Case Report

Treatment Decisions in Geriatric Cardiac Lymphoma Facilitated by Serial Cardiac Magnetic Resonance Imaging and Positron Emission Tomography

P. Timothy Pollak, MD, PhD, Gurbir Brar, MD, Krishna Poinen, MD, and Carmen P. Lydell, MD

ABSTRACT

A tumour encasing the right coronary was identified on computed tomography pulmonary embolism protocol in an 81-year-old man. Concerns regarding tolerability of chemotherapy in an octogenarian were addressed using cardiac magnetic resonance imaging to monitor a trial of modified-chemotherapy for his primary cardiac B-cell lymphoma. Residual activity on positron emission tomography computed tomography mandated consolidation with radiotherapy to achieve a tumor-free return to health. Despite advanced age, successful therapy in this, the oldest case of primary cardiac lymphoma reported, was facilitated by monitoring treatment effectiveness with advanced cardiac imaging and the use of standardized frailty scores in communicating his appropriate level of robustness for tolerating chemotherapy.

Cardiac masses are uncommon, the majority being benign myxomas (80%), with sarcomas outnumbering lymphomas among the malignancies. Of the lymphomas, B-cell subtype predominates, often presenting with tumour encroachment of the right heart. The resultant nonspecific symptoms related to obstruction, arrhythmias, and pulmonary embolism make diagnosis and assessment of prognosis heavily dependent on imaging.

When an older patient presented with an aggressive cardiac lymphoma at age 81 years, a decade older than any previously reported case, therapeutic decisions were challenging because of the added potential for frailty decreasing tolerance of chemotherapy. No published reports were found to suggest the best course in this patient. Such concerns raised by advanced chronological age and potential for decompensating under lymphoma treatment are embodied in the 2015 European Society for Medical Oncology Practice Guidelines for B-cell lymphoma. They suggested the cutoff for normal therapy is 80 years of age. However, it is increasingly recognized that chronological age is not entirely indicative of a patient’s suitability for aggressive therapy. As such, tools including the Canadian Study of Health and Aging (CSHA) Clinical Frailty Scale have been developed to improve communication surrounding decisions regarding therapeutic choices in the older patients.

Case Presentation

A previously healthy 81-year-old man presented with 2 weeks of progressive cough and bilateral leg edema, on a background of recent 5-kg weight loss, making malignancy or...
tuberculosis the top differential diagnoses. Given his acute dyspnea, reduced oxygen saturation, positive D-dimer, normal pro-brain natriuretic peptide, and normal white blood cell count, a diagnosis of malignancy-associated pulmonary embolism was anticipated. However, no clot was found on a pulmonary embolism protocol computed tomography (CT) study of the chest. Instead, a cardiac mass of $10 \times 8 \times 11$ cm was found, encasing the right coronary artery and encroaching on the right atrium and ventricle, with perivascular lymphadenopathy and a pleural effusion (Fig. 1A).

**Figure 1.** Cardiac tumour diagnosis. (A) Initial pulmonary embolism protocol computed tomography (CT) image revealing a large heterogeneous mass extending into the right heart chambers and encasing the right coronary artery (arrows). (B) Corresponding axial cardiac magnetic resonance (CMR) image and late gadolinium enhancement image showing heterogeneous late enhancement, consistent with tumor. (C-F) Short-axis CMR sequences with further tissue characterization suggestive of malignancy showing homogeneous T2-signal (C); heterogeneous T1-signal (D); heterogeneous T1-enhancement on postgadolinium with fat saturation (E); and first-pass perfusion T1-enhancement (F).
Axial cardiac magnetic resonance (CMR) imaging (1.5 Tesla Siemens Avanto; Washington, DC) confirmed a large cardiac mass invading the right atrium and ventricle from the adjacent atrioventricular groove. The left myocardium was spared. As typical for lymphoma, the encased aortic root and right coronary artery were not detectably narrowed. Further
characteristics suggestive of lymphoma included homogeneous signal increase on T2-weighted SPectral Attenuated Inversion Recovery (SPAIR) images, mildly hyperintense myocardial signal on T1-weighted dark blood sequences, heterogeneous enhancement on post-gadolinium T1-weighted images, and limited heterogeneous enhancement on first-pass perfusion and late gadolinium phase-sensitive inversion recovery images (Fig. 1B-F). Because endocardial vascular access was blocked by the tumour, an imaging-guided anterior thoracic node biopsy was used to confirm a diagnosis of stage IV diffuse large B-cell lymphoma.

The healthcare teams had concerns regarding exposure of an octogenarian, even a healthy one, to standard, potentially cardiotoxic, chemotherapy. In evaluating risk of treatment, the Oncology service rated his score on the Eastern Cooperative Oncology Group (ECOG) performance scale as 2 at the time of diagnosis, just shy of midway between fully active and dead. We preferred to gauge his suitability for therapy on the basis of his recent excellent health, reflected in a score of 1 on the (CSHA) Clinical Frailty Scale. This implied a high degree of robustness with an excellent 5-year life expectancy (> 80%), if he were again free of cancer. In the end, it was agreed that a trial of nonanthracycline chemotherapy (substituting the topoisomerase inhibitor, etoposide, for the standard hydroxydaunorubicin) and given at reduced-doses should be considered to mitigate the risk of direct cardiotoxicity. Because CMR was available, effectiveness assessment became a practical adjunct to such a compromise regimen. An initial test cycle of Rituximab, Etoposide, Oncovin (vincristine) and Prednisone (methylprednisolone) (R-CEOP) was administered with doses of cyclophosphamide and etoposide reduced by 50%. This proved to be highly tolerable, and cyclophosphamide and etoposide were then increased by 10% of the normal dose with each cycle. Given that his excellent tolerance to chemotherapy was maintained with escalating doses, and CMR documented 75% tumour regression by the end of cycle 3 of therapy (Fig. 2B), all 6 cycles of therapy were completed. Postchemotherapy, positron emission tomography (PET)-CT showed 2 loci of residual activity (Fig. 2E), requiring consolidation with radiotherapy. Follow-up PET-CT, the next year (Fig. 2F), showed no residual activity, and the patient returned to his previous level of independent function. Written informed consent was obtained from the patient for publication of this Case Report and any accompanying images before the writing of this manuscript.

Discussion

Diagnosis of cardiac lymphomas is frequently delayed by the gradual onset of nonspecific symptoms suggestive of other conditions, including congestive heart failure, superior vena cava syndrome, or thromboembolism. Both potential tumour encroachment restricting access to the right heart and the inherent risks of cardiac biopsy can make obtaining tissue for pathology difficult. As in this case, sampling extracardiac nodes or pericardial fluid may be preferable. Nonetheless, continuously advancing imaging techniques have improved the workup of cardiac lymphomas and, as demonstrated in this case, can be helpful in monitoring therapy.

Therapeutic decisions involve consideration of risk/benefit. Serial assessment showing progressive efficacy and a Clinical Frailty Scale rating suggesting excellent resilience in our patient supported a favourable risk/benefit for chemotherapy. Indeed, CMR imaging and PET provided us with objective evidence of superb tumour response. Of equal import, subjective assessment of the degree to which chronological age increases risk of therapy is fraught with errors. Thus, better tools for assessment of a patient’s robustness can be of help to health professionals faced with increasingly older patients for whom concerns exist around both mounting frailty and lack of testing of standard therapies in advanced age. Growth in the use of systemized frailty assessment can be seen in protocols for determining suitability for cardiac procedures such as transcatheter aortic valve replacement. In Europe, frailty assessment is becoming a routine in the workup of older patients for chemotherapy. Aging of the population will eventually demand a shift toward the use of frailty assessment tools such as the Clinical Frailty Scale and its Rockwood adaptation rather than chronological age when making therapeutic decisions.

Diagnosis of cardiac tumours has long relied on the excellent spatial resolution of electrocardiogram-gated cardiac CT. However, information provided by the superior tissue characterization and localization available from CMR can furnish better initial evaluation of a cardiac tumour. Dynamic visualization of the mass, its relationship to myocardium/pericardium, degree of enhancement, and delineation of fatty/edematous tissue by T1/T2 signal characteristics all help distinguish between benign or malignant masses. Serial imaging with CMR can provide accurate monitoring of left and right ventricular function during therapy, with specific attention to sites of myocardium that were involved by tumour. Thus, when available, CMR is generally recommended for help differentiating cardiac masses. PET-CT provides adjunctive information most useful in identifying residual active tumor that is not anatomically apparent and confirming complete response at the end of treatment.

In considering the case reported, the treating physicians needed to be satisfied that the risks of chemotherapy would be balanced by a reasonable expectation of success. This was achieved in a 3-pronged approach. First, the patient was deemed by the Clinical Frailty Scale to be sufficiently resilient to attempt chemotherapy. Second, the toxicity of standard lymphoma therapy was mitigated by scaling doses and substituting etoposide for the standard anthracycline. Third, the efficacy of the modified therapy was confirmed using serial CMR assessments to justify completing therapy. Thus, in this case, CMR not only assisted in diagnosis but also provided early proof of the efficacy of patient-customized chemotherapy. Chemotherapy and radiation were ultimately curative, returning him to his previous quality of life, despite initial concerns that standard chemotherapy might be too risky in this octogenarian.

This case demonstrates how successful therapy of the oldest reported case of primary cardiac lymphoma was facilitated by the use of advanced cardiac imaging to ensure treatment effectiveness and the use of standardized frailty scoring to facilitate discussion of his appropriateness for treatment.
Disclosures
The authors have no conflicts of interest to disclose.

References
1. Yuda S, Nakatani S, Yutani C, et al. Trends in the clinical and morphological characteristics of cardiac myxoma: 20-year experience of a single tertiary referral center in Japan. Circ J 2002;66:1008-13.

2. Petrich A, Cho SI, Billett H. Primary cardiac lymphoma: an analysis of presentation, treatment, and outcome patterns. Cancer 2011;117:581-9.

3. Mohsen A, Najafi AH, Zhou L, et al. Massive, rapidly growing cardiac lymphoma with rare valvular involvement showing excellent response to chemotherapy. Can J Cardiol 2013;29:1139.e3-4.

4. Habertheuer A, Laufer G, Wiedemann D, et al. Primary cardiac tumors on the edge of oblivion: a European experience over 15 years. J Cardiothorac Surg 2015;10:56.

5. O’Mahony D, Peikarz RL, Bandettini WP, et al. Cardiac involvement with lymphoma: a review of the literature. Clin Lymphoma Myeloma 2008;8:249-52.

6. Pistritto AM, Pavo N, Maurer G, Binder T, Golasch G. Multimodality imaging of a primary cardiac diffuse large B-cell lymphoma. Eur Heart J Cardiovasc Imaging 2015;2015.

7. Tilly H, Gomes da Silva M, Vitolo U, et al. Diffuse large B-cell lymphoma (DLBCL): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015;26(Suppl 5):v116-25.

8. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-95.