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Case Report

Atrial Myxoma Masquerading as Lyme Disease

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INTRODUCTION

Primary cardiac tumors are extremely rare, accounting for up to only 10% of cardiac neoplasms, and their incidence ranges from 0.001% to 0.03% in autopsy studies [1,2]. Myxoma represents the most common primary cardiac tumor in adults and is most prevalent in females aged 30-60 years [1,3]. Due to their various clinical manifestations, which can mimic diverse cardiac or systemic conditions, atrial myxoma represent a diagnostic challenge and are often initially misdiagnosed [4].

Because they gradually release inflammatory cytokines, including interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha (TNF-α), cardiac myxoma are associated with symptoms that overlap with those seen in other inflammatory conditions [2]. Previous case reports have documented cardiac myxoma initially misdiagnosed as infective endocarditis, respiratory conditions, schizophrenia, and other conditions [5-9].

Here we present a case of atrial myxoma initially misdiagnosed as Lyme disease. We then examine the specific clinical overlap between atrial myxoma and Lyme disease and propose evidence-based diagnostic strategies to reduce diagnostic delays and improve patient outcomes.

CASE PRESENTATION

A case of atrial myxoma presenting with syncope and complete heart block in a patient with Lyme disease

In 1991, a 55-year-old right-hand-dominant Caucasian woman presented with recurrent syncope over one week. Her past medical history was notable for a treated episode of Lyme disease six months earlier, confirmed by erythema migrans, positive serology, and a one-month course of doxycycline with full symptomatic resolution.

Clinical findings on admission to hospital

Neurologic exam: Receptive aphasia and left-sided hemiparesis..

Cardiac auscultation: Grade 1/6 systolic ejection murmur, maximal over the left sternal border.

Other: Vital signs were stable; no fever or ongoing signs of infection.

Diagnostic Assessment

Lumbar puncture: Cerebrospinal fluid analysis negative for *Borrelia burgdorferi* (Lyme) PCR and serologies.

Initial cardiac evaluation: Surface Transthoracic Echocardiography (TTE) was reported as normal, but image quality was limited by breast tissue attenuation.

Neurologic event in ICU: During continuous monitoring in the intensive care unit, the patient experienced a second syncope episode accompanied by sudden third-degree atrioventricular block.

Intervention: An emergent dual-chamber pacemaker was implanted to manage the complete heart block.

Definitive cardiac imaging: A Transesophageal Echocardiogram (TEE) subsequently identified a 3.0 cm pedunculated mass attached to the superior aspect of the left atrial wall, consistent with atrial myxoma.

Therapeutic intervention

Following the TEE diagnosis, the patient was referred for urgent surgical resection. Intraoperative inspection confirmed a pedunculated atrial myxoma attached near the atrial appendage. The mass was excised with a margin of normal tissue, and the atrial septum was repaired.

Outcomes and follow-up

Postoperatively, the patient's neurologic deficits improved over two weeks of an aggressive, in-patient rehabilitation unit admission, and there were no further syncopal episodes. Pacemaker dependency was re-evaluated; intrinsic conduction recovered sufficiently to allow device down programming. Histopathology confirmed benign myxoma without malignant features. At six-month follow-up, she remained asymptomatic,

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with no physical or cognitive deficits, and no evidence of recurrence on surveillance echocardiography.

Given that Lyme disease, which is caused by the tick-borne spirochete *Borrelia burgdorferi*, is endemic in the United States, Europe, and Asia, clinicians in these geographical areas have likely observed more tick-related illness than atrial myxoma and may therefore be primed to recognize the overlapping symptoms in the context of Lyme disease, leading to misdiagnosis [10,11]. While in this case study, the patient formerly suffered from Lyme disease, even in the absence of Lyme disease, it is possible that a clinician may misdiagnose atrial myxoma as the tick-borne illness due to the overlap in clinical presentation and laboratory results.

Atrial myxoma and Lyme disease overlap in their clinical presentation

Both atrial myxoma and Lyme disease characteristically present with nonspecific constitutional symptoms that reflect underlying inflammatory processes, and neurological manifestations occuring in both conditions can further complicate differential diagnosis [12-18]. Cardiac and skin manifestations also represent critical areas of symptom overlap. Lyme carditis occurs when *Borrelia burgdorferi* invade heart tissue, causing bacterial factors to colonize in the heart resulting in Atrioventricular (AV) electrical block, palpitations, chest pain, light-headedness, and shortness of breath [19-21]. Similarly, shortness of breath is very common in cardiac myxoma, and palpitations, chest pain, light-headedness also occur [14]. Both conditions also lead to skin changes, including livedo reticularis, as well as erythematous macules and papules [22-25].

In addition to overlapping constitutional symptoms and neurological, cardiac, and skin manifestations, both cardiac myxoma and Lyme disease can produce a range of similar rheumatologic findings, which are largely driven by cytokine-mediated inflammation in myxoma and spirochetal invasion in Lyme. For instance, arthralgias occur across all stages of Lyme disease, and in cardiac myxoma, tumor-derived cytokines (e.g., IL-6, TNF-α) frequently cause diffuse arthralgias, even in the absence of frank arthritis. Myalgias also frequently accompany erythema migrans and disseminated infection in Lyme disease, contributing to diffuse musculoskeletal pain, while myalgia and muscle weakness due to systemic inflammation are noted symptoms in cardiac myxoma [26,29].

Lyme arthritis is a late-stage manifestation of Lyme disease, characterized by mono or oligoarthritis with intermittent joint swelling and synovitis [30,31]. This arthritis most commonly occurs in the knee and is sometimes migratory. In atrial myxoma, paraneoplastic seronegative arthritis can be the first presentation, including involvement of entheses and purpuric lesions [27]. Often oligoarticular, this arthritis tends to be refractory to standard therapies. Early disseminated Lyme disease often involves tenosynovitis, bursitis, or periarticular pain affecting wrists, ankles, or other tendon regions, while tendon sheath inflammation and periarticular discomfort have been reported in cardiac myxoma [27,30,32].

Certain laboratory findings may be identical in Lyme disease and atrial myxoma

Both Lyme disease and cardiac myxoma may invoke an almost identical cytokine - driven laboratory signature, despite their divergent etiologies. Acute Lyme disease features a pronounced IL-6 elevation during active *Borrelia burgdorferi* infection, which often persists for months despite antibiotic therapy [37]. This IL-6 driven cytokine upregulation provokes an acute-phase response with raised C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR) in most cases, fueling a polyclonal B-cell response in patients with Lyme disease [38].

In cardiac myxoma, neoplastic myxoma cells constitutively secrete IL-6, with serum concentrations correlating to tumor burden and normalizing after resection [33]. This IL-6 surge stimulates hepatocytes to produce acute-phase reactants, leading to markedly elevated CRP and fibrinogen (reflected as a high ESR) in most patients with myxoma [34]. Chronically elevated IL-6 also drives broad B-cell activation and differentiation, manifesting as polyclonal hypergammaglobulinemia on serum protein electrophoresis in over 75% of cases [35]. Rarely, large or mobile myxomas mechanically shear platelets or induce splenic sequestration, resulting in mild thrombocytopenia [36].

Physiological features can distinguish Lyme disease and cardiac myxoma

There are physiological features of Lyme disease and cardiac myxoma that can help to distinguish them. For instance, the erythema migrans rash in Lyme disease has no equivalent in cardiac myxoma. Lyme disease symptoms also follow a temporal progression, whereas myxoma symptoms tend to be consistent and related to tumor size and appearance [14,39]. Though both conditions can present with constitutional symptoms that may initially obscure diagnosis, the systemic nature of Lyme disease with its multi-organ inovolvement contrasts with the primarily cardiovascular focus of myxoma symptoms. Cardiac-specific involvement is also distinct, with Lyme disease typically manifesting as conduction abnormalities and cardiac myxoma associated with mechanical obstruction and embolic events [14,20,40,41].

Laboratory findings may also help in differential diagnosis. While Lyme disease shows positive serology and may present with elevated inflammatory markers, cardiac myxoma is often associated with anemia, elevated ESR, and echocardiographic evidence of an intracardiac mass [34,37,40,42-45].

A systematic diagnostic approach is needed when clinicians encounter patients with symptomatology that is consistent with both Lyme disease and cardiac myxoma

Given the significant clinical overlap between cardiac myxoma and Lyme disease, we propose the following approach to diagnosis.

Initial assessment framework: When evaluating patients presenting with constitutional symptoms, cardiac manifestations, and rheumatologic findings in Lyme-endemic areas, clinicians should maintain diagnostic equipoise and pursue parallel investigative pathways.

Recommended diagnostic strategy:

1. Comprehensive history and physical examination

- Document temporal progression of symptoms. Gradual onset favors myxoma; episodic progression suggests Lyme
- Assess for pathognomonic features. (Erythema migrans rash definitively indicates Lyme disease (though does not exclude myxoma).
- Evaluate cardiovascular symptoms for mechanical versus electrical abnormalities

2. Laboratory evaluation

- Complete blood count with differential (anemia more common in myxoma)
- Comprehensive metabolic panel
- Inflammatory markers (ESR, CRP)
- Serum protein electrophoresis (polyclonal hypergammaglobulinemia in > 75% of myxomas)
- Lyme serology (ELISA followed by Western blot if positive)

3. Cardiac imaging protocol

- High-quality transthoracic echocardiography as initial screening
- *Critical recommendation:* Employ a low threshold for transesophageal echocardiography when initial Transthoracic Echocardiography (TTE) is suboptimal or clinical suspicion remains high
- Consider cardiac MRI for comprehensive tissue characterization if echocardiographic findings are inconclusive.

CONCLUSION

Cardiac myxoma and Lyme disease can present with strikingly similar, multisystem symptoms that make diagnosis challenging, particularly in endemic areas where availability bias may favor more common infections. The case described above underscores the importance of systematically evaluating each symptom complex and ensuring high-quality cardiac imaging. When clinical suspicion persists despite an initial lack of abnormal findings, advanced modalities should be leveraged. By keeping a low threshold for comprehensive cardiac assessment in patients with constitutional signs and cardiovascular manifestations, clinicians can recognize rare but curable conditions like myxoma early and avert life-threatening complications.

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