

## Laryngopharyngeal Diphtheria: Still a Diagnosis in Indian Adults

### ABSTRACT

Diphtheria is an acute, potentially fatal, and highly communicable bacterial infection caused by *Corynebacterium diphtheriae*. In India and the developing world, 100% immunisation is claimed against diphtheria through diphtheria, pertussis, and tetanus (DPT) vaccination. Only a negligible number of cases are seen in the western world. In India, a few outbreaks of diphtheria has been reported among children. But it is rarely diagnosed in Indian adults. Diphtheria has high morbidity due to nerve damage and high mortality because of respiratory obstruction or myocardial complications. PubMed data base was searched for case reports in last 10 years for respiratory diphtheria in adults. Here we are presenting our case and a review on laryngopharyngeal diphtheria in adults.

**Keywords:** *Corynebacterium diphtheriae*, DPT vaccine, respiratory obstruction, myocardial complication, Indian adults



### INTRODUCTION

*Corynebacterium diphtheriae* is the causative agent for potentially fatal and communicable laryngopharyngeal diphtheria infection, which is transmitted mostly by inhalation of aerosols. This agent releases exotoxins which is regulated by tox gene present in  $\beta$ -corynebacteriophage.<sup>1</sup> Mortality in this infection is either by due to pseudo membrane related airway obstruction or exotoxin mediated insult to cardiac wall muscles, brain, and kidneys. Case-fatality rates were up to 50% in the 1880 epidemic. Even now with antitoxins and modern facilities, 5% to 10% mortality is reported.<sup>1</sup>

Globally in 1950, up to 100 000 cases of diphtheria were reported. This number was decreased to about 8000 in 2009 and to 4530 in 2015.<sup>2</sup> This was reported by the World Health Organization (WHO) as a result of the widened and improved immunization coverage.<sup>2</sup> There is a continuous and regular diphtheria, pertussis, and tetanus (DPT) vaccination plan for all infants in India for about 3 decades. So it is rare to see clinically confirmed case of diphtheria in an Indian adult. We report our experience of diagnosing and managing an adult patient of diphtheria and with its significance in the era of compulsory vaccination and a review of laryngopharyngeal diphtheria in global scenario. Informed written consent was obtained from the patient and clearance was taken from the institutional research committee for the publication.

### METHODOLOGY

Information retrieval was done from PubMed database using MeSH words diphtheria, adults and case report for last 10 years from 2011 onward. Total 112 articles were retrieved. All articles reporting cutaneous diphtheria were not analysed. Only case reports mentioning pharyngeal and laryngeal or respiratory diphtheria were assessed.

#### Case Report

A 24-year-old Garhwali female was brought to the emergency department with on and off fever for last two weeks. Her fever was high grade with chills and used to relieved with paracetamol. She also complained of difficulty and pain while swallowing both solids and liquids for 5 days. This pain was moderate to severe in intensity, and radiating to head and not relieved with the use of analgesics. She also complained for change of voice, pain while speaking, decreased appetite, and generalized weakness. There was no history of

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weight loss. Patient did not remember about her childhood vaccination. On examination, the patient complained about pain on tongue protrusion. Greyish membrane was visualized over grade 3 enlarged tonsils approaching the soft palate which did not bleed on peeling. Bilateral palatal movement was equal, and gag reflex was present. On laryngeal endoscopy, membrane was extending to edematous arytenoids and the posterior pharyngeal wall. Bilateral vocal cord movement was normal. There were bilateral, enlarged, and tender jugulodigastric lymph nodes. Clinical examination of nose and bilateral ear was within normal limits. We made differential diagnosis of laryngopharyngeal diphtheria along with other differentials for membrane over tonsils. After first clinical assessment, patient was kept in isolation. On investigation, throat swab was positive for Albert's stain. Patient's electro-cardiography report showed a normal pattern. Other routine blood investigations were within normal limits except for raised total leucocyte and raised neutrophils. She was immediately started on intravenous fluids. She also received 60 000 IU of antidiphtheric serum. She also received injection of amoxicillin and clavulanic acid 1.5 g twice daily for 7 days. The patient also received metronidazole injections for 7 days. All close family members were also counseled and were prescribed with chemoprophylaxis. They were advised with erythromycin 500 mg tablet thrice a day for 14 days. On day 7, repeat throat swab was sent which came to be negative for Albert's stain. The patient was discharged and followed-up after a week with no new complaints.

## DISCUSSION

Diphtheria infection is usually reported among children up to 12 years. It is an acute, severely debilitating serious condition. Respiratory diphtheria is usually transmitted by droplets in humans. Berger A et al reported sexually transmitted diphtheria through orogenital route.<sup>3</sup> A thick greyish pseudomembrane forms on the posterior pharyngeal wall. This membrane causes a mechanical obstruction. It may lead to difficulty in swallowing and difficulty in breathing to the patient. *Corynebacterium diphtheriae* is an exotoxin-producing bacteria. Entrance of this exotoxin in systemic circulation is the cause of systemic complication among patients. This exotoxin is regulated by "tox" gene. This exotoxin works by cell death. There are no specific target cells for this exotoxin in the human body. But myocardium and peripheral nerves are the most common victims, which turns fatal. Myocarditis and/or peripheral nerve neuropathy is reported in 10-20% of patients with diphtheria. This has been seen that two out of three patients with severe diphtheria may have myocardial and neurological complications at

presentation. Both these involvements are considered as the major cause for diphtheria associated mortality.<sup>4,5</sup>

*Corynebacterium diphtheriae* can be differentiated according to structure involved. It may be faucial, laryngeal, or cutaneous. It may also involve both the pharynx and larynx, and described as laryngopharyngeal. There are three different strains of this infection. These are divided according to the intensity of severeness of the infection. The three types of strains are gravis, intermedium, and mitis. The gravis strain is the most severe, while mitis strain is only of mild variety.<sup>6</sup> The worldwide trend of diphtheria infection is declining with time. It decreased by more than 90% between 1980 and 2016. This is the result of the WHO-initiated immunization program in 1974.<sup>7</sup> The effect of this program was also reflected by the shifting age distribution from children to adolescents and adults.<sup>8</sup> In India, vaccination against diphtheria has good national coverage. However, despite the well-planned vaccination program, sporadic diphtheria outbreaks are still noticed. Immunity conferred by diphtheria vaccination may wane with time. This protection usually lasts for ten years on average. Consequently, there is a recommendation from the WHO for a booster diphtheria vaccine every 10 years. This booster dose can be given in combination in developing countries, along with anti-tetanus toxoid. Raja SA et al.<sup>9</sup> reported a case of adult diphtheria who was first diagnosed as acute tonsillitis with peritonsillar abscess as patient came with patch over tonsil. He emphasized that we should keep suspicion of diphtheria in every membrane over tonsil as delay in treatment may lead to morbidity and mortality. He also emphasized over universal availability of life saving anti diphtheric serum. Two indigenous cases of pharyngeal diphtheria was reported in France after 22 years interval from last case.<sup>10</sup> In this report emphasis was given over contact tracing as they traced 53 contacts and investigate all of them along with prophylactic treatment. Ornek E et al.<sup>11</sup> reported diphtheria related myocarditis in a 34 years female patient. They gave emphasis on suspicion of diphtheria in all patients with fever, sore throat and unwellness for early detection and life saving treatment. A case of pharyngeal diphtheria was reported in a 68 years Swedish national who returned from West Africa after travelling.<sup>12</sup> This highlights risk of transmission from endemic areas to European countries and advocate for vaccination of travellers to endemic countries. Adler NR et al<sup>13</sup> commented that diphtheria was most common infectious cause of death in Australia in pre-vaccination period. They further reported one case in Brisbane and two cases in Victoria. Monaco M et al<sup>14</sup> reported respiratory diphtheria in an adult in Italy which was transmitted by companion dog who had cutaneous diphtheria. This report suggest that diphtheria can be transmit in humans from close contact of infected pets. Berger A et al<sup>15</sup> reported 45 years male in Germany with diagnosis of pharyngeal diphtheria in 2015, however they couldn't find source of infection. Moor C C reported a 54 years Turkish female with non toxigenic *Corynebacterium diphtheriae* from tracheal lesion with minimum respiratory symptoms.<sup>16</sup> Okamoto K et al<sup>17</sup> reported a case of nasal diphtheria by non toxigenic strain in Japan and highlight importance of awareness among clinician about diphtheria in post vaccination era. Skogmar S.<sup>18</sup> reported a case of pharyngeal diphtheria in 55 years male who returned to Sweden 6 days back from Srilanka and emphasised importance of travel history in suspicion of diphtheria in tonsillitis case. Haywood MJ et al reported

## MAIN POINTS

- Diphtheria is a notifiable disease in most parts of the globe as it is a rare condition in western countries.
- In the developing world, cases are seen in children, but it is rare to find it in adults in developing countries also.
- So we should keep in mind the possibility of diphtheria in all adult patients with differential diagnosis for membrane over oropharynx and larynx.

a case of respiratory diphtheria who required multidisciplinary approach and percutaneous feeding gastrostomy.<sup>19</sup> This adult male was infected from his dog who was diagnosed as cutaneous diphtheria. Loganathan T et al reported a case of pharyngeal diphtheria in a partially immunized adult with no source of infection in Malaysia and highlighted the need of robust immunization and booster dose in adults.<sup>20</sup> Lai Y et al<sup>21</sup> reported a case of autocanthous diphtheria in a Bangladeshi construction worker who was working in Singapore for last 10 months. They highlighted significance of vaccination of international labourer from endemic areas. Scheifer C et al<sup>22</sup> reported respiratory diphtheria in an Afghani refugee staying in Europe who also had tuberculosis. Lucy Li et al<sup>23</sup> reported two cases of respiratory diphtheria in fully vaccinated United Kingdom born adults in Scotland. Both were reported as imported cases due to travel history of Tunisia. They highlighted importance of suspicion of re-emergence of diphtheria in high risk cases. Grigg S reported a case of toxigenic diphtheria in Australia with no travel history to endemic area.<sup>24</sup> De Jong W et al<sup>25</sup> reported a 22 years female with respiratory diphtheria in Indonesia. They highlighted the importance of vaccination in international religious traveller to prevent spread in non endemic area. Cholewa S et al<sup>26</sup> reported a case of toxigenic respiratory diphtheria in a 69 years visitor in Canada from India. He was admitted with in 48 hours of arrival to Canada with the complain of shortness of breath, sore throat and fever. A recent article reported an analysis of diphtheria in India over the past 2 decades (1996-2016). This report emphasizes the lack of progressive epidemiological data for diphtheria. This report suggests that diphtheria cases are frequent among school-going children and adolescents in India. The study had also noted that there was an 80% coverage of the initial 3 doses of vaccine. There is no reliable data for booster dose vaccination coverage among children in the literature.

## CONCLUSION

Diphtheria is a vaccine-preventable, highly fatal bacterial infection. Even after nationwide immunization coverage, we still see serious life threatening diphtherial infections among Indian adults. Along with India respiratory diphtheria is frequently reported in Asia and Africa. Due to increased global tourism for leisure, work or religious trip, risk of spread of diphtheria from endemic areas to non endemic nations is on rise. Another cause of diphtheria in adults seems to be fading immunity provided by childhood vaccination. So we recommend importance of booster dose of vaccination for adults against Diphtheria globally both for endemic and non endemic areas.

**Informed Consent:** Written informed consent was obtained from the participant who participated in this case.

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