BRIEF REPORT

DIPHTHERITIC MYOCARDITIS: CASE SERIES IN THE PRESENT ERA OF UNIVERSAL IMMUNIZATION PROGRAMME

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ABSTRACT
Diphtheria continues to be reported from the developing world and is a major preventable disease of childhood with high morbidity and mortality. It can affect many organ systems but the cardiovascular involvement in the form of myocarditis carries a high mortality. We report a case series of eight children with the diagnosis of diphtheria who presented with arrhythmias or cardiogenic shock suggestive of severe myocardial damage. Out of eight children, five (62.5%) died. Early detection, careful monitoring and aggressive management may result in improved outcomes in these critically sick children.

Methods & Materials
We conducted a retrospective observational study in the Department of Paediatrics at a tertiary care teaching institute from central India. Institutional Ethics committee approval was taken before the commencement of the study. Data was collected from the in-patient records of the patients retrieved from the Medical Records Department. The pediatric cases admitted within the study duration period of 4 months from August 2018 to November 2018 with the diagnosis of diphtheria with myocardial involvement were enrolled in the study. The diagnosis of diphtheria was made clinically on the basis of classic clinical findings of fever, throat pain, white membrane in the throat that bled on touching. The diagnosis of myocarditis was made on the basis of symptoms and signs of cardiac failure or arrhythmias or electrocardiographic (ECG) findings in the form of conduction abnormalities (heart block) or arrhythmias. ECG was done in all patients; however, echocardiography could be done only in one patient. Children with other causes of myocardial dysfunction were excluded from the study.

Results
A total of eight patients were enrolled during the study period of four months. Male to female ratio was 2:8. Eight children were between the ages of 8-13 years (mean age: 10.5 years). Hypotension was defined as systolic BP <2 SD below normal for age. Leucocytosis was defined as total leucocyte count more than 15,500/cumm (Age: 4-7 years) and 13,500/cumm (Age: 8-13 years). Hypotension was defined as systolic BP <2 SD below normal for age. The identity of the patients was not revealed in the study. Data was tabulated and analyzed.
equal. Mean age was 8.75 years. In all patients, the history of immunization was either incomplete or none. History of high-grade fever was present in all patients. Bull neck was present in all except one patient. On throat examination, white membrane was present in all cases. It caused airway obstruction in one case. Neurological involvement in the form of palatal palsy and nasal twang of voice was present in three patients. All patients had leucocytosis on complete blood count except one and deranged renal function test were seen in two patients. All the patients had cardiac complications after 5 to 7 days of illness. Clinically they presented with either arrhythmia, bradycardia/tachycardia, hypotension, and breathlessness. Bacteria (Klebs-Loeffler bacillus KLB) was isolated on throat swab smear examination by Albert’s stain in two cases. Mean duration of hospital stay was 7 days. Out of 8 children, 5 (62.5%) died. Four patients succumbed within 24 hours of admission. All patients received anti-diphtheritic serum (40,000-1,00,000 IU) intravenously, erythromycin (40-50 mg/kg/day) orally in 4 divided doses, and intravenous fluids, if needed inotropes in the form of dobutamine (10 mcg/kg/min), ventilation and defibrillation. Still, 5 patients could not be salvaged. Clinical and laboratory features are tabulated in Table 1.

**Discussion**

The pharyngo-tonsillar is the classic presentation of diphtheria characterized by sore throat, fever, pseudomembrane, cervical lymphadenopathy/bull neck appearance, dysphagia, drooling. The bacteria produce a powerful exotoxin, responsible for its virulence. Toxin mediated inhibition of protein synthesis is reported as a mechanism of all systemic manifestations. Degenerative changes in tissues, which include heart, muscle, peripheral nerves,

| Table 1. Clinical features and investigations of patients admitted with diphtheria |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **Patient 1**                  | **Patient 2**                  | **Patient 3**                  | **Patient 4**                  | **Patient 5**                  | **Patient 6**                  | **Patient 7**                  | **Patient 8**                  |
| ---                            | ---                            | ---                            | ---                            | ---                            | ---                            | ---                            | ---                            | ---                            |
| **Age (years)**                | 5                              | 13                             | 3                              | 11                             | 7                              | 13                             | 8                              | 10                             |
| **Gender**                     | Female                         | Male                           | Female                         | Female                         | Female                         | Male                           | Male                           | Male                           |
| **Day of presentation of myocardial involvement after illness** | 7th                            | 7th                            | 5th                            | 5th                            | 4th                            | 5th                            | 5th                            | 7th                            |
| **Clinical Features**          | Fever, Bull neck, Membrane in throat, Nasal twang | Fever, Bull neck, Membrane in throat, Palatal Palsy | Fever, Membrane in throat | Fever, Bull neck, Membrane in throat, Airway obstruction | Fever, Bull neck, Membrane in throat, Nasal twang | Fever, Bull neck, Membrane in throat | Fever, Bull neck, Membrane in throat, Aphon | Fever, Bull neck, Membrane in throat |
| **ECG Findings**               | Complete Heart Block           | Escape ventricular Rhythm      | Sudden Ventricular tachycardia  | Left Bundle branch block type ventricular tachycardia | Sinus tachycardia               | Sinus bradycardia               | Ventricular tachycardia with capture beats | Sinus tachycardia |
| **WBC count (cells/cumm)**     | 34,900                         | 14000                          | 25000                          | 40000                          | 13983                          | 14000                          | 30800                          | 26000                          |
| **Urea/Creatinine (mg/dl)**    | 35/0.8                         | 213/0.5                        | 28/0.4                         | 34/0.7                         | 26/0.8                         | 30/0.5                         | 77/1.63                        | 38/0.46                        |
| **Throat Swab positive for diphtheria bacillus** | No                             | No                             | No                             | No                             | Yes                            | No                             | No                             | Yes                             |
| **Immunization**               | Incomplete                     | Incomplete                     | Not Known                      | Incomplete                     | Incomplete                     | Not Known                      | Incomplete                     | Not Known                      |
| **Outcome**                    | Survived                       | Died                           | Died                           | Died                           | Survived                       | Died                           | Died                           | Died                           |
| **Duration of Hospital Stay (Days)** | 23                             | 1                              | 11                             | 1                              | 8                              | 12                             | 1                              | 1                              |
adrenals, kidneys, liver and spleen result in systemic pathology of the disease. The cardio-vascular involvement leads to the highest mortality as compared to other system involvement. Myocarditis occurs in 10-20% of all diphtheria patients. Few Indian studies done on diphtheria report incidence of 16-66% of myocarditis in cases of diphtheria. Our study had similar mortality of 62.5%. Myocardial dysfunction as well as bradyarrhythmia and tachyarrhythmia are common but the most dreaded one is the complete heart block and ventricular tachycardia which are fatal in almost all cases. Ventricular tachycardia occurs in later stages of illness and is usually refractory and all the patients who developed this arrhythmia in our series died. Conduction system abnormalities are a marker of severe damage and pacing does not help much. Elevated renal function tests are indicators of advanced disease and seen in all cases who died. Hence are a poor prognostic marker. Lack of early identification and treatment leads to high mortality in diphtheritic myocarditis.

Anti-toxin administration forms the mainstay of treatment, but it has limited action against penetrating toxins or toxin already absorbed inside the cells. Hence it does not help much in cases presenting in advanced stage of the disease. The role of immunosuppressive agents such as steroids and immunoglobulins are not approved. Hence we did not use it in any of our patients. Proper airway management, supportive measures like inotropes, oxygen, and temporary pacemaker insertion may improve survival in critical cases of severe myocardial damage.

Limitations:
This case series describes only 8 patients. The organism was isolated in only two cases. Pacemaker insertion and ECMO facilities were not available to critically ill patients with cardiogenic shock and complete heart block that could improve outcomes.

Conclusion
Diphtheritic myocarditis has a high mortality (60%). Such patients require monitoring in pediatric cardiac intensive care units to enable early detection of serious arrhythmias like ventricular tachycardia and complete heart block so that timely treatment can be provided. It highlights the urgent need to fill the gaps in the universal immunization programme and ensure complete immunization of children.

Compliance with Ethical Standards
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