Case Report

Diphtheria: The Patch Still Remains—A Case Report From the State of Uttarakhand

Aroop Mohanty¹, Mohit Bhatia¹, Pratima Gupta¹, Saurabh Varshney², Manu Malhotra², Balram J. Omar¹

¹Department of Microbiology, ²Department of ENT and Head & Neck Surgery, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India

ABSTRACT

Diphtheria is a potentially fatal, toxin-mediated, infectious disease of children caused by Corynebacterium diphtheriae, which may cause obstructive pseudomembranes in the upper respiratory tract or damage to myocardium and other tissues. It spreads through close contact or droplet infection from a case or carrier. Carriers are an important source of infection, the ratio being 95 carriers for 5 clinical cases. Despite the Universal Immunization Programme (UIP) of India, which offers 3 doses of the Diphtheria, Pertussis, and Tetanus (DPT) vaccine starting at 6 weeks of age, there have been a number of reports of either reemergence or persistence from several Indian states in the last 5–10 years. There are, however, no published reports of diphtheria from the state of Uttarakhand, India, in the recent years. We hereby report a confirmed case of diphtheria from this region, which reiterates the fact that there is impending potential of reemergence of this infection.

KEYWORDS: Corynebacterium diphtheriae, DPT, UIP, Uttarakhand

INTRODUCTION

Diphtheria is a potentially fatal, toxin-mediated, infectious disease of children caused by Corynebacterium diphtheriae, which may cause obstructive pseudomembranes in the upper respiratory tract or damage to myocardium and other tissues. It spreads through close contact or droplet infection from a case or carrier. Carriers are an important source of infection, the ratio being 95 carriers for 5 clinical cases. Despite the Universal Immunization Programme (UIP) of India, which offers 3 doses of the Diphtheria, Pertussis, and Tetanus (DPT) vaccine starting at 6 weeks of age, there have been a number of reports of either reemergence or persistence from several Indian states in the last 5–10 years. There are, however, no published reports of diphtheria from the state of Uttarakhand, India, in the recent years. We hereby report a confirmed case of diphtheria from this region, which reiterates the fact that there is impending potential of reemergence of this infection.

CASE HISTORY

A 12-year-old male child was brought to the emergency department of a tertiary care teaching hospital of Rishikesh, Uttarakhand, in August 2018 with chief complaints of acute onset of fever, productive cough, and dyspnea with odynophagia for 5, 3, and 2 days, respectively. His parents revealed that the pattern of fever had changed from low grade and intermittent to high grade and continuous in the preceding 5 days. He was finding it extremely difficult to swallow both solids and liquids of late and had labored noisy breathing. His voice had also changed with slight hoarseness in character for 2 days. The child was repeatedly coughing and expectorating yellow-colored, non-foul-smelling, non-blood-stained sputum. As per the information given by his mother, the immunization status of this child was inappropriate for age.

General physical examination revealed that the child had appropriate height for age and weight for height and therefore was neither stunted nor wasted respectively. He was conscious and oriented but looked toxic. He was febrile with a temperature of 102°F, heart rate of 120/min, and respiratory rate of 24/min. Inspiratory...
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stridor was also present. No other abnormality was detected on systemic examination. Oropharyngeal examination revealed that the soft palate was congested with poor oro-dental hygiene. There were grayish-white membranous patches on the medial aspect of both the tonsils. Tonsils were hypertrophied (grade III) and uvula, soft palate, anterior pillar, and posterior pharyngeal wall were congested and edematous. Posterior pillar was not visible.

Investigations were carried out, the results of which are as follows: hemoglobin 9.1 g/dL; total leucocyte count 29,950/mm³; and deranged differential leucocyte count (neutrophils 85%, lymphocytes 6%, monocytes 8%, and eosinophils 0%). Two throat swabs were sent for microscopic examination and aerobic culture, respectively. Microscopic examination of Gram stained smear revealed few pus cells and occasional gram-negative bacilli. No structures morphologically resembling *C. diphtheriae* were observed on microscopic examination of Albert stained smears. Blood, MacConkey, and chocolate agar plates were respectively inoculated and incubated under aerobic conditions. Raised, gray colonies approximately 2–3 mm in size were obtained on chocolate agar after 48 hours of aerobic incubation [Figure 1]. Gram and Albert stained smears were prepared from these colonies, which respectively revealed the presence of pleomorphic gram-positive bacilli with swollen ends arranged in palisades and angular fashion [Figure 2] and green colored bacilli with bluish-black granules at their ends [Figure 3]. The isolate was confirmed as *C. diphtheriae* using MALDI-TOF-MS system (Bruker Daltonics, Bremen, Germany) with a high confidence identification score of 2.19. Owing to lack of resources, analysis for toxin production could not be performed.

Meanwhile, keeping the possibility of faucial diphtheria in mind, the patient was subjected to electrocardiography, which revealed the presence of inverted p waves. He was started on injections amoxicillin–clavulanic acid, amikacin, and metronidazole. However, his condition deteriorated rapidly with increasing difficulty in breathing. He was subjected to emergency tracheostomy and maintained on mechanical ventilation on the second day after admission. Chest X-ray revealed the presence of pneumothorax in both lung fields and therefore bilateral intercostal drains were placed and secured.

By the time aerobic culture report was released, the patient's condition had worsened further. Owing to nonavailability of diphtheria antitoxin, the parents of this child were counseled about the grave prognosis of this disease. On the fourth day of admission, oxygen saturation of this patient decreased to 18%.

Figure 1: Growth obtained on chocolate agar

Figure 2: Gram stained smear showing Gram stained bacilli arranged in palisades and angular fashion

Cardiopulmonary resuscitation was started by critical care team but unfortunately, the patient could not be revived.

The hospital and state health authorities were notified about this case as per Integrated Disease Surveillance Programme (IDSP) guidelines. Appropriate measures were also employed by Hospital Infection Control team in order to prevent a nosocomial outbreak of diphtheria as per Centers for Disease Control, Atlanta, guidelines.[8]

**DISCUSSION**

Diphtheria manifests as either an upper respiratory tract or cutaneous infection with faucial diphtheria...
being most common.[7] Oropharyngeal infection is associated with formation of a tough, gray, fibrous pseudomembrane, which might extend into the larynx and bronchial airways leading to fatal airway obstruction. Owing to this potentially fatal complication, a timely microbiological diagnosis of diphtheria is imperative as this infection is often confused with other clinical conditions such as severe streptococcal throat infection, Vincent’s angina, or glandular fever.[8]

Detection of the lethal and potent exotoxin produced by the causative organism is considered to be the definitive test for the diagnosis of toxigenic *C. diphtheriae*.[8] In this case, although we succeeded in identifying *C. diphtheriae*, analysis for toxin production could not be performed. However, clinically the patient was toxic and rapidly deteriorated within a span of 4 days. This can be considered as an indirect evidence of toxin-mediated disease caused by *C. diphtheriae*.

Although cases of diphtheria have been reported from across the globe, it is endemic primarily in developing regions of Africa, Asia, and South America. As a preventive strategy against this infection, the World Health Organization (WHO) started Expanded Program of Immunization, which recommends three doses of DPT vaccine starting at 6 weeks of age with booster doses of diphtheria vaccine in countries where resources permit. In India, the UIP offers two booster doses at 18 months and 56 to 72 months of age apart from the routine doses given at 6, 10, and 14 weeks of age, respectively.

According to the data on vaccine-preventable diseases provided by the Government of India to WHO during 1980–2008, diphtheria continues to persist in India without much decline over the last 25 years. India accounted for 19–84% of the global burden from 1998 to 2008.[9] During 2001–2015, nearly half of the diphtheria cases reported globally were from India. As per CBHI data, during 2005–2014, India reported 41,672 cases (average: 4167 per year) with 897 deaths (case fatality ratio: 2.2%).[10] Ten Indian states namely Kerala, Assam, Delhi, Gujarat, Haryana, Karnataka, Nagaland, Maharashtra, Rajasthan, and West Bengal accounted for 84% of these cases. Data published from some of these states in the last 4 years have been depicted in Table 1. According to WHO, India contributed 3830 (53.9%) out of the 7097 diphtheria cases reported globally in the year 2016.

The aforementioned data bring out two important features about the epidemiology of diphtheria in India. First, this disease is now commonly affecting older children (5–19 years) and adults instead of under-five children. Second, majority of the cases were reported from children who were unimmunized/partially immunized against diphtheria. Because the immunity acquired through primary immunization wanes in early childhood, adequate coverage of booster doses is equally important. Unfortunately, data about coverage

![Figure 3: Albert stained smear showing green colored bacilli with bluish black terminal granules](image)

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| State             | Year of study | Total no. of suspected cases | No. of lab confirmed cases | Age (years) ≤5 (%) | Age (years) 6–10 (%) | Age (years) ≥10 (%) | Gender Male (%) | Gender Female (%) | Mortality (%) |
|-------------------|---------------|------------------------------|---------------------------|-------------------|---------------------|-------------------|-----------------|------------------|---------------|
| Kerala            | 2018          | 554                          | 29                        | 8                 | 30                  | 62                | 47              | 53               | 0             |
| Kerala            | 2016          | 533                          | 533                       | 7                 | 14                  | 79                | 52              | 48               | NA            |
| Assam             | 2016          | 33                           | 10                        | 0                 | 0                   | 100               | 30              | 70               | 20            |
| Rajasthan         | 2016          | 180                          | 180                       | 48                | 37                  | 15                | 63              | 37               | 24            |
| Karnataka         | 2015          | 432                          | 38                        | NA                | NA                  | NA                | 76              | 24               | NA            |
| Andhra Pradesh    | 2015          | 19                           | 13                        | 16                | 63                  | 21                | 58              | 42               | 37            |
| Delhi             | 2014          | 941                          | 218                       | 58                | 27                  | 15                | NA              | NA               | NA            |

NA = Data not available
of first and second boosters are not routinely collected in India. The patient under study in this report was 12 years old and partially immunized.

The vaccination status of children between 12 and 23 months of age in Uttarakhand is dismal, with only 67% having received 3 doses of DPT. About 9% of all children in the state have not received any vaccine till date. These figures are alarmingly low and point toward the possibility of an impending outbreak in the state. According to IDSP, there were no reported cases of diphtheria for the past 3 years from Uttarakhand. To the best of our knowledge, ours is the first confirmed case of diphtheria from this region in recent years. In a study conducted by Singh et al. in 2013, a total of 61 suspected cases of diphtheria were reported during the period from 2005 to 2010, from the Kumaun region of Uttarakhand. However, none of these cases could be confirmed microbiologically as smear examination and culture were negative in all cases.

The mainstay of treatment in diphtheria is Diphtheria Anti Toxin (DAT) or Anti Diphtheritic Serum. There are limited number of manufacturers of this lifesaving medicine in India and owing to paucity of demand, DAT is not manufactured regularly. The shortage of DAT calls for serious consideration about our understanding of success of the UIP. Given the rarity of this infection and insufficient inducement for pharmaceutical companies for continuous production of older or improved versions of DAT, the supply of this drug will continue to be scarce. The patient under study could not be saved because of nonavailability of DAT, as a result of which the toxin-mediated complications of diphtheria could not be subdued.

This case highlights the need of having a high index of clinical suspicion for diphtheria and the importance of vigilance in the laboratory, while managing a patient with membranous tonsillitis. Because antibiotic therapy can only eliminate the infection but not reverse the effects of the diphtheria toxin, making diphtheria antitoxin readily available at health-care centers is the need of the hour. Adequate immunization with emphasis on taking booster doses along with generation of high-quality data on coverage of DPT vaccination as per UIP will go a long way in eliminating this dreaded infectious disease.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Dikid T, Jain SK, Sharma A, Kumar A, Narain JP. Emerging & re-emerging infections in India: An overview. Indian J Med Res 2013;138:19-31.
2. Das PP, Patgiri SI, Saikia L, Paul D. Recent outbreaks of diphtheria in Dibrugarh district, Assam, India. J Clin Diagn Res 2016;10:DR01-3.
3. Mahanta TG, Nath B. Investigation of an outbreak of diphtheria in Borborooah block of Dibrugarh district, Assam. Indian J Community Med 2010;35:436-8.
4. Meera M, Rajarao M. Diphtheria in Andhra Pradesh—a clinical epidemiological study. Int J Infect Dis 2014;19:74-8.
5. Sangal L, Joshi S, Anandan S, Balaji V, Johnson J, Satapathy A, et al. Resurgence of diphtheria in north Kerala, India, 2016: Laboratory supported case-based surveillance outcomes. Front Public Health 2017;5:218.
6. Kretsinger K, Broder KR, Cortese MM, Joyce MP, Ortega-Sanchez I, Lee GM, et al. Preventing tetanus, diphtheria, and pertussis among adults: Use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP) and recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health-care personnel. MMWR Recomm Rep 2006 Dec;55:1-37.
7. Lakshmi P, Narsimloo K, Archana GJ, Leela K. Diphtheria in Telangana state—A case report. J Basic Clin Res 2016;3:35-8.
8. Efstratiou A, Engler KH, Mazurova IK, Glushkevich T, Vuopio-Varkila J, Popovic T. Current approaches to the laboratory diagnosis of diphtheria. J Infect Dis 2000;181 Suppl 3:S138-45.
9. Murhekar MV, Bitragunta S. Persistence of diphtheria in India. Indian J Community Med 2011;36:164-5.
10. Murhekar M. Epidemiology of Diphtheria in India, 1996-2016: Implications for Prevention and Control. Am J Trop Med Hyg 2017;97:313-8.
11. Immunization Programme: Department of Medical Health and Family Welfare, Government of Uttarakhand, India; [cited 2018 Sep 7]. Available from: http://health.uk.gov.in/pages/display/77-immunization-programme
12. Singh N, Singh AK, Gaur S. A study of diphtheria in Kumaun region of Uttarakhand state in India. J Drug Del Therapeutics 2013;3:105-7.
13. Jain Y. Persistence of diphtheria in India signals need for accessible drugs for neglected illnesses [Internet]. The Wire; 2017 [cited 2018 Sep 7]. Available from: https://thewire.in/health/diptheria-india-accessibility-drugs-neglected-illnesses.