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Hiccups as an Atypical Presentation of Complete Heart Block and Cardiac Amyloidosis with Multiple Myeloma

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Abstract Cardiac amyloidosis typically causes heart failure due to restrictive cardiomyopathy. Along with structural defects, cardiac amyloidosis can also cause conduction abnormalities, especially bradyarrhythmias. When suspected, cardiac amyloidosis can be diagnosed via cardiac imaging modalities or biopsy. However, due to various atypical patient presentations, diagnosing cardiac amyloidosis requires a high index of suspicion and can often be cryptic in nature. We present the rare case of a 71-year-old male who presented with hiccups as his primary symptom and was found to have complete heart block in the setting of cardiac amyloidosis from multiple myeloma in the absence of restrictive cardiomyopathy.

Keywords: *Multiple Myeloma, Cardiac Amyloidosis, AL Amyloidosis, 3rd degree AV block*

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1. Introduction

Amyloidosis is a systemic disease characterized by extracellular deposition of fibrils which are usually composed of a variety of misfolded proteins. These protein deposits can result in a wide range of clinical manifestations depending on the location, amount, and specific type of protein [1]. The subunit proteins that form amyloid deposits are usually a result of abnormal secondary structure of the proteins that lead a predominantly antiparallel beta-pleated sheet configuration. These amyloid proteins have a characteristic apple-green birefringence microscopic appearance when placed under polarized light of Congo red stained tissue [2].

Cardiac amyloidosis typically manifests as symptoms of heart failure due to restrictive cardiomyopathy. These symptoms commonly include lower extremity swelling, shortness of breath, elevated jugular venous pressure, and hepatic congestion from right ventricular failure. Angina is often thought to be an uncommon symptom of cardiac amyloidosis although microvascular dysfunction has also been noted occasionally. Patients have also frequently presented with syncope or pre-syncopal episodes as their main symptom. This is usually a result of symptomatic bradyarrhythmia or advanced atrioventricular block (AV block) as was the case with this patient [3,4,5]. Due to the multisystem nature of the disease, along with the various presentations, the diagnosis can often be cryptic in nature and requires a high index of suspicion. This is a case of a 71 year old male who initially presented with hiccups as his main symptom and was found to be in 3rd degree AV block and acute renal failure and was diagnosed with AL cardiac amyloidosis from multiple myeloma.

2. Case

A 71 year old African American male with no known medical history who presented to the emergency department (ED) with frequent, intermittent hiccups with associated nausea for the past 1 month. He denied any abdominal pain, decreased appetite, constipation, diarrhea, chest pain, shortness of breath, palpitations, leg swelling, fevers, chills, or weight changes. The remainder of the review of systems was unremarkable. In the ED, the patient's heart rate was noted to be ranging from 31-35. He was afebrile, normotensive, and oxygen saturation via pulse oximetry was 98% while breathing room air. A complete blood count showed hemoglobin level of 7.7 mg/dL and MCV of 92.7, representing normocytic anemia. The patient's baseline hemoglobin level from one year prior was 13 mg/dL. Complete metabolic panel was remarkable for a BUN level of 46.6 and a creatinine level of 7.27. The patient's baseline creatinine level from one year prior was 0.8. The BUN:Creatinine ratio was 6.4, suggesting acute kidney injury from intrinsic renal disease. Electrolytes and liver enzymes were within normal limits. Due to significant bradycardia, the patient had continuous cardiac monitoring. An electrocardiogram (EKG) was performed, which showed complete AV dissociation with underlying sinus and idioventricular rhythms. Chest X-ray was unremarkable. Cardiology was consulted, transcutaneous pacing pads were placed on the patient

without pacing, and the patient was admitted to the medical unit with telemetry monitoring. On day two of hospital admission, a permanent dual chamber pacemaker was placed and the patient's hiccups and nausea resolved shortly afterwards. A serum and urine protein electrophoresis was done due to suspicion of multiple myeloma based on the patient's age, ethnicity, anemia, and acute kidney injury. The results showed two abnormal protein bands migrating in the gamma globulin region, measuring 0.17 g/dL (2.4% of total serum protein) and 0.18 g/dL (2.6% of total serum protein). Serum free light chains were also tested, which showed elevated lambda free light chain of 1,304 mg/L and kappa free light chain of 200.5 mg/L an abnormal kappa:lambda light chain ratio of 0.15. The oncology team was consulted next and a bone marrow aspiration and biopsy was performed which showed 60-70% neoplastic plasma cells, diagnostic of multiple myeloma. Skeletal survey was negative for lytic lesions. On the third day of hospital admission, an echocardiogram was done which showed a normal ejection fraction of 65% with moderate left ventricular hypertrophy in a restrictive pattern; there were no wall motion abnormalities or valvular abnormalities found. Over the next two days, the patient's renal function worsened and a decision was made to start the patient on outpatient hemodialysis after discharge. The patient was started on cyclophosphamide, bortezomib, and dexamethasone (C1D1 CyBorD regimen) for multiple myeloma and the patient was discharged from the hospital in stable condition.

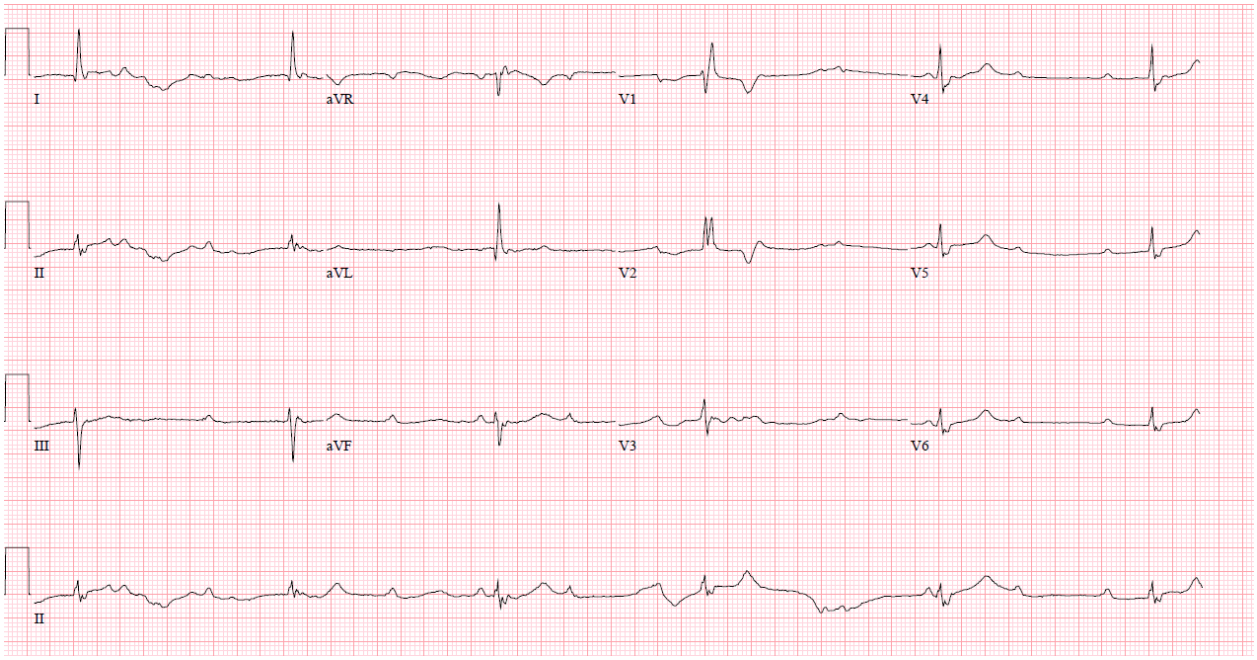

Figure 1. EKG taken prior to pacemaker placement showing sinus rhythm with AV dissociation and idioventricular rhythm with right bundle branch block

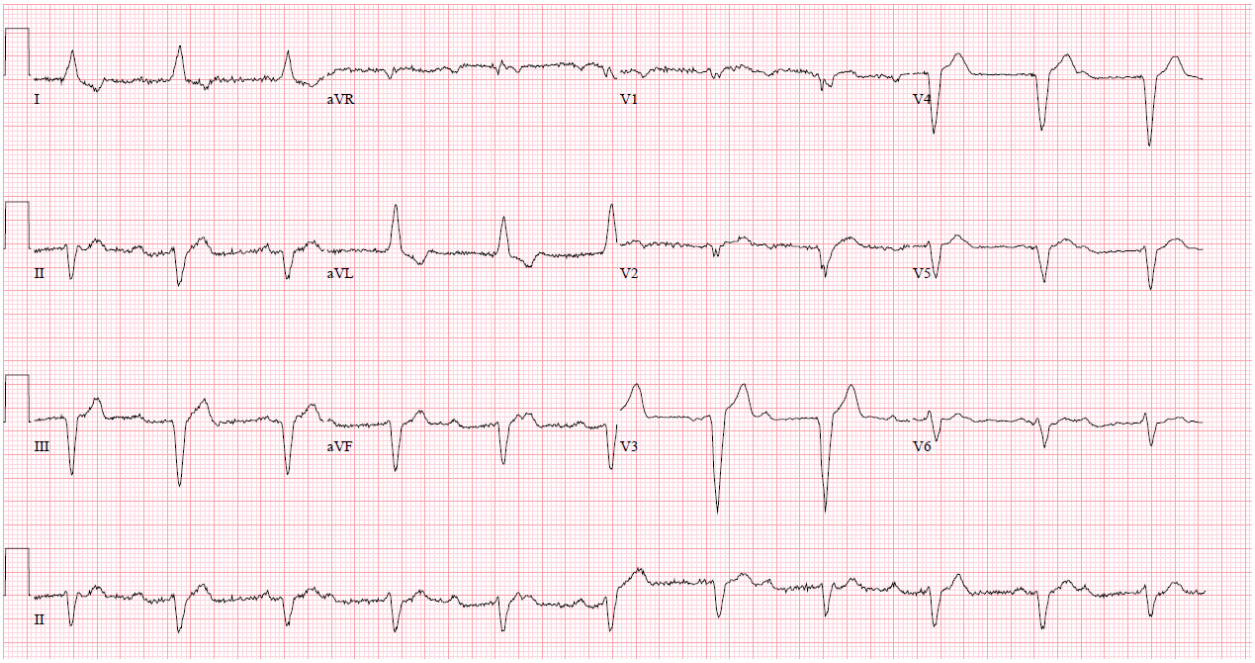

Figure 2. EKG taken after pacemaker placement showing sinus rhythm with ventricular paced rhythm with ventricular pacing at 65bpm

3. Discussion

The clinical manifestations of amyloidosis are diverse in nature and depend largely on the organs that are affected. Patients with light chain amyloidosis typically present with symptoms after the age of 40 [6]. Common organs affected include the liver, kidneys, spleen, and the nervous system. Although there are many different subtypes of amyloidosis, about 95% of all cardiac amyloidosis cases are caused by two main subtypes: light chain amyloidosis (AL) and transthyretin amyloidosis (ATTR) [7].

Cardiac involvement presents with symptoms of heart failure including lower extremity edema, hepatic congestion, elevated jugular venous pressure, ascites, and dyspnea. These symptoms are caused by the restrictive cardiomyopathy that develops as a result of the light chain deposition. Specific transthoracic echocardiogram findings for cardiac amyloidosis are thickening of the posterior wall and interventricular septum [13]. Angina is an uncommon symptom as microvascular dysfunction is rarely reported. Patients with cardiac amyloidosis also frequently present with symptoms of syncope/presyncope. This is usually caused by bradyarrhythmia or high degree AV block which was the case with our patient [Figure 1]. Since amyloidosis is a multi-system disorder, the diagnosis is often a difficult one to make. In the case of cardiac amyloidosis, there are a few clinical clues for which cardiac amyloidosis should be suspected. First, patients with unexplained left ventricular hypertrophy (LVH) seen on echocardiography with or without heart failure can raise suspicion for amyloidosis although this is not a specific finding. This was the case with our patient whose echocardiogram revealed moderate LVH in a restrictive pattern. A more specific echocardiogram finding seen cardiac amyloidosis is reduction in global longitudinal strain with relative apical sparing. This pattern has been reported to have a high sensitivity (93%) and specificity (82%) for cardiac amyloidosis [8,9]. One should also suspect cardiac amyloidosis in patients who have already had an established diagnosis AL Systemic Amyloidosis or ATTR. Establishing the diagnosis should start with a thorough physical examination and history focusing on the cardiac and extracardiac manifestations, laboratory tests, EKG, and echocardiogram. For patients with unexplained LVH seen on echocardiogram or heart failure with signs concerning of amyloidosis, a cardiac MRI should be done to confirm the diagnosis along with serum kappa/lambda free light chain ratio, and serum and urine protein immunofixations. If testing reveals ATTR amyloidosis, a bone tracer cardiac scintigraphy is the next best step to confirm the diagnosis [10,11,12].

4. Conclusion

Cardiac amyloidosis typically causes restrictive cardiomyopathy which can initially be seen on echocardiogram and may lead to progressive heart failure. Conduction abnormalities such as advanced AV blocks can also occur alongside. Due to the multisystemic nature of the disease, patients can present in many different ways. This is a rare case of a patient presenting with hiccups who was found to have complete heart block from cardiac amyloidosis in the setting of multiple myeloma without evidence of restrictive cardiomyopathy on echocardiogram. This case points out some of the challenges clinicians may face in diagnosing cardiac amyloidosis.

Consent

Informed oral consent was given by the patient.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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