CASE REPORT

Haemodynamic instability secondary to cardiac involvement by lymphoma

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SUMMARY

Cardiac involvement in lymphomas is not uncommon, but it is often missed due to the variability in its presentation. We present a case of bradycardia and complete heart block resulting in haemodynamic instability in a patient with recurrent diffuse large B-cell lymphoma. Timely diagnosis and appropriate management of such patients is crucial and requires a high index of suspicion. Our patient required temporary pacemaker implantation and intravenous corticosteroid therapy. His complete heart block and bradycardia eventually resolved after a course of radiation therapy.

BACKGROUND

Our case illustrates the need for a high index of suspicion for cardiac involvement in a patient with known (current or previous) history of lymphoma presenting with arrhythmias or other cardiac symptoms. In addition to aiding immediate management decisions and possibly saving the patient's life, such recognition could be the initial pathway to diagnosing recurrence of past lymphoma. In addition to lymphoma, other neoplasms such as lung, breast, leukaemia and melanoma should also be considered due to their tendency for cardiac involvement.

CASE PRESENTATION

A 68-year-old man with stage IV diffuse large B-cell lymphoma (DLBCL), coronary artery disease with coronary artery bypass grafting performed 6 years earlier and atrial fibrillation, presented with a 2-week history of progressive dyspnoea, cough and fatigue. Two months prior, he had completed six cycles of chemotherapy consisting of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP). Transthoracic echocardiogram (TTE), performed at the end of his chemotherapy regimen and prior to this admission, was normal, with no cardiac masses noted. Chest CT scan on presentation showed mediastinal lymphadenopathy, and the patient was subsequently admitted for a mediastinal lymph node biopsy.

The initial ECG on admission showed new-onset atrial flutter with intermittent asymptomatic bradycardia (figure 1). TTE was performed and showed a left atrial mass with mitral valve involvement, and mild-to-moderate mitral regurgitation (figure 2A, B). During the planned lymph node biopsy procedure (prior to surgical incision), the patient developed severe bradycardia (heart rate of 23 bpm) and hypotension (55/30 mm Hg) requiring cardiac resuscitation. He was immediately transferred to the Cardiac Intensive Care Unit, where a temporary

Figure 1 Initial 12-lead ECG on admission showing atrial flutter (seen most clearly in lead II) with a ventricular rate of 62 bpm.

pacemaker was implanted and vasopressor support with epinephrine and norepinephrine was started.

Given his medical history and echocardiographic findings, there was concern for lymphomatous infiltration of the heart as the cause of his acute episode of hypotension and bradycardia. A cardiac MRI could not be completed due to haemodynamic instability and the temporary pacemaker in place. A cardiac CT was therefore performed and showed diffuse pericardial, myocardial, bypass graft and aortic involvement, presumably from his previously diagnosed lymphoma (figure 3).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for the patient's left atrial mass found on TTE and cardiac CT scan can be divided into primary and secondary neoplasms. Primary neoplasms in adults include benign (myxoma, papillary fibroelastoma, lipoma, haemangioma and paraganglioma), as well as malignant (sarcoma, lymphoma and mesothelioma) aetiologies. Neoplasms that metastasise to the myocardium could present similarly—these include lung, breast and haematological malignancies (ie, leukaemia and lymphoma), and melanoma.^{1 2} Our patient's history of DLBCL made a diagnosis of secondary cardiac involvement by lymphoma the most likely aetiology.

Figure 2 (A and B) Transthoracic echocardiogram: (A) apical 4-chamber view showing left atrial mass (arrow) involving the lateral mitral annulus/basal leaflets, as well as the lateral wall of the left atrium. (B) The same left atrial mass (arrow) on parasternal long axis view.

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Figure 3 Cardiac CT showing lymphomatous involvement of the left atrium, mitral valve and descending aorta (red circle), as well as diffuse pericardial involvement (yellow arrows) with tumour necrosis (green circle).

TREATMENT

High-dose intravenous corticosteroid therapy was initiated to help reduce inflammation and oedema around the cardiac mass. The patient also received radiation therapy to the entire mediastinum (total dose of 400 cGy over 2 days). He was subsequently induced with one 5-day cycle of etoposide, methylprednisolone, ara-C and cisplatin (ESHAP) chemotherapy and one dose of intrathecal chemotherapy with methotrexate and cytarabine. After completion of chemotherapy, his temporary pacemaker was removed and a prophylactic single-chamber permanent pacemaker implanted.

OUTCOME AND FOLLOW-UP

Our patient's heart block and pacemaker dependence resolved with the initial dose of corticosteroid and radiation therapy. He converted from bradycardia with complete heart block to normal sinus rhythm with brief intermittent episodes of atrial fibrillation. He tolerated chemotherapy well and remained in normal sinus rhythm for the remainder of his hospital stay. He was discharged with a plan to follow-up for further cycles of ESHAP chemotherapy as an outpatient.

DISCUSSION

While primary cardiac neoplasms are rare, the incidence of cardiac metastases in the literature ranges from 2.3% to 18.3%. Postmortem studies have shown that cardiac involvement is present in 16% of patients with Hodgkin's lymphoma and 18% of patients with non-Hodgkin's lymphoma.³ The clinical presentation varies depending on the neoplasm's location, size, growth rate, degree of invasion and friability. Complete heart block, as seen in our patient, is an uncommon presentation.^{3 4} Metastasis to the pericardium commonly results in haemorrhagic pericardial effusions. Myocardial infiltration can present as arrhythmias (eg, atrial flutter, atrial fibrillation or premature atrial/ventricular complexes), conduction disturbances and congestive heart failure with systolic or diastolic dysfunction. On physical examination, the signs and symptoms could include chest pain, dyspnoea, hypotension or superior vena cava syndrome. While ECG changes are common, differentiating changes due to metastasis from changes due to myocardial damage from therapeutic antineoplastic agents can also be difficult.³

Lymphomatous metastasis to native valves is extremely rare, with a limited number of case reports in the literature.^{5–8} This low incidence is possibly due to the absence of vessels in the

valvular stroma and constant cusp motion.³ However, our patient had evidence of mitral valve involvement on TTE. The likely mechanism of metastasis varies depending on the cardiac structure involved. Pericardial involvement is the most common type of metastasis, and can be due to direct invasion of a mediastinal tumour, retrograde lymphatic spread or local advancement from other involved cardiac tissue. Metastases to the myocardium and epicardium are usually due to retrograde lymphatic spread or diffusion of the neoplasm from the pericardium. Finally, endocardial involvement is usually the result of haematogenous spread or diffusion from local myocardial metastases. Our patient's mitral valve tumour burden could be due to direct infiltration of the lymphoma from myocardial involvement or haematogenous spread.^{3 7}

The variability in presenting symptoms for lymphomatous cardiac involvement often causes these neoplasms to go unrecognised until autopsy.^{4 9} A high index of suspicion is necessary to identify cardiac involvement in these patients. While endocardial metastases usually localise to the right atrium and ventricle, myocardial metastases can involve any of the heart chambers.³ Diagnosis of these cardiac metastases requires leveraging multiple imaging techniques, including echocardiography, cardiac CT, cardiac MRI and fluorodeoxyglucose positron emission tomography. Pathological and immunohistochemical characterisation may also be helpful in guiding chemotherapy, and could be performed with thoracotomy or less invasively by pericardiocentesis with cytology.^{3 4 9}

Our patient was initially treated for stage IV DLBCL, with R-CHOP as first-line chemotherapy. However, 5–10% of patients will have disease progression despite primary therapy with R-CHOP, and 30–40% experience disease relapse requiring second-line therapy.¹⁰ Our patient's relapse was managed with mediastinal radiation and induction of ESHAP chemotherapy. While no clear gold standard exists for second-line therapy in these cases, ESHAP with or without rituximab is commonly used in patients who intend to proceed to autologous stem cell rescue.^{10–12} Unfortunately, despite intervention with salvage therapy with ESHAP, the progression-free and overall survival in patients with refractory DLBCL remains poor.¹⁰

Learning points

- ▶ Cardiac arrhythmias, including symptomatic bradycardia and/or complete heart block, could be the presenting symptoms of cardiac lymphoma.
- ▶ Cardiac involvement should always be considered in a lymphoma patient with cardiac arrhythmias or signs/symptoms.
- ▶ Valvular involvement is an atypical but possible presenting symptom of cardiac lymphoma.
- ▶ Transthoracic echocardiogram and cardiac CT can aid in the diagnosis of cardiac involvement by lymphoma.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Bruce CJ. Cardiac tumours: diagnosis and management. *Heart* 2011;97:151–60.
- 2 Goldberg AD, Blankstein R, Padera RF. Tumors metastatic to the heart. *Circulation* 2013;128:1790–4.
- 3 Bussani R, De-Giorgio F, Abbate A, et al. Cardiac metastases. *J Clin Pathol* 2007;60:27–34.

- 4 O'Mahony D, Piekarz RL, Bandettini WP, *et al.* Cardiac involvement with lymphoma: a review of the literature. *Clin Lymphoma Myeloma* 2008;8:249–52.
- 5 Abdullah HN, Nowalid WK. Infiltrative cardiac lymphoma with tricuspid valve involvement in a young man. *World J Cardiol* 2014;6:77–80.
- 6 Zlotchenko G, Futuri S, Dillon E, *et al.* A rare case of lymphoma involving the tricuspid valve. *J Cardiovasc Comput Tomogr* 2013;7:207–9.
- 7 Chisté M, Vrostos E, Zamora C, *et al.* Chronic lymphocytic leukemia/small lymphocytic lymphoma involving the aortic valve. *Ann Diagn Pathol* 2013;17:295–7.
- 8 Khanna A, Burkhart HM, Manduch M, *et al.* Composite Hodgkin and non-Hodgkin lymphoma of the mitral and aortic valves. *J Am Soc Echocardiogr* 2010;23:1113e.5–e7.
- 9 Jorge VJ, Bernardino V, Araujo AC, *et al.* Complete heart block as a complicating feature of a mediastinal lymphoma. *BMJ Case Rep* 2012;2012:pii: bcr1020114890.
- 10 Telio D, Fernandes K, Ma C, *et al.* Salvage chemotherapy and autologous stem cell transplant in primary refractory diffuse large b-cell lymphoma: outcomes and prognostic factors. *Leuk Lymphoma* 2012;53:836–41.
- 11 Zelentz AD, Gordon LI, Wiera WG, *et al.* Non-Hodgkin's lymphomas, version 4.2014. *J Natl Compr Canc Netw* 2014;12:1282–303.
- 12 Philip T, Guglielmi C, Hagenbeek A, *et al.* Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy sensitive non-Hodgkin's lymphoma. *N Engl J Med* 1995;333:1540–5.

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