

# Diphtheritic myocarditis: An unusual and reversible cause of heart failure

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## ABSTRACT

Diphtheria is a life-threatening infectious disease caused by *Corynebacterium diphtheriae*. Although the disease is seen infrequently in the postvaccination era, sporadic cases continue to occur. Cardiac involvement, in the form of myocarditis, is the most serious manifestation of diphtheria and is the most common cause of mortality in these patients. The features of diphtheritic myocarditis on cardiac magnetic resonance imaging (MRI) have not been reported previously. In this brief report, we describe the cardiac MRI and histopathologic features on endomyocardial biopsy of a patient with acute heart failure who was later diagnosed to be a case of diphtheritic myocarditis.

**Keywords:** Diphtheria, heart failure, myocarditis

## INTRODUCTION

Cardiac involvement is the most serious manifestation of diphtheria and is the most common cause of mortality in these patients. Myocardial involvement leads to a spectrum of changes on electrocardiogram (ECG) and endomyocardial biopsy (EMB). In this report, we present the ECG and EMB features along with the cardiac magnetic resonance imaging (MRI) findings in an adolescent male with diphtheritic myocarditis, who was managed with a successful outcome.

## CASE REPORT

A 12-year-old adolescent male presented with dyspnea on exertion which progressed to NYHA Class 3 within a period of 10 days. At admission, he was in acute decompensated heart failure with elevated jugular venous pulse and pedal edema. Blood pressure was 110/70 mmHg in the right arm. Chest radiograph

revealed cardiomegaly with a cardiothoracic ratio of 65%. ECG revealed a junctional escape rhythm at a rate of 65 beats/min and a QRS duration of 100 ms [Figure 1a]. Blood investigations showed an elevated total leukocyte count with leukocytic predominance with no abnormalities detected in the renal and hepatic function parameters. The brain-type natriuretic peptide level at presentation was 1200 pg/mL, and the creatine kinase myocardial band was 35 U/L, both of which were elevated. Transthoracic echocardiography showed global hypokinesia of the left ventricle (LV) with an ejection fraction of 35% by Simpson's method. A thin rim of circumferential pericardial effusion was also noted. He was started on diuretics and angiotensin-converting enzyme inhibitors with which there was partial improvement. A cardiac MRI was performed, as a part of evaluation for acute heart failure, which showed subepicardial T2 hyperintensity (edema) and late

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**How to cite this article:** Arvind B, Ojha V, Arava SK, Seth S, Ramakrishnan S. Diphtheritic myocarditis: An unusual and reversible cause of heart failure. *Ann Pediatr Card* 2022;15:311-3.

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10.4103/apc.apc\_144\_21

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Submitted: 23-Jul-2021

Revised: 30-Nov-2021

Accepted: 05-Apr-2022

Published: 16-Nov-2022

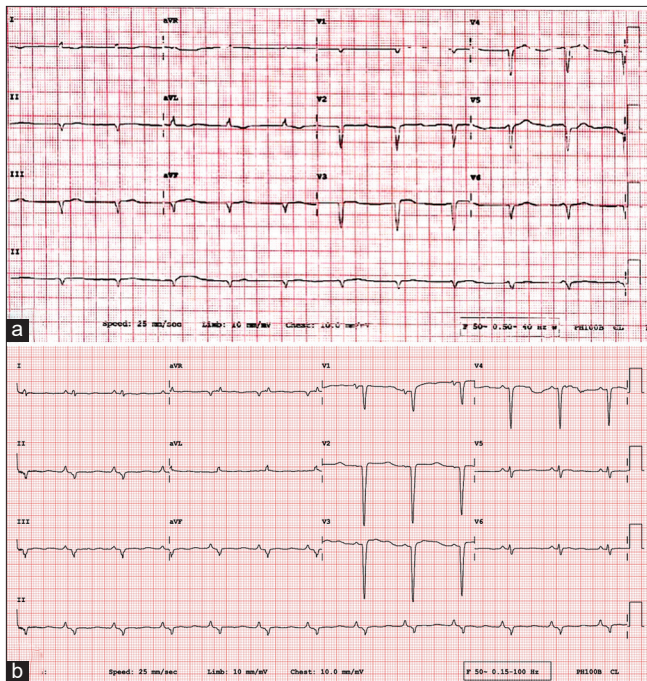
gadolinium enhancement (necrosis) in the anteroseptal segment of basal LV, suggestive of myocarditis [Figure 2]. Subsequently, the patient was subjected to an EMB as a part of workup for myocarditis and evaluate for the underlying etiologies.

While awaiting biopsy result in the ward, an astute resident doctor noticed that the patient had a nasal twang to his voice. On further questioning, he accepted to have had an episode of fever that lasted for 4 days associated with throat pain and swelling 2 weeks before the onset of his heart failure symptoms for which he was prescribed a course of oral amoxicillin. He had also been experiencing nasal regurgitation of feeds and drooling of saliva for few days after the febrile episode. However, he did not have weakness of any limbs, gait disturbances, visual disturbance, seizures, or headaches. Bladder and bowel continence was preserved. His immunization status was verified to be incomplete. This clinical presentation is consistent with *Corynebacterium diphtheriae*-associated myocarditis. Throat examination did not show any evidence of pseudomembrane. Throat swab also did not demonstrate any evidence of the suspected organism on Albert's staining. However, in view of strong clinical suspicion, he was administered one lakh units of antidiphtheritic serum after which he showed marked improvement. The rhythm reverted to sinus 2 days following the administration of antiserum [Figure 1b]. The EMB showed patchy areas of myocyte necrosis

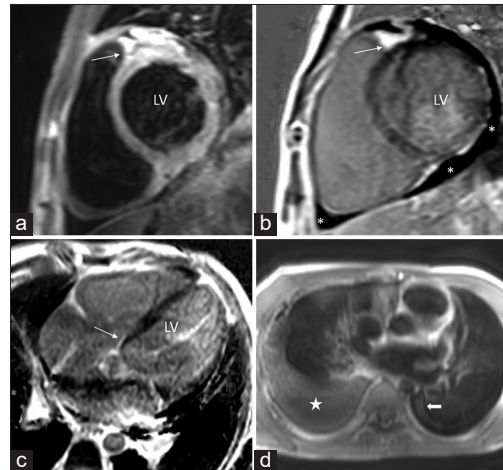
with mononuclear cell infiltration accompanied by interstitial fibrosis and edema suggestive of acute myocarditis [Figure 3]. At 6-month follow-up, the patient had near-normal LV function and continued to be in sinus rhythm along with the complete resolution of neurologic symptoms.

## DISCUSSION

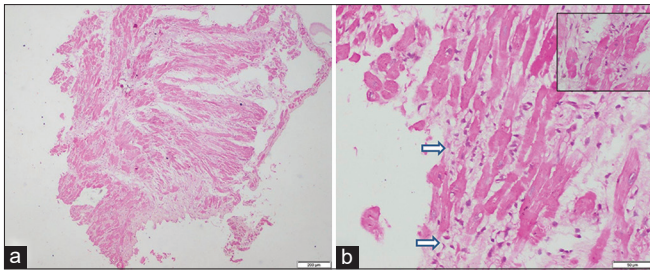
Diphtheria is a life-threatening condition caused by toxigenic *C. diphtheriae*. However, being a potentially reversible cause of myocarditis, a very high index of suspicion should be kept in patients presenting with acute-onset heart failure along with history of sore-throat, coexisting neurologic manifestations, and cranial nerve involvement, especially in an unimmunized individual. Visualizing a pseudomembrane in the oropharynx strengthens the clinical suspicion. Demonstration of *C. diphtheriae* by Albert stain or throat swab culture or demonstration of diphtheria toxin helps confirm the diagnosis. Although the global incidence of this disease has substantially decreased, with effective vaccination programs, the disease remains endemic in few regions where the vaccine programs are not sustained where increasing proportions of adults are affected. The diagnosis of diphtheria is made based on the clinical presentation, which is supported by microbiologic confirmation. EMB or cardiac MRI is not necessary for its diagnosis. However, since they were performed in our patient before diphtheria was



**Figure 1: ECG of the index patient with diphtheritic myocarditis. (a) At presentation showing junctional escape rhythm at a rate of 65 beats/min and a QRS duration of 100 ms, (b) After treatment with antidiphtheritic serum the rhythm has converted to sinus. ECG: Electrocardiogram**



**Figure 2: Cardiac MRI T2-weighted fat-saturated short-axis image (a) shows the presence of T2 hyperintensity (thin white arrow in a) in the anterior and anteroseptal segment of basal LV, suggestive of edema. LGE short axis (b) and four chambers (c) images show enhancement (thin white arrow in b and c) in the basal septum (anteroseptal segment) extending into superior RV insertion point, suggestive of necrosis and fibrosis. Thin rim of pericardial effusion (asterisks) is seen in b. (d) Axial black blood image of the thorax shows bilateral effusion (star for right and block white arrow for left), right much more than left. MRI: Magnetic resonance imaging, LGE: Late gadolinium enhancement, LV: Left ventricle, RV: Right ventricular**



**Figure 3: Endomyocardial biopsy (Hematoxylin and Eosin stain): (a) Lower magnification reveals patchy areas of myocyte damage with interstitial widening by fibrosis and edema. (b) Higher magnification shows the presence of myocyte damage/necrosis by mononuclear cells (arrow and inset). Adjacent cardiac myocytes show degenerative changes**

suspected, it provided an opportunity to retrospect these findings.

Cardiac damage is the leading cause of mortality in these patients, which is seen in 10%–20% of the patients with oropharyngeal diphtheria.<sup>[1]</sup> Histopathologic features of diphtheritic myocarditis have only been studied in autopsy series.<sup>[2]</sup> Myocardial autopsy specimen showed extensive areas of hyaline degeneration and myocardial necrosis along with active inflammation in the interstitial spaces. Infiltrates of mononuclear cells with eosinophilic cytoplasm are also found in these areas similar to the findings in our patient. Fluorescent antibody staining of tissue sections demonstrates diphtheria toxin in a patchy distribution within the myocardial fibers, which could possibly explain the role of the toxin in mediating myocardial injury. Electron micrography shows striking ultrastructural changes within involved myofibers predominantly involving the mitochondria which appear swollen with loss of matrix and disorganized cristae which is also associated with the depletion of glycogen and accumulation of lipid droplets.<sup>[2]</sup> The myocarditis process also involves the cardiac conduction tissue and results in a spectrum of electrocardiographic changes. Almost half of the patients with diphtheritic myocarditis develop severe conduction disturbances, the most serious being complete heart block.<sup>[3]</sup> It was observed in a study that the presence of left bundle branch block pattern and T-wave inversions predicts poor long-term survival in these patients.<sup>[4]</sup> Because of the high risk of cardiac mortality, patients with these high-risk ECG changes should be closely followed up even after the resolution of acute phase. The cardiac MRI findings in our patient suggest the presence of myocardial edema and necrosis in regions not restricted to one coronary territory, similar to that seen in other etiologies of inflammatory myocarditis.

## CONCLUSIONS

Myocardial involvement is the most serious manifestation of diphtheria which may present as acute heart failure with dysrhythmias. It is characterized by myocardial necrosis with mononuclear cell infiltration and areas of interstitial fibrosis on histopathology. Cardiac MRI shows evidence of myocardial edema and necrosis. Although it is considered a life-threatening condition, with timely administration of antidiphtheritic serum and aggressive supportive care, the outcome might be successful.

## Consent

Appropriate consent for the publication of anonymized patient material was obtained from the patient and guardian.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published, and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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