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Burkitt Lymphoma Presenting as an Intracardiac Mass: Case Report and Review of Literature

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Conflict of interest: None declared

Patient: Male, 27
Final Diagnosis: Burkitt lymphoma with intracardiac mass
Symptoms: Dizziness • fatigue • palpitations • weight loss
Medication: —
Clinical Procedure: Catheter-directed thrombolytic therapy with intracardiac infusion of alteplase
Specialty: Hematology

Objective: Rare disease

Background: Non-neoplastic causes such as infections and thrombi account for most intracardiac masses. Primary tumors such as myxomas and metastasis from breast cancer, lung cancer, or melanomas account for many of the remaining cases. Burkitt lymphoma manifesting as an intracardiac mass is a rare entity, with 21 cases reported in the English literature.

Case Report: We report the case of a man infected with human immunodeficiency virus (HIV) who presented with non-specific cardiac symptoms and was later found to have intracardiac mass caused by Burkitt lymphoma. His rapid decline with unexpected complications was reversed with prompt management. Subsequent to induction, the patient achieved a near complete response with considerable improvement in his condition.

Conclusions: Lymphoma should be considered in the differential diagnosis of intracardiac masses. Associated cardiac symptoms are frequently non-specific and can often be overlooked or underappreciated. Burkitt lymphoma has a short doubling time and an intracardiac lesion can become life-threatening in a matter of days. Early recognition and prompt treatment are crucial to achieving optimal outcomes.

MeSH Keywords: Burkitt Lymphoma • Heart Neoplasms • Lymphoma, Non-Hodgkin

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/899022

Background

Burkitt lymphoma (BL) constitutes less than 1% of all non-Hodgkin lymphomas (NHL) [1], and this percentage increases to 25% to 30% in patients with human immunodeficiency virus (HIV) infection [2]. The incidence of cardiac involvement with NHL ranges from 9% to 24% in autopsy series [3–6]. This has increased steadily over time [7] due to increased life expectancy of immunocompromised individuals and improvement in diagnostic tests [2]. Diffuse large B cell lymphoma is the most common lymphoma involving the heart. BL manifesting as an intracardiac mass is extremely rare, with only 21 reported cases in the English literature. We report a case in an HIV-infected patient followed by a review of the published literature.

Case Report

A 27-year-old white man presented with palpitations and dizziness of a few days duration. He also complained of 3 months of fatigue and an 18-kg weight loss. He was diagnosed with HIV infection 5 years ago and was compliant with his antiretroviral therapy (combination of elvitegravir, cobicistat, emtricitabine, and tenofovir). The patient denied any history of substance abuse. Pertinent physical findings included irregular pulse with tachycardia, tachypnea, and elevated blood pressure. His oxygen saturation was normal (95%) on room air. An ejection systolic murmur was heard at the left lower sternal border, and his liver was palpable 3 cm below the costal margin. Laboratory work-up revealed a CD4+ T cell count of 79 cells/μL with HIV RNA copies of 90/mL. Complete blood count revealed a white blood count of 9100/μL, hemoglobin 12.3 g/dL, and platelet count of 701 000/μL. Occasional premature ventricular complexes were noted on his electrocardiogram.

Computed tomography (CT) scan of the abdomen and pelvis showed multiple liver lesions, the largest measuring 7.8×6.2×10.1 cm (Figure 1A). A CT scan of the chest demonstrated a 7-cm lesion within the right atrium (Figure 1B) with bilateral pleural effusions. Masses were noted in the mediastinum, lungs, pancreas, kidneys, and ilium. An initial transthoracic echocardiogram (TTE) revealed a solid (5×4.3 cm) right atrial mass, invading the base of the right ventricular free wall and the interatrial septum (Figure 2A, 2B). A small amount of pericardial effusion was also noted. There was no valvular involvement and the ejection fraction was preserved. Three-dimensional transesophageal echocardiography (TEE) showed that the quantitated volume of the right atrial mass was 29 mL.

An ultrasound-guided biopsy of the largest liver lesion revealed a diffuse sheet-like proliferation of intermediate-to-large lymphoid cells with irregular nuclei (Figure 3A). Many areas demonstrated a prominent starry sky appearance with scattered macrophages (Figure 3B). Scattered mitotic activity was noted with areas of apoptosis. On immunoperoxidase stains, the neoplastic cells were strongly and diffusely positive for LCA, CD20, BCL6, and CD10 and had a Ki-67 positivity of 100%. They were negative for CD45RO, BCL1, BCL2, PLAP, AE1/AE3, and Cam 5.2. Fluorescence *in situ* hybridization (FISH) showed rearrangement of *myc* and *IgH* t (8, 14) genes.

A diagnosis of acquired immunodeficiency syndrome (AIDS) with stage IVB Burkitt lymphoma was made. The insertion of an Ommaya reservoir was planned in anticipation of intrathecal chemotherapy. However, the surgery was abandoned when the patient became hypoxic during induction of general anesthesia. He subsequently developed hypotension and went into cardiogenic shock. A repeat echocardiogram revealed severe tricuspid valve stenosis due to the rapidly growing intra-atrial tumor, which now extended into the right ventricle. A new

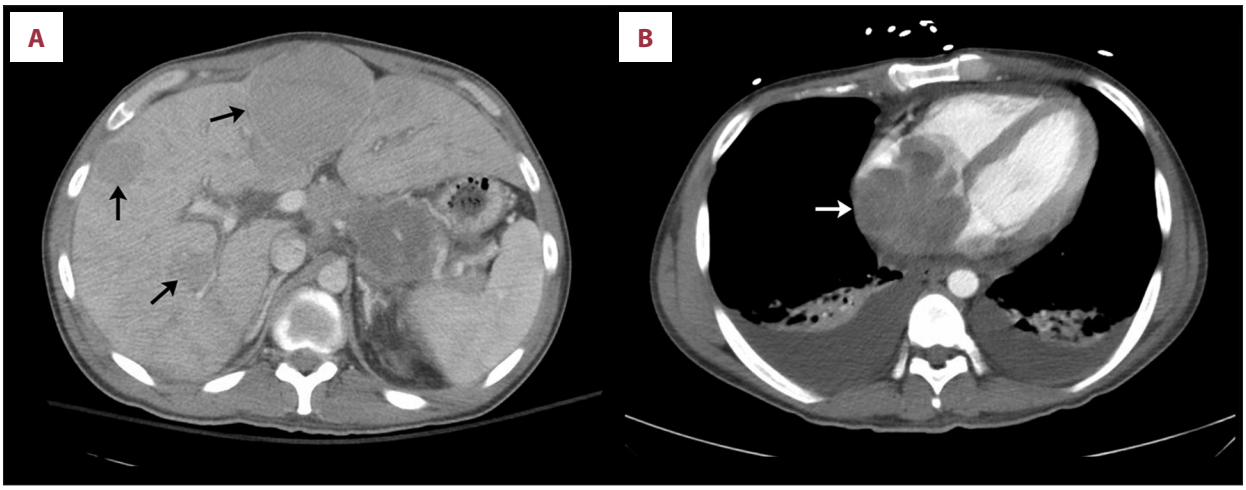

Figure 1. (**A**) CT scan of the abdomen and pelvis shows multiple, hypodense lesions in the liver (arrows). (**B**) CT scan of the chest shows the right atrial mass (arrow).

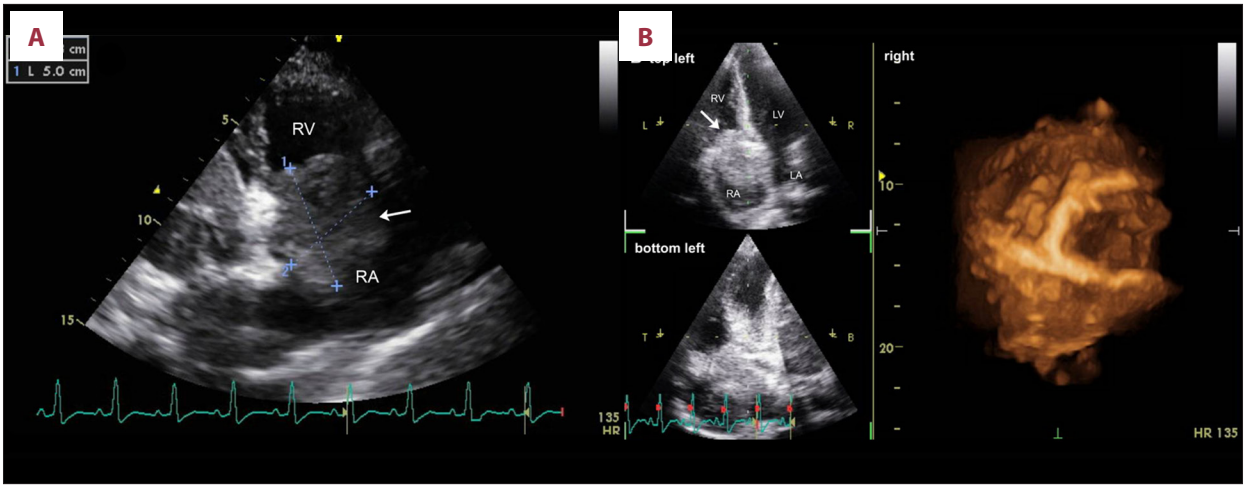

Figure 2. (**A**) Pretreatment 2-dimensional TTE shows a 5×4.3-cm right atrial mass (arrow) (crosshairs represent dimension measurements). (**B**) Apical 4-chamber view (top left) of the mass (arrow) and another image plane (bottom left) combined to generate a 3-dimensional reconstruction of the mass (right). LA – left atrium; LV – left ventricle; RA – right atrium; RV – right ventricle.

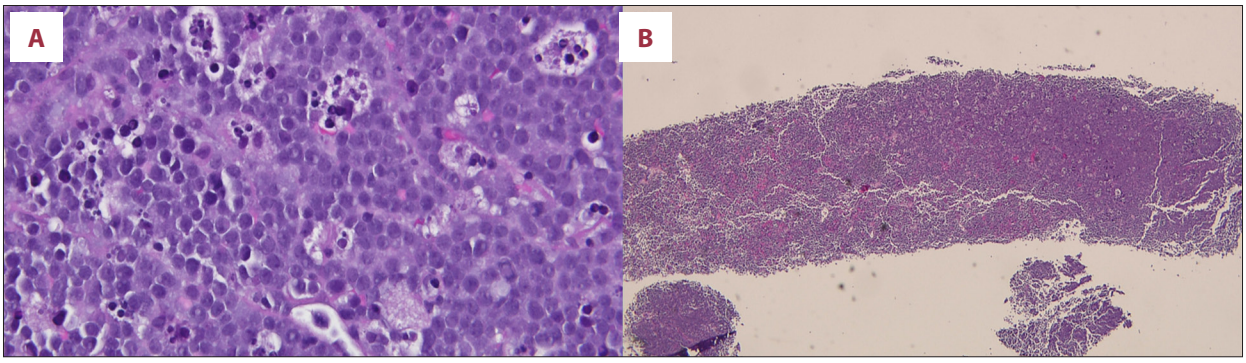

Figure 3. (**A**) Hematoxylin and eosin stains of liver biopsy at 400× magnification demonstrate diffuse sheet-like proliferation of intermediate to large tumor cells with irregular nuclei. (**B**) Hematoxylin and eosin stains of liver biopsy at 40× magnification demonstrate areas of prominent starry sky appearance with scattered macrophages.

right atrial mass consistent with a thrombus was also noted. A diagnosis of cardiac thrombosis overlying the intracardiac tumor was made.

Chemotherapy with modified cyclophosphamide, vincristine, doxorubicin, and methotrexate/ifosfamide, etoposide, cytarabine (CODOX-M/IVAC regimen) was started. The reason this regimen was chosen instead of a regimen with rituximab is because HIV-positive patients with low CD4 counts often do poorly with rituximab and have increased rates of infection-related deaths. Although recent studies suggest there might be some benefits, these data were not available at the time of this patient's care, and thus it was not incorporated into our management decision. Catheter-directed thrombolytic therapy with intracardiac infusion of alteplase was given for 5 days. The patient showed a rapid response to therapy with improvement in organ function and he was discharged 3 weeks later. He completed 4 cycles of chemotherapy with a complete

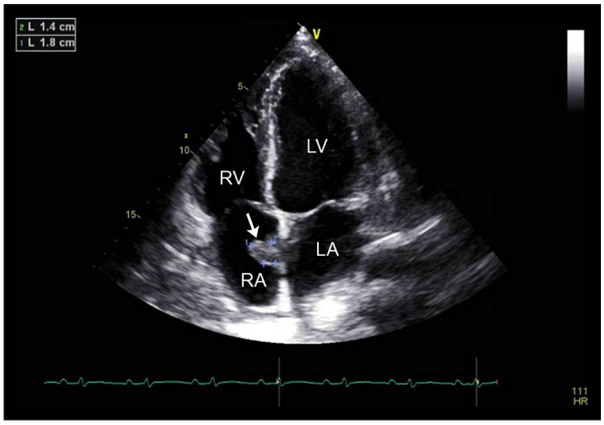

Figure 4. Post-treatment 2-dimensional TTE shows a 2.0×1.4 cm right atrial mass (arrow). LA – left atrium; LV – left ventricle; RA – right atrium; RV – right ventricle.

Table 1. Published case reports of Burkitt lymphoma causing intracardiac mass.

Year	Age	Sex	HIV	Pertinent symptoms	Intracardiac mass location	Diagnostic procedure	Treatment	Outcome	Reference
1975	12	M	N/A	SOB, anorexia, palpitation	RA	Autopsy	No treatment	D (days)	Cole [15]
1990*	35	M	+	SOB, WL, orthopnea	RV	Pericardiotomy	Vincristine	D (days)	Helfand [16]
1992	29	M	N/A	SOB, WL, F	RA, LA	Laparotomy	N/A	D (days)	Zyssman [17]
1992**	13	M	N/A	F, cough	LA	Mediastinoscopic biopsy	N/A	R	Moore [18]
1992**	55	W	N/A	Syncope	RA	Autopsy	No treatment	D (days)	Bestetti [19]
1998	47	M	+	SOB	TV, RV, RA, LA	Cytology of pericardial fluid	EPOCH, bleomycin	R (3+ yrs)	Brinkman [20]
2000	78	W	N/A	SOB	RA	Thoracotomy	N/A	D (days)	Carfagna [21]
2004	10	M	Neg	SOB, cough, fatigue	RA, inter-atrial septum, pulmonary infundibulum	Thoracotomy	Patient was in a study: 1 x COP, COPADM, CYM	R (3+ yrs)	Chalabreysse [12]; Meshref [22]
2005	9	M	N/A	SOB	RA	N/A	N/A	R (4 wks)	Ahmad [23]
2006*	70	M	Neg	SOB	RA	Endomyocardial transvenous biopsy	N/A	N/A	De Filippo [13]
2006	4	M	+	SOB, orthopnea	RA	Median sternotomy	N/A	D (days)	Singh [24]
2007	41	W	+	BLE weakness, lower back pain	LV	Vertebral mass biopsy	EPOCH	R	Mendiolaza [25]
2007	52	M	+	SOB, CP, night sweats	RA, LA	N/A	R-CHOP	R	Poh [26]
2008	61	W	Neg	SOB, palpitation	RV	Thoracotomy	Hyper-CVAD	D (days)	Stefani [27]
2009	33	M	Neg	SOB	RA	Thoracotomy	N/A	N/A	Peng [28]
2009	67	M	Neg	Syncope	RA, LA	Resection	CODOX-M, Ara-C	R (12 m)	Santini [29]
2009*	74	M	Neg	SOB	RA	Intracardiac mass biopsy	CHOP	D (6 wks)	Legault [30]
2010*	9	M	Neg	SOB, cough, palpitations	RA	Fine needle cervical node biopsy	CHOP	D/C after 3 wks, LTF	Mocumbi [31]
2014*	45	M	+	F, WL, night sweats	LV	Liver biopsy	R-EPOCH	D (days)	Bush [2]
2014	26	F	+	SOB, leg edema, fatigue	RA	Laminectomy	CHOP	D (days)	Basavaraj [32]
2015	38	M	+	SOB, palpitations	RA	Open sternotomy	R-EPOCH	R	Lazkani [33]

* Burkitt-like or highly likely Burkitt; ** small non-cleaved cell type. Ara-C – cytarabine; BLE – bilateral lower extremity; CHOP – cyclophosphamide, doxorubicin, vincristine, prednisone; CODOX-M – cyclophosphamide, vincristine, doxorubicin, and methotrexate; COP – cyclophosphamide, vincristine, prednisone; COPADM – cyclophosphamide, vincristine, prednisone, doxorubicin, methotrexate; CP – chest pain; CVAD – cyclophosphamide, vincristine, doxorubicin, dexamethasone; CYM – Ara-C, methotrexate; D – deceased; D/C – discharged; EPOCH – etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin; F – fever; HA – headache; HD – high-dose; LA – left atrium; LN – lymph node; LTF – lost to follow-up; LV – left ventricle; m – month(s); M – man; MTX – methotrexate; N/A – information not available; Neg – negative; + – positive; R – remission; R-CHOP – rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; R-EPOCH – rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin; RA – right atrium; RV – right ventricle; SOB – shortness of breath; TV – tricuspid valve; W – woman; wks – weeks; WL – weight loss; yrs – years.

resolution of his symptoms and cardiac murmur. The intracardiac mass was notably decreased to 2.0×1.4 cm (previously 5×4.3 cm) on TTE (Figure 4) with quantitated volume reduced to 5 mL (previously 29 mL) on TEE. CT scans of the chest and abdomen revealed complete resolution of his pleural effusions and renal masses, with the mediastinal and retroperitoneal lymphadenopathy showing significant response.

Discussion

BL is a highly aggressive subset of B cell NHL. It is an uncommon disease in adults, accounting for less than 1% of all NHL [1]. HIV patients have a 200-fold increased risk of developing NHL, with 25% to 30% of these being BL or Burkitt-like lymphoma [2]. Unlike other types of HIV-associated lymphomas, these patients often have CD4 counts greater than 200 cells/μL [8]. HIV-associated BL are more likely to have atypical presentations with extra-nodal disease and liver, lung, and other organ involvement [8].

Intracardiac mass secondary to BL is rare. The usual causes of intracardiac masses are non-neoplastic (e.g., structural abnormalities, infections, thrombi, and hamartomas). Neoplastic causes can be metastasis to the heart or primary cardiac tumors, with the former being more common [9]. About 90% of all primary cardiac tumors are benign and include myxomas, papillary fibroelastomas, fibromas, lipomas, angiomas, and rhabdomyomas [10]. Sarcomas are the most common malignant primary cardiac tumors, accounting for 95% of cases, and mesotheliomas and lymphomas account for the rest [9,10]. The metastatic intracardiac tumors usually arise from breast or lung cancer, melanoma, or lymphomas [10].

Primary cardiac lymphomas (PCL) or lymphomas involving only the heart and/or pericardium has an estimated incidence of less than 0.05% [3, 11]. According to the largest published review of PCL, only 197 published cases of PCL were reported from 1949 to 2009. Of these, only 13 (6.6%) were BL [3]. Disseminated NHL with cardiac involvement has a higher incidence (9% to 24%) [3–6] compared to PCL, but there are suggestions that these entities might not be as distinct as previously thought. PCL has a propensity to involve the superior vena cava (SVC) and the right side of the heart, which are the areas that receive lymph drainage from the thoracic duct. It is hypothesized that PCL could be merely a manifestation of occult systemic lymphoma (spreading to the heart by the thoracic duct) instead of a primarily cardiac issue [3]. Regardless of the origin, an intracardiac mass caused by BL is exceedingly rare. To the best of our knowledge, there are only 21 reported cases in the English literature (Table 1). We excluded 4 cases that might have met our criteria, because the articles were not available in English. Older cases reported as Burkitt-like or small non-cleaved cell type on pathology were included unless otherwise specified.

Among the 22 cases (including present case), all 3 types of BL were represented (9/22 (41%) sporadic, 4/22 (18%) endemic, and 9/22 (41%) immunodeficiency-associated). Most were men (17/22 (77%)). The age ranged from 4 to 78 years, with a median of 38 years, much younger than the median age for PCL in adults, which is approximately 60 years [3,12]. The reason for this predilection for intracardiac involvement in younger patients remains unclear. Common presenting symptoms include dyspnea, palpitation, dizziness, and B-symptoms, which are consistent with prior studies on cardiac lymphoma [2,3,12]. There were 9/22 (41%) HIV-positive cases, 7/22 (32%) HIV-negative cases, and HIV status was not reported in 6/22 (27%). The disease was right-sided in 16/22 (82%) cases. Patients received standard chemotherapy regimens such as EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) or CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) with or without rituximab, Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone), and CODOX-M. A total of 10/22 (45%) patients died. No treatments were reported for 6/10 (60%) patients that died. Most of these patients died within a few days of diagnosis, 9/10 (90%), and 1 died 6 weeks after diagnosis. BL was diagnosed at autopsy in 2 cases. The longest surviving patient was reported to be alive at 36 months after diagnosis. It is well known that BL is a highly aggressive tumor, but in the presence of cardiac involvement, it seems to lead to even more complications and worse outcomes.

Symptoms of dyspnea or palpitations are common in BL patients, most of whom do not have any intracardiac involvement. BL has a rapid doubling time, and intracardiac involvement can become life-threatening very quickly, as seen in our patient. Keeping a high index of suspicion for possible intracardiac involvement is vital. Pericardial effusion and arrhythmias frequently accompany intracardiac lymphomas [9]. TTE is the preferred diagnostic modality [10,13]. Trans-esophageal echocardiogram (TEE) and magnetic resonance imaging (MRI) are helpful in equivocal cases [6,14]. Immunosuppression, presence of extra-cardiac disease, left ventricle involvement, and absence of arrhythmia are associated with poor prognosis [3]. Surgery and radiation therapy have not shown any benefit [3,6,11]. Early treatment with anthracycline-based chemotherapy is associated with the best outcome [12,14].

Conclusions

BL causing intracardiac mass is rare, with only 21 cases reported in the English literature. The cardiac symptoms are frequently non-specific and can often be overlooked or underappreciated

in the presence of the impressive extra-cardiac disease. Due to the aggressive nature of BL, the cardiac tumor can progress and become life-threatening very quickly. Any delay in diagnosis or treatment can decrease the chances of survival. Our patient is a good reminder that early detection, treatment, and optimization of cardiac parameters can potentially mean the difference between life and death in these patients.

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Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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