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CASE STUDY OPEN ACCESS

SYSTEMIC AMYLOIDOSIS WITH CARDIAC INVOLVEMENT IN A 47 YEAR OLD NIGERIAN: A CASE REPORT

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ABSTRACT

Cardiac amyloidosis is a rare clinical disorder caused by extracellular deposition of insoluble fibrils within the myocardium. The rarity of the condition makes it difficult to diagnose, hence a high index of suspicion on the part of the physician is needed. Cardiac amyloidosis should be suspected in patients with unexplained congestive heart-failure symptoms accompanied by low-voltage complexes on ECG, and ventricular hypertrophy with abnormal myocardial texture, described as 'granular sparkling' on echocardiogram.

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INTRODUCTION

Systemic amyloidosis constitutes a group of heterogeneous disorders caused by deposition of amyloid fibrils, which are composed of misfolded proteins in one or more organs (Kyle, 2001). The protein misfolding abnormalities may manifest as primary, secondary, or familial amyloidosis. Amyloid deposition can occur in multiple organs (eg, heart, liver, kidney, skin, eyes, lungs, nervous system) resulting in a variety of clinical manifestations (Cohen, 1967). Cardiac involvement is a progressive disorder resulting in early death due to congestive heart failure (CHF) and arrhythmias. Cardiac involvement can occur as part of a systemic disease or as a localized phenomenon (Selvanayagam, 2007 and Desai, 2010). We report a case of systemic amyloidosis with cardiac involvement in a 47 year old male. The case highlights the difficulties in recognition of the disease and it's adverserognosis. The role of echocardiography and tissue biopsy in its diagnosis is emphasized.

Case Presentation

A 47-year-old man with no significant medical history developed shortness of breath on exertion over a three month prior to his presentation to our outpatient clinic. At the time of presentation, he also reported a dry cough, paroxysmal nocturnal dyspnoea, orthopnea, and progressive billateral leg swelling. Other complaints were of epigatric pain and an episode of haematochezia. Social history was negative for smoking, alcohol or illicit consumption drugs. Physical examination revealed purpura and ecchymosis on the trunk and abdomen (Fig 1), bilateral pitting pedal oedema, tachycardia, blood pressure of 90/70 mmHg, elevated jugular venous pressure, soft S1,S2 and apical S3, hepatomegaly, and bilateral crackles on lung auscultation.

Investigations: Chest X-ray showed a normal cardiac size, pulmonary oedema and small-sized right-sided pleural

effusion. The haemogram was normal and ESR was 45 mm/hr. Urine routine examination showed RBC of +1 but no proteinuria. Renal and liver function tests were normal.Low voltage complexes in limb and augmented leads were present in ECG (Fig. 2). Two dimensional echocardiography (Fig 3 and 4) revealed marked thickening and speckled appearance of interventricular septum, left ventricular and right ventricular posterior wall, and left ventricular ejection fraction (LVEF) of 24%. Atrioventricular valves were normal. Restrictive filling pattern was demonstrated on Doppler at mitral and tricuspid valves along with moderate pulmonary arterial hypertension. Tissue Dopplerconfirmed the restrictive pattern (reduced annular diastolic velocities). Endoscopic duodenal biopsy showed blood vessels within the wall of submucosa appearing thicker with features of hyalinization and positive for congo red stain which is consistent with amyloidosis (Fig 5). Bone marrow aspiration cytology suggested abnormal plasma cells. Despite intensive chemotherapy using alkylating agent melphalan, immunomodulator thalidomide and steroids, patient continued to deteriorate and died after 4 weeks.

DISCUSSION

Amyloidosis is a clinical disorder caused by extracellular deposition of insoluble fibrils (approximately 7.5-10 nm wide) in organs and tissues that alter their normal function. Systemic amyloidosis can be classified by the etiology of the underlying disease and include: Immunoglobulin (AL) amyloidosis, Familial amyloidosis (or hereditary amyloidosis), Secondary (SAA) amyloidosis (or reactive amyloidosis), and Senile systemic amyloidosis. Another type of systemic amyloid has been described in patients with chronic renal failure on hemodialysis (Benson, 2001 and Westermark, 1990). AL amyloidosis is the most common type (Kyle, 1992). Cardiac involvement is most common and most severe in AL amyloidosis, but can occur in all types of systemic amyloidosis (Kyle, 2001). The patient possibly had AL amyloidosis involving the skin, gastrointestinal tract and heart as seen from his symptoms and signs which includes purpura, ecchymosis, epigastric pain, haematochezia, paroxymal nocturnal dyspnoea, orthopnoea etc. Cardiac amyloidosis presents as restrictive cardiomyopathy characterized by progressive diastolic and subsequently systolic biventricular dysfunction. Patients initially commonly present with signs of right-sided heart failure, including an elevated jugular venous pressure, right-sided third heart sound, peripheral edema, and hepatomegaly (Falk, 1997). These signs were present. Characteristic electrocardiogram features include Low voltage complexes (QRS amplitude $\leq$ 0.5 mV in limb leads or $\leq$ 1.0 mV in all precordial leads) are seen in 46% of cases. Loss of anterior forces consistent with anteroseptal infarction is seen in 46% of cases (Ridolfi, 1977). LV hypertrophy is unusual. Echocardiography plays a pivotal role in diagnosis and shows several features that can be suggestive of cardiac amyloidosis but these features are commonly present only in the later stages of the disease.The most common echocardiographic feature is thickening of the LV wall, particularly in the absence of hypertension. This is often referred to incorrectly as "hypertrophy" because the pathological process is infiltration, not myocyte hypertrophy. This feature has a poor specificity for amyloidosis because of its occurrence with other conditions such as hypertensive heart disease, hypertrophic cardiomyopathy and other infiltrative diseases (Westermark, 1990). A speckled or granular myocardial (sparkling) appearance (as in this case) has been reported to be characteristic of amyloidosis. However this finding should be interpreted within the clinical context as this finding is dependent on machine gain settings and can also occur in other causes of LV hypertrophy. A thickened interatrial septum is very specific for amyloid in the later stage of the disease, has 100% specificity (Siqueria, 1981). Other features of cardiac amyloid include bilaterally enlarged atria, thickened valves and pericardial effusion. Diastolic dysfunction is the hallmark and majority of patients show a restrictive pattern on mitral inflow assessment. Endomyocardial biopsy has been considered to be gold standard for demonstrating cardiac amyloid deposition (Cristina, 2012). In clinical practice it is rarely necessary to biopsy the heart if clinical, echocardiographic and biochemical information is sufficient for diagnosis and a histopathological data is available from other tissues as seen in this case. The treatment and prognosis of cardiac amyloidosis directly depends on the underlying etiology of amyloid deposition. Cardiac amyloidosis has a poor prognosis (Dubrey, 1997). In general, calcium channel blocking agents are contraindicated because of their negative inotropic effects, as they can precipitate congestive heart failure. Beta blockers are often avoided for the same reason (Falk, 1997). Digoxin should be used with caution because it is bound extracellularly by amyloid fibrils, which may cause patients with amyloidosis to be "hypersensitive" to its effects (Gertz, 1985). Pacemakers may be required depending on the degree of conduction system disease. Anticoagulation is also advocated because of the higher incidence of intrachamber thrombi seen in cardiac amyloidosis, even in the absence of atrial fibrillation (Rubinow, 1981). Treatment that suppress production of amyloid fibril precursor protein include drugs like melphalan, prednisone, thalidomite etc. The prognosis for patients with AL amyloidosis is poor as such treatment rarely results in complete remission of disease or reversal of end organ dysfunction because of amyloid deposits (Kyle, 1999).

Conclusion

Cardiac amyloidosis, although uncommon, is most common and most severe in AL amyloidosis. It is characterized by a typical appearance on electrocardiogram and echocardiography, the recognition of which should alert the clinician to the probable diagnosis. Cardiac involvement is progressive resulting in early death due to congestive heart failure (CHF) and arrhythmias. In AL amyloidosis, chemotherapy may arrest or possibly reverse the disease, with resultant stabilization or improvement of symptoms. Thus, early diagnosis is critical because patients with advanced disease are usually too ill for intensive chemotherapy.

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