CASE REPORT

Non-compaction cardiomyopathy and visceral leishmaniasis: uncommon combination with therapeutic challenges in a resource limited-setting

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ABSTRACT

Non-compaction cardiomyopathy (NCCM) or spongy myocardium is a rare type of congenital cardiomyopathy. Visceral leishmaniasis is a protozoal disease caused by *Leishmania donovani* and transmitted by the bite of female sand-fly species of *Phlebotomus argentipes*, which is common in tropical areas like Sudan. We report a 6-year-old female, presented with a fever of unknown origin, weight loss, anemia that necessitated multiple blood transfusions and had hepatosplenomegaly. Developed heart failure later on admission the current case narrates an unusual combination of diseases with therapeutic challenges in a resource-limited setting.

KEYWORDS

Non-compaction cardiomyopathy; Leishmaniasis; Challenges of therapy.

INTRODUCTION

Non-compaction cardiomyopathy (NCCM) is a type of cardiomyopathy in which there is an increase in trabeculations of the left ventricle, where the endocardial thickening of the non-compacted layer is more than twice that of the epicardial compacted one. Previously known as a 'spongy' heart, it draws attention because of progress in cardiac imaging modalities [1].

It is abroad spectrum, ranging from asymptomatic to severe congestive heart failure, classified by the American Heart Association into a genetic category in 2006 [1]. Most of these genetic types were described in patients with hypertrophic and dilated cardiomyopathy [2,3]. Children with NCCM usually had a normal cardiac function and were below risk of adverse cardiac events [1].

Recently studies proved that many factors might be implicated in hypertrabeculation of the left ventricle and expanded the cardiac preload as pregnancy, sickle cell anemia and in-depth sports [4–6]. The legitimate prevalence of the disease in children ranges between 0.02% and 0.014%, and the mortality rate is estimated to be 13% [7,8]. It listed third to hypertrophic and dilated ones [9]. The diagnosis depends on morphological criteria detected on echocardiography and cardiac magnetic resonance. Treatment relies on the

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management of heart failure, other complications and heart transplant. Gene editing technology is a promising future therapy [7].

Visceral leishmaniasis (VL), named kala-azar, is caused by *Leishmania donovani* and transmitted by female sand-fly species of *Phlebotomus argentipes*. In respect of the global affliction of the disease, the incidence is 0.5 per year and the prevalence of cases is 2.5 million. According to the World Health Organisation, >90% of the global cases were detected in India, Bangladesh, Sudan, South Sudan, Ethiopia and Brazil [10,11]. The disease is characterised by prolonged fever, hepatosplenomegaly, emaciation and pancytopenia of blood indices, and it is deadly if left untreated [12,13]. The diagnostic methods depend on the detection of the parasite in bone marrow, spleen, lymph node, liver and immunological tests or molecular study. Chemotherapy has remained the anchor for the control of leishmaniasis due to the lack of effective vaccines. Drug regimens sufficiently effective against leishmaniasis are amphotericin B, pentavalent antimonial drugs, paromomycin and miltefosine [13]. Leishmaniasis and the heart were studied as a part of neglected tropical diseases and other infectious diseases affecting the heart project using midline database meta-analysis (1990–2020) including case reports/series and studies. The study concluded that the incidence is underestimated due to infrequent diagnosis and reporting. Heart involvement was detected in some cases in the form of myocarditis and pericarditis. Cardiac sequalae as sudden death and arrythmia were reported related to drug effects in both the antimony and amphotericin B [12].

CASE REPORT

A 6-year-old Sudanese female, from Eastern Sudan, presented with a fever of unknown origin for 26 days, which was high-grade on and off, associated with weight loss but strikingly good appetite, vomiting on and off, with normal bowel habit and marked fatigability. Two days prior to admission patient developed lower limb swelling, with mild facial puffiness. She had no difficulty in breathing, neither cough nor chest tightness but she felt palpitation. There were no signs of increased intracranial pressure, no change in urine amount or frequency and neither skin nor joints abnormality. She was admitted twice during her illness at rural hospitals in Eastern Sudan, where she was born and lived, and received a blood transfusion on two occasions. Diagnosed as a case of anemia on the first admission, and malaria on the second one. The mother denied any history of fatigability or reduced activity before this onset, and she had no past history of pica, jaundice or blood loss. There was no history of contact with chronic cough or history of traveling. She passed the natural steps of milestones but did not attend school. Her nutrition was satisfactory with no habit of raw milk ingestion, and she completed immunisation. The parents are first-degree cousins and had five alive and well sibs. There was no family history of anemias, cardiac diseases or sudden deaths. She was not on any long-term medication. The patient presented to the emergency room very ill-looking, distressed, febrile and very pale, but not jaundice, with positive periorbital and lower libs edema. Her anthropometric measurements were normal apart from the weight was just below the 3rd percentile vital signs; were respiratory rate (53 breaths/minute), pulse (120 beats/minute) weak volume and the cardiovascular system revealed displaced apex and galloping rhythm. Two days later after the patient was shifted to the ward, still there was tachypnea and tachycardia with persistent fever, her apex beat was at the 6th intercostal space, palpable second heart sound (S2), positive left parasternal heave pansystolic murmur and which indicated heart failure with pulmonary hypertension. There was no clubbing or sign of infective endocarditis. There was a palpable liver of 12 cm span and spleen of 6 cm, but no palpable lymph node or ascites and no abnormalities related to the musculoskeletal or neurological system.

The preliminary investigations on arrival showed low haemoglobin (5 g/dl) with normal other blood indices. After the transfusion, her haemoglobin raised to (7.4 g/dl) but low platelets (65×10^9/l). The peripheral blood picture of both reports showed a dimorphic picture of anemia. The last result of complete blood counts showed low leukocyte count (3.2×10^9/l), low haemoglobin

(5.2 g/dl) and low platelet count (116 × 10^9/l) indicating pancytopenia. C-reactive protein was high. The blood film for malaria was negative. Screening for human immunodeficiency virus and hepatitis were negative. Screening for sickle cell anemia was negative. Ultrasound abdomen showed a liver of 13.3 cm with normal texture and a spleen of 10.8 cm with normal kidney and no ascites. Chest X-ray demonstrated a cardio-thoracic ratio ≈ 80% indicating cardiomegaly.

Echocardiography revealed dilated four chambers and low ejection fraction (20%) and reported as showing non-compacted cardiomyopathy with congestive heart failure and pulmonary hypertension.

Bone marrow examination revealed active bone marrow with no abnormal cells, proved the presence of *Leishmania donovani* bodies and confirmed the diagnosis of VL.

Further patient course of management at the emergency level included receiving oxygen therapy, diuretic intravenous injection and top up with blood transfusion. After a cardiologist consultation, she was started on frusemide 10 mg three times per day and captopril 6.25 mg twice a day and referred to another hospital in Omdurman City for the availability of visceral *Leishmania* treatment for free. Unfortunately, the patient passed while waiting for therapy at the referral hospital as her condition necessitated multiple blood transfusion sessions.

DISCUSSION

This case is one of the extraordinary combinations of diseases in which there were challenging therapeutic options in poor resource settings. The patient most probably had cardiomyopathy and contracted leishmaniasis later because she was born and lived in a region of high endemicity of VL. The first presentation of heart signs at age 6 years in a previously well-female child with a negative family history could occur in such a limited type of myopathy, similar to that reported by van Waning et al. [1]. We depended on the two-dimensional echocardiography as a standard tool for the diagnosis of non-compaction, similar to that reported by Ergul et al. [14]. The main presenting symptoms of this child and the blood indices results will not be explained by the cardiomyopathy alone. However, she was from the area of high endemicity of *Leishmania*, so bone marrow aspiration was our second line of investigation. There are reported cases of myocarditis and pericarditis in children who had VL [15]. Furthermore, there is no reported case of NCCM and VL. Bandeira et al. [15] reported a case of human immunodeficiency virus who developed reversible cardiomyopathy secondary to amphotericin B and was the sixth reported case in the literature. Unfortunately, our patient passed away before starting treatment for VL. A study in Brazil [16] reported that deaths related to *Leishmania* was significantly associated with congestive heart failure. Our patient had an ejection fraction of 20%, which is very low for the pediatric heart, mortality in patients with low ventricular ejection is doubling to those with normal one; furthermore, treatment modalities for both the antimony group and amphotericin B are cardiotoxic [7,15]. It seemed that the degree of anemia associated with *Leishmania* provoked the myopathy of the patient's heart as non-compacted layers had typically low perfusion, which was demonstrated in multiple modalities [1]. Recent studies endorsed the hypothesis that acquired causes might lead to characteristic hyper-trabeculation due to an increase in cardiac preload [4–6]. In the current case, VL could be one of these contributing factors, and further studies are needed. However, treatment for *Leishmania* is not provided for free except in a few hospitals, so treatment for such a combination of diseases is currently beyond the means of people of low socioeconomic status. Many poor prognostic factors were implicated in worsening patient condition, and adding burden to heart status including depressed ejection fraction, frank congestive heart failure refractory to medication and the requirement for multiple blood transfusion sessions.

CONCLUSION

We highlight a case of an extraordinary combination of diseases with multiple poor prognostic factors that contributed to the worsening of patient medical condition, and the

availability of treatment modalities that cost the heart more burden in a limited resource- setting. We recommended further studies in leishmaniasis as an implicated factor for cardiomyopathy, and to increase awareness among health providers in endemic areas and to encourage diagnosis and reporting of similar cases.

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CONFLICT OF INTEREST

None.

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ETHICAL APPROVAL

Ethical approval from the Academy University Teaching Hospital and informed consent from the guardian of the patient were obtained. Confidentiality was ensured at all stages.

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