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CASE REPORT: CLINICAL CASE: ACC.24

Mantle Cell Lymphoma With Cardiac Involvement Presenting as Complete Heart Block

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ABSTRACT

A 50-year-old woman presented with complete heart block on electrocardiogram. Echocardiogram revealed an intracardiac mass with extensive cardiac involvement. The patient was diagnosed with mantle cell lymphoma, confirmed via lymph node biopsy. Pacemaker implantation and chemotherapy were initiated, with subsequent improvement noted. This showcases an unusual manifestation of intracardiac metastasis with conduction system infiltration. (JACC Case Rep 2024;29:102416)

HISTORY OF PRESENTATION

A 50-year-old woman presented with worsening exertional dyspnea, lower extremity edema, and cervical adenopathy. On initial evaluation, the patient was found to have a heart rate of 45 beats/min, blood pressure of 116/74 mm Hg, jugular venous distention, bilateral pitting lower extremity edema, and diffuse lymphadenopathy in the submandibular, submental, and anterior/posterior cervical chains; otherwise, cardiopulmonary examination was unrevealing.

LEARNING OBJECTIVES

- To understand the potential cardiac involvement in MCL and its implications for diagnosis and treatment.
- To identify the role of multimodality imaging techniques, including transthoracic echocardiography and PET-CT scan, in staging and managing cardiac masses associated with MCL.
- To recognize the challenges and considerations in pacemaker lead placement in patients with intracardiac involvement of MCL, highlighting the importance of procedural planning and imaging-guided interventions.

PAST MEDICAL HISTORY

Past medical history was significant for type 2 diabetes.

DIFFERENTIAL DIAGNOSIS

Intracardiac masses have an extensive differential diagnosis, including tumors, lipoma, infective vegetation, calcified lesions, and thrombus.[1] Although exceedingly rare, primary cardiac tumors can be benign or malignant. Intracardiac tumors secondary to metastasis are far more common than a primary cardiac neoplasm and can be caused by metastases from malignant melanoma, soft tissue sarcoma, primary lymphoma, leukemia, breast, esophageal, and

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ABBREVIATIONS AND ACRONYMS

CT = computed tomography

FDG = fluorodeoxyglucose

ICE = intracardiac echocardiogram

MCL = mantle cell lymphoma

PET = positron emission tomography

PET-CT = positron emission tomography-computed tomography

TTE = transthoracic echocardiogram

lung cancer. Pericardial involvement of cardiac masses is more likely to be related to metastasis or lymphoma. Cardiac masses can present with a wide array of findings on history and physical examination. Transthoracic echocardiography can help with identifying the myocardial or chamber involvement.[2] Transesophageal echocardiography provides increased spatial and temporal resolution.[3] Other imaging modalities include cardiac magnetic resonance, positron emission tomography (PET), and computed tomography (CT). Cardiac magnetic resonance has the advantages of using T1- and T2-weighted sequences to delineate the tumor further.[4] Positron emission tomography-computed tomography (PET-CT) is useful in establishing disease stage and provides a baseline for treatment response especially with lymphomas because most lymphomas are 18F-fluorodeoxyglucose (FDG) avid. Contrast-enhanced CT can be helpful in staging the mass along with PET-CT.[5]

INVESTIGATIONS

Initial electrocardiogram revealed complete heart block with a stable junctional escape rhythm. The patient underwent urgent bedside transthoracic echocardiogram (TTE), which showed a giant mass obliterating the right atrium and invading multiple cardiac structures including the tricuspid annulus, right ventricle, and left atrium, and encasing the aortic root (**Figures 1A and 1B**). Additionally, there was a separate mass in the inferolateral segment of the left ventricle and a large pericardial effusion without cardiac tamponade. The patient had no previous TTE reports from before for comparison.

Pericardiocentesis was performed for diagnostic and therapeutic purposes, yielding 380 mL of serous fluid, and the patient underwent permanent pacemaker implantation. Because the diagnosis was made via TTE and the patient required an emergent pacemaker, a cardiac magnetic resonance was not performed.

A bone marrow biopsy and PET-CT scan were obtained to complete the staging workup. Bone marrow biopsy showed no evidence of malignancy, and pericardial fluid cytologic analysis was also negative for malignancy. An ^{18}F-FDG PET-CT scan was obtained and revealed widespread FDG-avid disease in multiple organs both above and below the diaphragm, including the neck, chest, retroperitoneal lymph nodes, nasal cavity, skull base, pericardium, small bowel, bilateral renal parenchyma, and right thigh (**Figure 1C**). A contrast-enhanced CT scan showed that the mass measured 74 mm (left-right), 43 mm (superior-inferior), and 62 mm (anterior-posterior) (**Figures 2A and 2B**). A left cervical lymph node fine needle aspiration revealed a diffuse infiltrate of medium-sized atypical lymphoid cells with distinct characteristics, including powdery chromatin, small nucleoli, irregular nuclear contours, and limited cytoplasm. This was observed against a backdrop of tingible body histiocytes forming a starry sky pattern. Immunohistochemical analysis showed positivity for CD20 (Cluster of Differentiation 20), PAX5 (Paired Box 5), IgM (Immunoglobulin M), and cyclin D1; high expression (90%) of Ki-67; partial positivity for BCL6 (B-Cell Lymphoma 6 protein) and BCL2 (B-Cell Lymphoma 2 protein); equivocal positivity for CD43 (Cluster of Differentiation 43); and negativity for all other markers assessed. Fluorescence In Situ Hybridization (FISH) analysis demonstrated CCND1/IGH fusion and a BCL6 rearrangement in nearly 100% of nuclei, confirming a diagnosis of mantle cell lymphoma (MCL), blastoid variant.

MANAGEMENT

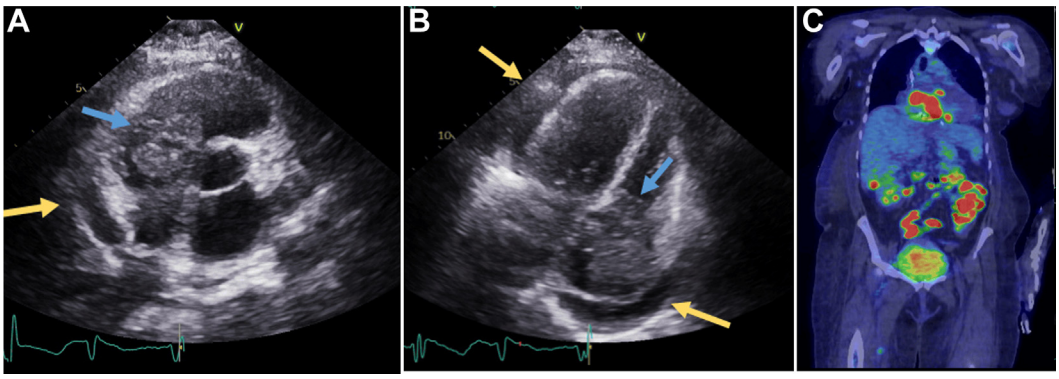
The decision to place a traditional dual-chambered pacemaker was made. Intracardiac echocardiogram (ICE) was used to enhance the infiltrative cardiac mass visualization and to assess the feasibility of lead placement. ICE revealed an extensive mass extending from the right atrium through the tricuspid annulus to the right ventricle with tricuspid inflow stenosis (**Figures 3A and 3B**). A 150-cm, 0.089 cm angled Glidewire (Terumo Interventional Systems) was used to traverse through the narrow tricuspid inflow, and a Worley sheath (Merit Medical) was advanced into the right ventricle over the Glidewire. A 65-cm right ventricular pacing lead was advanced through the long sheath and screwed into the right ventricular apical septum. Given the friable mass's extensive involvement in the right atrium, including portions of the right atrial appendage, the right atrial lead was placed on the inferoposterior aspect of the interatrial septum (**Figure 3C**). The procedure was tolerated without significant complications.

The patient was initiated on systemic therapy with the Nordic regimen (dose-intensified rituximab, cyclophosphamide, vincristine, doxorubicin, and prednisone alternating with rituximab and high-dose cytarabine).

DISCUSSION

We present a unique case of widespread MCL with the involvement of multiple cardiac structures leading to

FIGURE 1 **At Presentation**



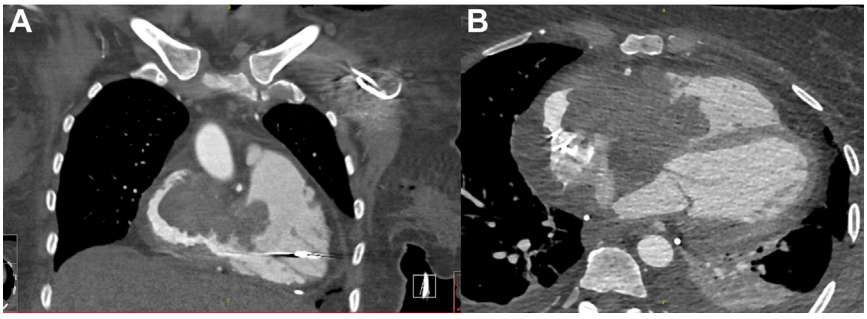
(A) Parasternal short-axis view. (B) Apical 4-chamber view. (C) Increased fluorodeoxyglucose uptake in the right atrium, right ventricle, pericardium, small bowel, and liver. Blue arrow: intra-cardiac mass; yellow arrow: pericardial effusion.

third-degree atrioventricular block. This case highlights the following: 1) the potential for extranodal involvement of MCL in the cardiac conduction system; 2) multimodality imaging used for the staging and management; 3) unique pacemaker lead placement given intracardiac involvement; and 4) Nordic protocol chemotherapy as a treatment of MCL.

Multiple imaging modalities were used, including TTE, ICE, and PET-CT, to assist with mass characterization, to assist with staging, and to guide proper pacemaker lead positioning. PET-CT showed FDG-avid intracardiac lesions with widespread FDG-avid disease in multiple organs above and below the diaphragm. The patient had experienced a complete heart block, which required urgent placement of a dual-chamber permanent pacemaker. ICE enhanced the infiltrative cardiac mass visualization to ensure proper positioning of myocardial tissue instead of the infiltrative mass. A very large mass encompassing the right ventricular inflow, periaortic, and right atrial region was visualized. It also demonstrated tricuspid inflow stenosis, which was not fully appreciated on other imaging modalities. This allowed for successful ventricular lead placement by traversing the inflow stenosis. Tissue biopsy was ultimately pursued for definitive diagnosis and guided chemotherapy selection.

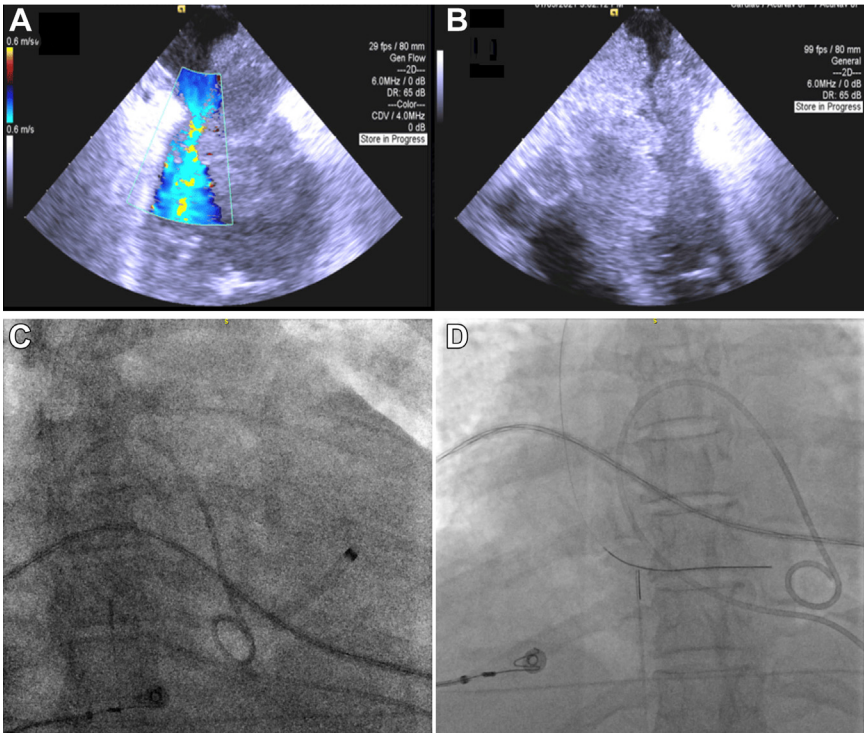
The decision to implant a dual-chambered pacemaker was a judgment call and influenced by various factors. A leadless pacemaker was considered but was not done considering anticipated challenges in passing a 27-F sheath through the tricuspid annulus obstructed by the tumor mass. A temporary pacing wire was also considered. However, at our institution, we do not retain temporary pacemakers beyond a week. Uncertainties regarding chemotherapy efficacy

FIGURE 2 **Contrast-Enhanced CT Scan Before Pacemaker Implantation**



(A) Apical computed tomography. (B) Coronal computed tomography.

FIGURE 3 Images During Pacemaker Implantation Procedure (ICE and Flouroscopic Images)



(A and B) Intracardiac echocardiography reveals significant stenosis through the tricuspid valve orifice secondary to malignant obliteration. (C and D) Right anterior oblique and left anterior oblique fluoroscopic images.

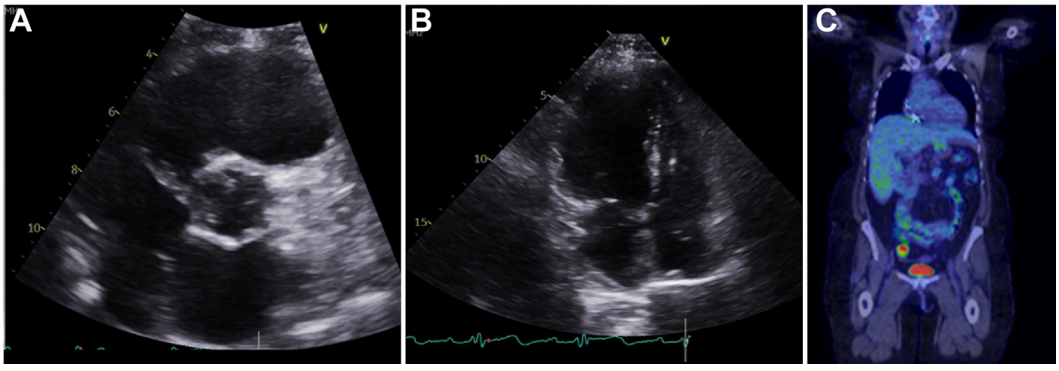
and its impact on heart block led us to forego temporary pacing. Furthermore, a single-chambered pacemaker would have hindered achieving atrioventricular synchrony. Finally, given the potential challenges of cytopenia with chemotherapy, we thought that a definitive strategy would help her in the long run and acted on the narrow window of intervention opportunity.

Opting for a permanent pacemaker implantation, rather than a temporary one, ultimately proved beneficial. Even after the mass resolved post-chemotherapy, the patient required a high burden of pacing, validating the appropriateness of our decision.

MCL is an aggressive subtype of B-cell non-Hodgkin lymphoma that typically presents at an advanced stage at diagnosis and rarely results in cardiac involvement. Classic MCL arises from naïve B cells expressing SOX11 and tends to involve lymph nodes and extranodal sites. The annual incidence is thought to be 1 to 2 per 100,000 people, with a median age of 60 to 70 years of age at diagnosis and a 3:1 male predominance.[6] Roughly 75% of patients present with lymphadenopathy, and common sites of involvement include the lymph nodes, bone marrow, and spleen, and extranodal sites include the gastrointestinal tract, Waldeyer's ring, and orbit.[7] Up to one-third of patients may present with B-symptoms, including drenching night sweats, fever, and unintended weight loss. Cardiac involvement of MCL is unusual, with few reported cases in the existing literature. Apart from one case report, and Surveillance, Epidemiology, and End Results (data on 4,477 patients with MCL), which showed only 4 cases with primary lymphoma in the thymus, mediastinum, or heart, there is no additional data on MCL's involvement with the heart.[8] The exact cause of conduction issues related to cardiac tumors is unclear, but it is thought to stem from either local pressure or direct invasion of the heart's conduction pathways.[9]

At present, there is significant controversy and ambiguity regarding the optimal treatment for

FIGURE 4 On Follow-Up



(A) Parasternal short-axis view. (B) Apical 4-chamber view. (C) Increased fluorodeoxyglucose uptake in the right atrium, right ventricle, pericardium, small bowel, and liver.

patients with MCL. Most patients with MCL require treatment at the time of diagnosis, although a minority of patients with low-risk disease may be observed clinically. Multiple chemotherapeutic induction regimens have been described in the literature, and treatment is dependent on the patient's disease stage, performance status, and eligibility for autologous hematopoietic cell transplantation. Those with aggressive, extensive stage, bulky disease who are thought to be candidates for consolidative autologous hematopoietic cell transplantation are typically treated upfront with aggressive chemotherapy regimens. Surgical resection is not usually used unless gastrointestinal bowel obstruction or bleeding is present. As in the present case of a patient with extensive symptomatic disease burden including cardiac involvement and good baseline performance status, intensive chemoimmunotherapy with a protocol such as the Nordic regimen may be considered.[10] Encasement of the aortic root affecting the conduction system is the most likely cause of her complete heart block. PET-CT is useful in establishing disease stage and provides a baseline for treatment response as MCL is ^{18}F-FDG avid.

FOLLOW-UP

After completing the first cycle of the chemotherapeutic regimen, a repeat TTE showed a significant reduction in the intracardiac mass size with a tricuspid inflow stenosis resolution. Also, the initial mass along the left ventricle was effaced with complete resolution of the prior pericardial effusion (**Figures 4A and 4B**). PET-CT after two chemotherapeutic cycles showed significant metabolic response to both extranodal and nodal lymphoma. On 21-month follow-up, the PET-CT showed no FDG uptake (**Figure 4C**).

All serial follow-up device interrogation reports consistently indicated that the patient's underlying rhythm was sinus with first-degree atrioventricular block. Furthermore, the patient's right ventricle and right atrium were paced approximately 98% and 1%, respectively.

CONCLUSIONS

This case of widespread MCL with myocardial and conduction system infiltration resulting in a complete heart block highlights the importance of multimodality imaging and the role of ICE in aiding pacemaker lead implantation. A permanent pacemaker may be necessary when patients present with masses involving the conduction system leading to complete heart block.

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KEY WORDS **complete heart block, intracardiac mass, mantle cell lymphoma**