FAMILIAL CARDIOMYOPATHY IN NIGERIA: A CASE REPORT.

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ABSTRACT

Background: **Familial DCM (FDCM) is identified when two or more first-degree relatives have idiopathic dilated cardiomyopathy (DCM) or unexplained death at a young age. This report aims to highlight the clinical manifestations of FDCM in a Nigerian family, emphasizing the importance of genetics while addressing the paucity of local data.**

Case Presentation: **This report describes a 22-year-old male with DCM whose elder sibling died from DCM, and a younger one had similar echocardiographic features as the index patient, highlighting the hereditary nature of the disease within his family**

The patient, initially asymptomatic, reported easy fatigability, breathlessness, and cough, which worsened over three months. Clinical examinations revealed signs of advanced heart failure, including elevated jugular venous pressure and fine bibasal crepitations. Echocardiography confirmed DCM. Despite initial treatment, the patient developed an intracardiac clot and required an extensive medication regimen. Family history indicated an autosomal dominant inheritance pattern, with a younger sibling also showing features of DCM.

Conclusion: **This case underscores the importance of genetic factors in the pathogenesis of FDCM and highlights the challenges of managing the disease, particularly in resource-limited settings. Early family screening, patient education, and adherence to treatment protocols are crucial for improving outcomes. There is a need for accessible genetic testing to facilitate early diagnosis and intervention in at-risk populations.**

Keywords: Familial cardiomyopathy, Genetic predisposition, Heart failure, Genetics, Inherited heart disease

INTRODUCTION

Dilated Cardiomyopathy(DCM) is a syndrome characterized by cardiac enlargement and impaired systolic function of one or both ventricles in the absence of abnormal loading conditions such as hypertension, valve disease, or congenital heart disease, or coronary artery disease of sufficient severity to cause global impairment of ventricular function.[1] The importance of genetics in DCM cannot be overestimated. Earlier work on this in the early 80s documented a prevalence of 2% in Italy.[2] With improvements in technology and interest in the disease, recent prospective studies have highlighted the importance of genetics in the aetiopathogenesis of DCM.[3-5]

Familial DCM (FDCM) is diagnosed when two or more first-degree relatives have "idiopathic" DCM and unexplained death at a young (< 35 years) age[6]. Recent studies suggest that the prevalence of FDCM in DCM patients is about 23% with high heterogeneity (prevalence ranging between 2-65%).[6]

Clinically, there are no recognizable clinical or morphological differences between sporadic and familial DCM.[6] The pattern of transmission of FDCM is mainly autosomal dominant.[7] Autosomal recessive and X-linked patterns of inheritance have also been described.[4,8,9] In addition, polygenic and mitochondrial inheritance have also been described.[10] To the best of our knowledge, there have not been reports on FDCM in Nigeria. A report from Uganda in 1974 described a familial cardiomyopathy case where a 16-year-old male, along with his elder brother and father, died from idiopathic congestive cardiomyopathy[11]. There have also been reports from other African countries, such as Ethiopia[12,13], Malawi[12,13], Tanzania[12-14], and South

Africa.[12,13,15] We report a case of this condition in a Nigerian family.

Case summary

A 22-year-old male university student presented to the medical outpatient clinic due to cardiomegaly discovered during a screening prompted by a diagnosis of DCM in his elder brother. He was initially asymptomatic and was prescribed oral lisinopril, spironolactone, and bisoprolol, but he was not compliant with the medications. He is the third child in a monogamous, non-consanguineous family of six children (Figure 1). His brother died from DCM at the age of 19 years, and a younger male sibling also showed features of DCM on echocardiography at age 22 years. Figure 2 shows the echocardiograms of the index case and those of his younger sibling.

He presented with easy fatigability, breathlessness, and cough, which had progressively worsened two years after initial diagnosis. On general examination, he appeared mildly distressed but was not pale. His pulse rate was 96 beats per minute, blood pressure of 103/65 mmHg, and jugular venous pressure was elevated. The apex beat was at the sixth left intercostal space, lateral to the midclavicular line. Heart sounds included S1, S2, and S3. Respiratory examination showed a rate of 28 breaths per minute with fine bibasal crepitations. His abdomen was full, with mild tenderness over the liver, which was palpable 4 cm below the right costal margin. Electrocardiography (ECG) revealed sinus arrhythmia, bi-atrial enlargement, left ventricular hypertrophy, and poor R wave progression. Thransthoracic echocardiography showed dilated cardiac chambers (left atrial dimension =5.1cm, left atrial volume=76mls, right atrial volume =99mls, right ventricular internal dimension in diastole =4.5cm and left ventricular internal dimension in diastole =5.6cm) The left ventricular ejection fraction was 24% and the tricuspid annular plane systolic excursion (TAPSE) was 1.1cm. There was type II diastolic dysfunction (E/A=1.54, E/E'= 14.80) There was moderate mitral and tricuspid regurgitation (Right Ventricular Systolic Pressure-RVSP=31mmHg) and circumferential pericardial effusion (2.0 cm over the right atrium and ventricule) The inferior venacava was dilated..

He was initially treated with intravenous torsemide 20 mg daily, followed by oral torsemide. Oral lisinopril 2.5 mg daily and digoxin 0.125 mg daily were also added. He received subcutaneous clexane 40 mg daily (for prophylaxis against thrombosis) while on admission and was administered intravenous antibiotics for five days before discharge. Two months after discharge, he presented with cough and bilateral leg swelling. A repeat echocardiography indicated worsening cardiac function and the presence of a huge immobile intracardiac clot measuring 1.9 x 4.8cm localised at the apex of the left ventricle and a small thrombus at the apex of the right ventricle. (Figure 3) He was treated with ramipril 1.25 mg on alternate days, subcutaneous clexane 40 mg daily, dapagliflozin 10 mg daily, and metolazone 1.25 mg on alternate days, in addition to his routine medications. He improved on

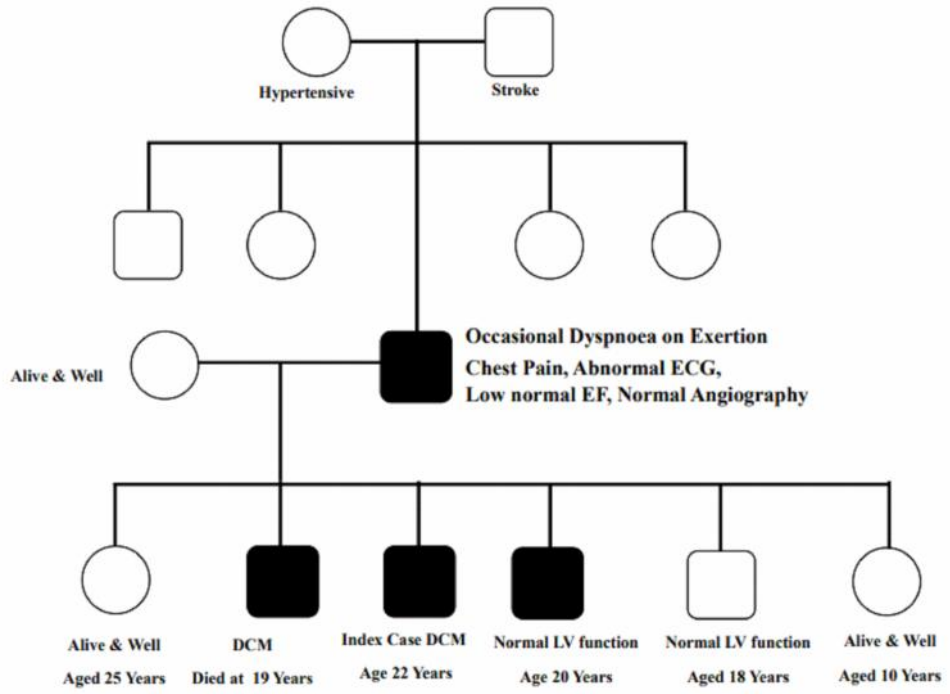

Figure 1: Family tree of the index patient showing three generations

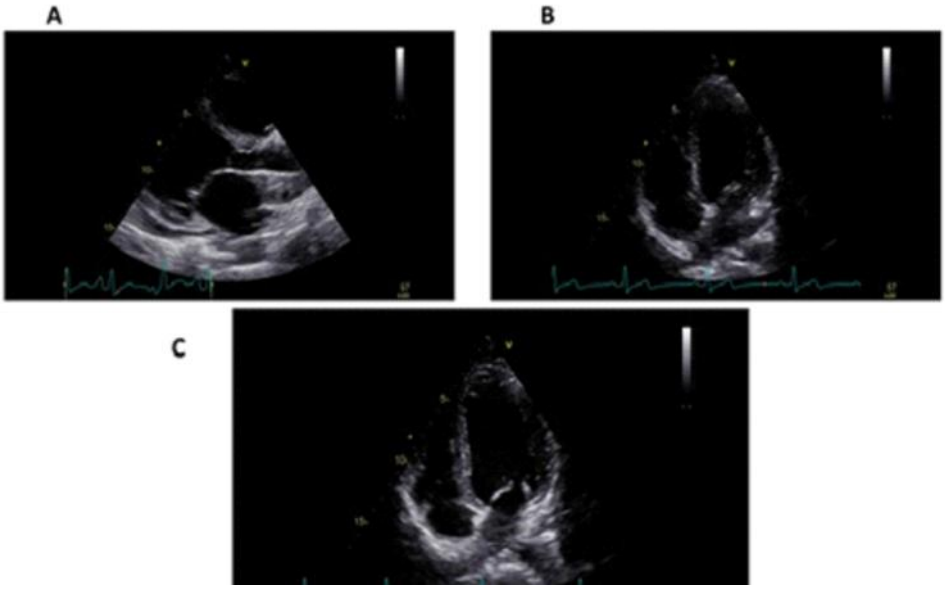

Figure 2: A. Parasternal long-axis view echocardiogram of the index case, **B.** Apical four-chamber view echocardiogram of the index case. **C.** Apical four-chamber view echocardiogram of the sibling

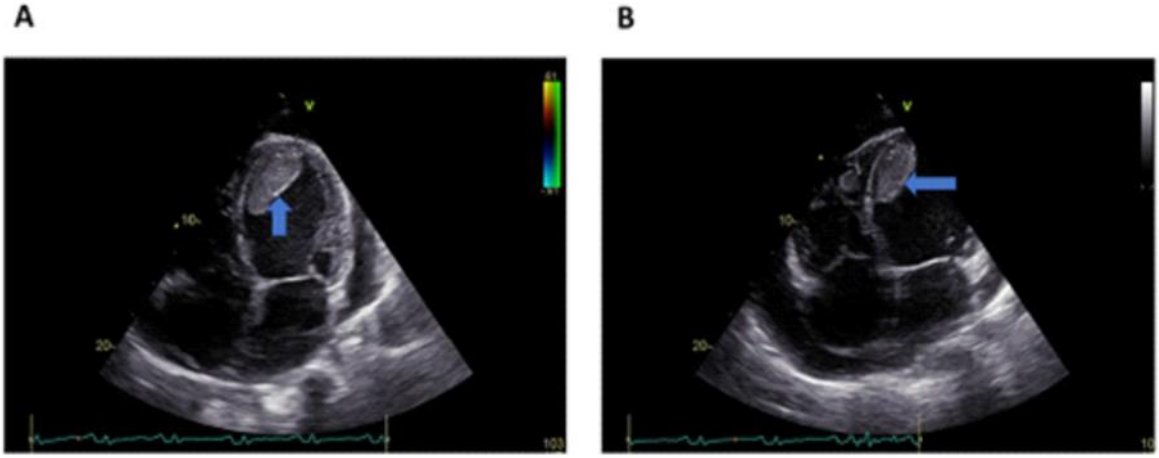

Figure 3: A. Apical four-chamber view echocardiogram of the index case with a huge thrombus in the apex of the left ventricle. **B.** Modified apical four-chamber view echocardiogram of the index case with a small thrombus in the apex of the right ventricle

medical therapy and was discharged home to be followed up at the Cardiology Outpatient Clinic. At the most recent follow-up, he was relatively stable on a comprehensive medication regimen, which includes diuretics (torsemide and spironolactone), digoxin, bisoprolol, warfarin, dapagliflozin, and candesartan. A repeat echocardiography still showed severely impaired LV systolic function and an organised clot at the apex of the LV.

Discussion

Familial DCM encompasses a spectrum of genetic cardiac disorders, such as DCM, atrial cardiomyopathy with heart block, and restrictive cardiomyopathy.[16] These pathologies are defined by structural and functional anomalies in the myocardium, resulting in compromised cardiac performance and heart failure.[16] Familial DCM is diagnosed when two or more first-degree relatives have idiopathic DCM and or unexplained death at a young (< 35 years) age.[17] This report describes a 22-year-old male with DCM whose elder sibling died suddenly, and a younger one had similar echocardiographic features as the index patient, highlighting the hereditary nature of the disease within his family. Familial dilated cardiomyopathy is a genetically heterogeneous disease with evidence of a Mendelian inheritance pattern and a prevalence of 23% among DCM patients.[16] The distinct patterns identified based on transmission patterns and phenotypic characteristics include: autosomal Dominant FDCM without extracardiac manifestations- 50-60%, autosomal recessive FDCM- < 1%, X-linked FDCM- 5-10%, autosomal dominant FDCM with subclinical skeletal muscle involvement- 5-10%, autosomal

dominant Left Ventricular Non-Compaction (LVNC)- 3-5% and unclassifiable FDCM with retinitis pigmentosa and hearing Loss- <1%.[5]

The family history of the index case depicts an autosomal dominant inheritance pattern. Evidence of incomplete and age-dependent penetrance exists, as many individuals carrying the mutations do not develop overt disease until their fifth or sixth decade. Our report aligns with the observed age-dependent penetrance demonstrated by the patient's initial asymptomatic status that evolved into overt cardiac failure. The American College of Cardiology recommends screening all relatives when evaluating patients with DCM, especially when there is a family history of cardiomyopathy or unexplained sudden deaths at a young age.[18]

Familial DCM can remain silent until advanced stages, where the prognosis becomes guarded. Our patient's initial presentation was asymptomatic; his non-compliance with medications may have exacerbated his condition, necessitating a more complex treatment protocol. Moreover, the presence of an intracardiac thrombus and the need for an extensive medication regimen show disease progression and the complexity of managing FDCM. Continuous patient education, stringent adherence to treatment, and regular follow-up should be encouraged for all patients.

Several genes are implicated in familial DCM, with mutations in the TTN gene being the most common.[19] Others include LMNA, MYH7, BAG3, and TNNT2[20-33]. These genes encode proteins vital for the structure and function of cardiac muscle cells[34]. Identifying pathogenic variants through genetic testing can confirm the diagnosis, guide treatment decisions, and allow for predictive testing in at-risk family members[19, 20, 34,]. This facility comes at a very high cost and is not available in Nigeria; therefore, none of the ECHO-confirmed patients in the index case had genetic testing. Our findings call for increased awareness, improved access to diagnostic resources, and robust family screening programmes to mitigate the impact of FDCM and improve patient outcomes.

CONCLUSION

Cases of familial DCM and first-degree relatives are at risk of developing the disease at a young age. Therefore, the identification of newly affected individuals with DCM may benefit from early management, even if they are asymptomatic, to prevent overt disease and its complications

The case presented indicates that the disease is not rare in our environment. There is a need for increased community awareness to encourage family screening of all DCM patients.

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