Case Series

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High mortality diphtheritic myocarditis with conduction disturbance, case series, and review of literature

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Introduction: Diphtheria cases are still being reported in various parts of the globe. Although complete heart block resulting from diphtheric myocarditis is infrequent, it can lead to fatality. Awareness and recognition of this help strengthen the importance of vaccines and their proper management.

Case presentation: The authors report two young patients who presented in the interval of a month, to the emergency department with signs and symptoms of diphtheria. Both developed diphtheric myocarditis with complete heart block and severe left ventricular systolic dysfunction, which did not respond to temporary pacing.

Discussion: Diphtheria remains rare but few cases continue to emerge, especially in developing countries. Those who develop it have high mortality, particularly from cardiomyopathy, airway compromise, and organ failure. Conduction abnormalities are diagnostic of diphtheric myocarditis and have a grim prognosis and treatment options are limited.

Conclusion: Diphtheric myocarditis has a poor prognosis and is an independent predictor of mortality. Since aggressive invasive treatment has not been shown to improve survival, early recognition along with antitoxin at the earliest suspicion and proper supportive care are the current best available options.

Keywords: case series, complete heart block, conduction disturbance, diphtheritic myocarditis, mortality

Introduction

Diphtheria, a vaccine-preventable disease that continues to affect many, is still infrequently reported in developing countries[1]. Complete heart block (CHB) is a rare but potentially fatal complication of diphtheric myocarditis. Marked electrocardiographic abnormalities such as Bundle branch block (BBB), AV dissociation, and CHB are diagnostic of diphtheric myocarditis. Transient non-specific electrocardiographic abnormalities are frequent but their significance remains unclear. This article presents two cases of diphtheric myocarditis with CHB and severe left ventricular systolic dysfunction that did not respond to temporary pacing. Apart from supportive measures, other treatment options for diphtheritic myocarditis have not been shown to improve outcomes. This article aims to raise awareness and improve understanding of the prompt detection and management of such complications.

HIGHLIGHTS

- The importance of recognizing and managing diphtheric myocarditis, a rare but fatal complication of diphtheria.
- Two cases presented here severe left ventricular systolic dysfunction that did not respond to temporary pacing.
- Fatalities in diphtheria are primarily due to complications such as myocarditis, respiratory failure, or peripheral neuropathy.
- Early recognition and prompt supportive care are critical in improving outcomes.

Method

This case series incorporates two consecutive cases that were treated in a teaching hospital. This case series has been reported in line with the Preferred Reporting of Case Series in Surgery (PROCESS) Guideline[2].

Case presentation

Case 1

An 18-year-old Brahmin boy from Sindhupalchowk presented to the emergency department with a history of fever, shortness of breath, and dizziness for 5 days. He was vaccinated against diphtheria as per the national guideline till 5 years of age but did not receive any booster doses of the vaccine. On examination, the pulse was regular, but at 20 beats per minute, with a blood pressure of 110/70 mmHg. Examination of the oral cavity showed tonsillar enlargement with pseudomembrane (Fig. 1). Respiratory examination showed mild bilateral wheeze and basal crepitation. ECG

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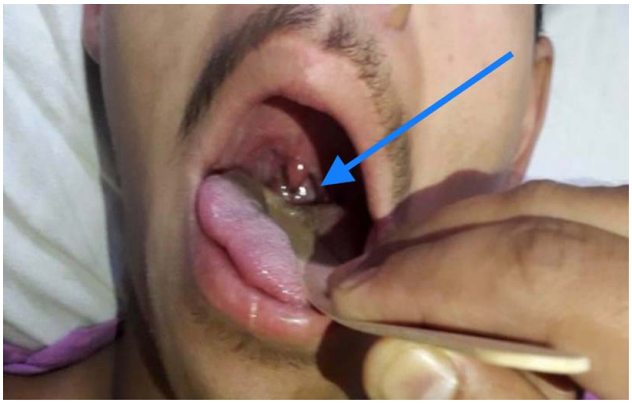

Figure 1. Oral cavity of case 1 with arrow pointing enlarged tonsil with gray white exudates (blue arrow in the figure points to the oral cavity of the patient).

revealed a high-degree AV block with intermittent CHB with a pause of 4 s. Echocardiography revealed severe left ventricular systolic dysfunction with an ejection fraction of 30%. Chest radiograph showed signs of congestive heart failure and blood investigations revealed CPK-MB at 252 U/l and a positive qualitative Antistreptolysin O and c-reactive protein. A provisional diagnosis of diphtheric myocarditis was made based on the clinical findings and ECG changes, which was later confirmed by throat swab culture. A temporary cardiac pacemaker was inserted immediately and he was given appropriate antibiotics, antitoxin, and intravenous immunoglobulin. Despite this, the patient expired after 5 days of cardiac care unit stay due to refractory malignant ventricular arrhythmia.

Case 2

After a month, a similar case visited the teaching hospital. A 12-year-old Newari male child from Thimi, presented with difficulty swallowing, fever, and bilateral peritonsillar abscess of 4 days' duration. He was living in foster care and his immunization history was not known. On examination, his pulse was found to be regular and measured at 60 beats per minute, while his blood pressure was recorded as 100/60 mmHg. ECG revealed a right bundle branch block type interventricular block. His echocardiography showed global hypokinesia with an ejection fraction of 25%. Investigations revealed a CPK-MB 346 U/l and troponin I 26.4 U/l. Antistreptolysin O titer was negative and qualitative c-reactive protein was positive. A provisional diagnosis of diphtheric myocarditis was made and a throat swab was taken for culture, which later came positive for diphtheria. The patient expired on the second day of his cardiac care unit stay when he developed bradycardia and went into an asystole (Fig. 2) that did not respond to emergency management including cardiac pacing, antibiotics, antitoxin, and intravenous immunoglobulin.

Discussion

Epidemiology

Diphtheria is a significant preventable disease that primarily affects children and has high morbidity and mortality rates[1]. While developed nations no longer consider it a public health concern, it persists in developing countries, where mortality rates remain around 10%, with little improvement over the past century[3]. Even in the 2000s, parts of India reported case fatality rates exceeding 12%[4]. There is a paucity of evidence on the prevalence of diphtheria in Nepal. A study published by Jha *et al.*[5] in 2013, where they surveyed 20 major pediatric hospitals in Nepal, found a documented 774 cases of diphtheria with 13.4% mortality between 1983 and 2003. This disease caused by toxins, affects multiple body systems, with cardiovascular involvement being a major contributor to illness and death. Fatalities in diphtheria are primarily due to complications

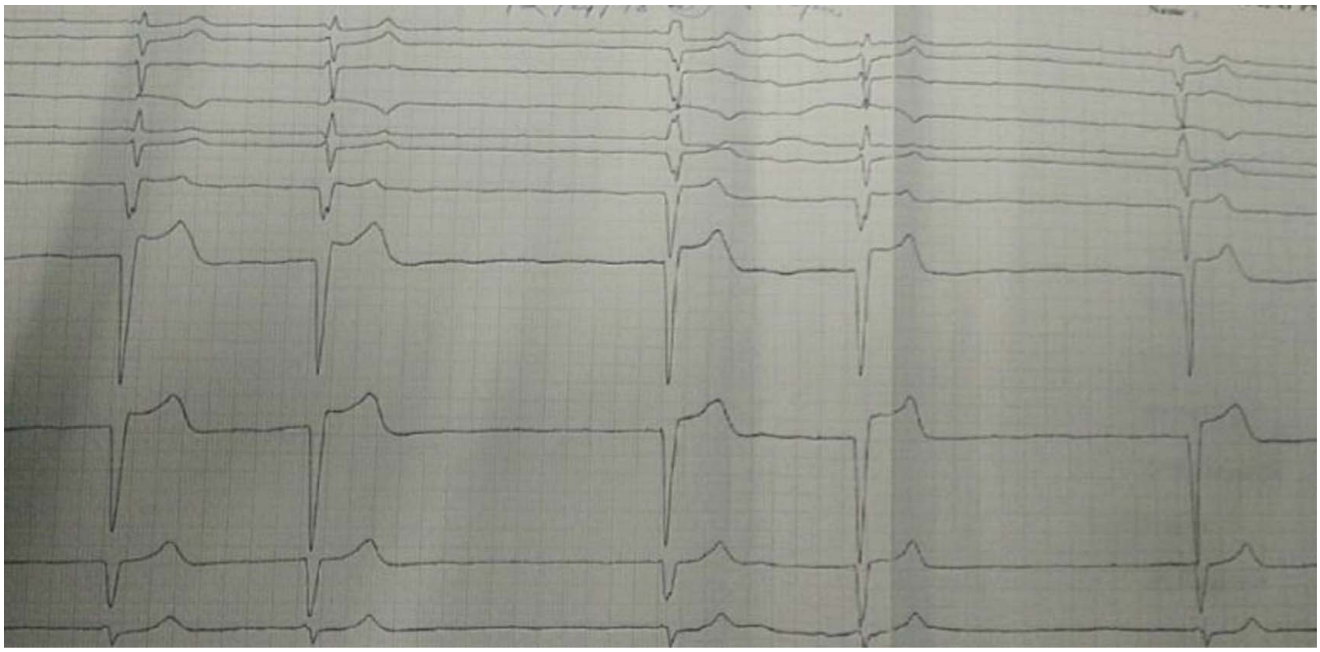

Figure 2. A segment of 12 lead ECG of case 2 with irregular rhythm and bradycardia with absent P waves with deep Q waves.

caused by toxins, such as myocarditis, respiratory failure, or peripheral neuropathy. Other significant contributors to associated mortality are upper airway obstruction, renal failure, and disseminated intravascular coagulation.

The two cases that presented to our center were young and sought medical attention after 4–5 days of symptoms, which is considered a delayed presentation and is associated with a poor prognosis[6]. At presentation, both patients had ECG changes, and the presence of arrhythmia and cardiogenic shock is also associated with poor survival[6].

Mortality and the heart

The major contributors to acute mortality in diphtheria are toxin-mediated diphtheritic cardiomyopathy and airway compromise from pseudomembrane. Other causes include disseminated intravascular coagulation and renal failure[7]. Following diphtheria, 10–20% of patients are likely to develop diphtheritic cardiomyopathy. The associated mortality is above 75% in under five children, which gradually decreases with increasing age[8]. Severe disturbances in cardiac conduction, which encompass the development of CHB, arise in roughly 50% of individuals afflicted with diphtheritic myocarditis and are consistently associated with a fatal outcome.

Diphtheria toxin exerts inhibitory effects on elongation factor 2 activity, which is a critical step in protein synthesis. In addition, it causes DNA fragmentation and cytolysis. Histopathological analysis of affected individuals reveals the presence of active inflammation in the interstitial space, hyaline degeneration, and necrosis in the myocardium. The conduction tissue is also affected, and about half of patients with diphtheric myocarditis develop severe conduction abnormalities. A study conducted by Jayashree *et al.* revealed that a paucity of immunization, hypotension during admission, and the existence of complicating factors such as respiratory obstruction, myocarditis, and renal insufficiency had a noteworthy detrimental impact on the disease prognosis. Through the utilization of multiple regression analysis, it was discerned that the sole autonomous factor predicting fatality was the occurrence of myocarditis[6].

Conduction abnormality

Currently, available literature offers limited information on the subject of conduction abnormalities observed in myocarditis, including the ones caused by diphtheria. Conduction system disturbances in patients with diphtheritic myocarditis are indicative of severe myocardial injury and are typically fatal even with ventricular pacing. While Dung *et al.*[9] claimed that the use of temporary cardiac pacemakers led to a reduction in the mortality rate to 74% in a prospective study of 34 patients, other studies, such as a 10-year retrospective analysis of 46 patients with myocarditis conducted from 1976 to 1986, have suggested that cardiac pacing is unlikely to improve survival in cases of CHB and BBB[10]. The unfavorable prognosis associated with CHB and BBB can be attributed to the marked decline in systolic function that accompanies AV block. Therefore, despite ventricular electrical stimulation, the mechanical response is inadequate, and most patients die from cardiogenic shock.

Our cases also showed poor responses to cardiac pacing. This further emphasizes the importance of supportive care rather than aggressive intervention in the patient's survival.

Treatment options

The treatment options for diphtheritic myocarditis are limited, with supportive measures being the primary form of management. The administration of antitoxin in the early stages of the illness has been shown to have some benefit, although its efficacy is limited against toxins that have already penetrated the cells[11]. Despite this, it is recommended that antitoxin be administered to all individuals suspected of having diphtheritic myocarditis. Steroids and immunosuppressive therapy have not been found to be beneficial in the treatment of this condition[12].

Conclusion

In conclusion, diphtheritic myocarditis continues to occur in underdeveloped countries, particularly in under-vaccinated children and is associated with very high mortality. Conduction system disturbances in patients with diphtheritic myocarditis are markers of severe myocardial damage and have a poor prognosis. Treatment options are limited and ventricular pacing does not improve survival. Antitoxin, particularly in early disease, and proper supportive care are currently the best available interventions. More studies are needed to prognosticate and evaluate the proper treatment of myocarditis in diphtheria.

Ethical approval

Ethical approval is not required because the information regarding the patients in this case series are gathered retrospectively and there are no concerns regarding patient safety in the process. So our institution has exempted case series from ethical review.

Consent

Written informed consent was obtained from the patient for case 1 and from the parents for case 2 to publish the cases with the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

C.M.P. was involved in the initial concept of the case series and was directly involved in patient care. All the authors were involved in data curation, drafting the manuscript and reviewing process.

Conflicts of interest disclosure

The authors declare that there are no conflicts of interest regarding the publication of this article.

Research registration unique identifying number (UIN)

This is not an original research project involving human participants in an interventional or an observational study, but a case series. This registration is not required.

Guarantor

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Data availability statement

Data and information generated during the study of the cases are available upon reasonable request to the corresponding author.

Provenance and peer review

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