymphoma tumor mass that mimicked cardiac myxoma on echocardiography. A polypoid PCL has also been reported to simulate prosthetic mitral valve thrombus on echocardiography.8 Two cases of fatal pulmonary tumor embolus arising from a PCL of the right atrium are reported.9,10 Wargotz et al11 describe a patient presenting with central nervous system complaints and radiographic lesions of the left cerebral hemisphere. At autopsy, the sole site of lymphoma involved the posterior walls of the atria. It is worthwhile noting that in each of these reported cases, the intracavitary mass was associated with an invasive component.

An additional point of interest is the identification of a CD30+ large B-cell lymphoma with anaplastic cytologic features. Anaplastic large cell lymphomas (ALCLs) are most often of T-cell or null phenotype and characteristically express CD30.12 B-cell ALCL is a relatively rare entity that shares the cytologic features and CD30 expression of T-/null-cell ALCL, but lacks the t(2;5) translocation and expression of the nuclear protein nucleophosmin/anaplastic lymphoma kinase fusion protein.13 B-cell ALCL presenting as a primary cardiac tumor has not been previously described. The finding of EBV nucleic acid sequences in the malignant cells by in situ hybridization has not been previously observed in PCL in immunocompetent patients.13,14 However, B-cell ALCL has been associated with EBV infection in some cases.15,16

A unique aspect of this case is the intimate association of the malignant lymphoid cells with a mural fibrin thrombus, without cardiac wall invasion. There are several possible explanations for how this lesion developed. The neoplastic process may have arisen within and remained localized to a previously formed thrombus, with growth and invasion limited by a reliance on atrial cavity blood flow. This hypothesis is supported by the superficial location of the neoplastic cells and an absence of nutrient vessels within the thrombus. Alternatively, an initial cardiac wall lymphoma may have spontaneously regressed, leaving only residual tumor within thrombus protected in this location from either vascular compromise or immune surveillance. A third possibility is that a primary lymphoma remote from the heart and clinically occult seeded an existing atrial mural thrombus.

We have described the unique presentation of B-cell ALCL as a noninvasive atrial thrombus in an immunocompetent patient with no evidence of systemic lymphoma.

Figure 2. Pathologic findings. (A) Gross photographic image of resected specimen. Arrowhead identifies the tumor stalk. Scale = 1 inch. (B) Histologic sections showed an organizing thrombus with a polypoid architecture (hematoxylin and eosin [H&E] stain). (C) Dense focus of atypical cells were predominantly arranged along the surface (H&E stain). (D) Malignant cells were round to lobated, with vesicular chromatin and prominent nuclei. Apoptotic cells and mitoses were numerous (H&E stain). (E) Occasional cells with cytoplasmic pseudoinclusions were observed (H&E stain). (F) Positive immunohistochemical staining with antibody to CD20 (immunoperoxidase). (G) Positive immunohistochemical staining with antibody to CD30 (immunoperoxidase). Original magnifications: panel B, ×2; panels C and F, ×10; panels D and E, ×100; panel G, ×40.

Figure 1. Transesophageal echocardiogram. (A) Left atrial intraluminal mass. (B) Atrial mass protruding into the left ventricle during diastole. LV indicates left ventricle.

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References