DOI: 10.7860/JCDR/2021/49665.15409

Case Report

Microbiology Section

Diphtheria in an Adult: A Paradigm of Waning Immunity

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ABSTRACT

In the past 10 years, there have been several reported cases of the existence of a vaccine-preventable disease from several Indian states. Diphtheria, re-emerge as a major public health problem as this fatal infection used to be noticed in toddlers and school-going has now been stated to occur amongst adults also despite the fully functional Universal Immunisation Program (UIP) in India. India contributed about 53.9% of diphtheria cases globally in the year 2016. In cases, the reason for the upsurge could be attributed to lack of proper immunisation or waning of vaccine-induced immunity with increasing age. Here, a case of a 24-year-old adult male was reported who presented with acute membranous tonsillitis, a preliminary diagnosis made on physical examination. *Corynaebacterium diphtheriae* was isolated. Finally, the isolate was confirmed as *C. diphtheriae* using Matrix Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS) system.

Keywords: Adult diphtheria, Pseudomembrane, Vaccine preventable infection

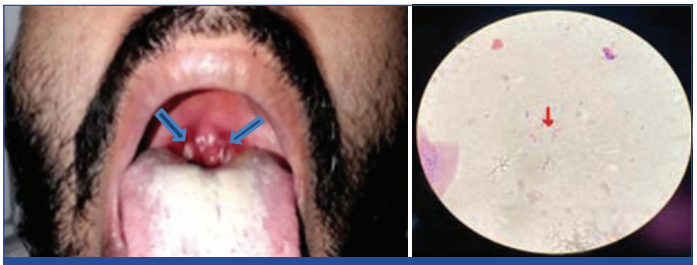
CASE REPORT

A 24-year-old male presented to Emergency Department with chief complaints of fever, sore throat leading to pain and difficulty while swallowing from past five days. The patient was apparently well, few days back when he developed fever which was low grade and intermittent. His condition worsened and he came to the emergency with odynophagia which was more for solids than liquids, fever, and slight hoarseness of voice. On physical examination, he was febrile with a temperature of 101°F, heart rate of 120/min, and respiratory rate of 22 beats/min. No abnormality was detected on systemic examination. In the oropharynx, the anterior pillars were congested bilaterally with grade IV tonsillar enlargement along with greyish white membrane visible on the medial aspect of both the tonsils as shown in [Table/Fig-1] with oedematous and congested uvula.

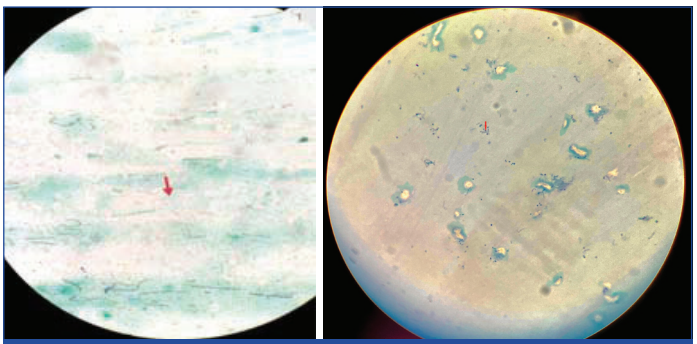
The posterior pharyngeal wall was congested but soft palate movements were normal. In the neck, mild lymphadenopathy was present which was unusual as the patients with diphtheriae presents with typical "Bull neck". Based on physical examination, a preliminary diagnosis of acute membranous tonsillitis was made. Upon eliciting the immunisation history, his mother stated that he had missed primary immunisation or incompletely vaccinated as no records of any childhood vaccination could be retrieved.

History also revealed that the patient had recurrent episodes of a sore throat for the last two years but he never noticed any membrane over his tonsils and used to take medicines from local chemist nearby. Investigations revealed haemoglobin of 12.9 g/dL, total leucocyte count was 29,950/mm^3; and differential leucocyte count (neutrophils was 85%, lymphocytes was 6%, monocytes was 8%, and eosinophils was 0%).

Two throat swabs were collected and sent for microbiological examination. Microscopic examination of gram stained smear revealed occasional pus cells, gram positive cocci in chains and few gram positive bacilli as shown in [Table/Fig-2]. Albert stained smear revealed green coloured bacilli with blue black metachromatic granules and reported bacilli morphologically resembling *C. diphtheriae* [Table/Fig-3]. The second swab received was inoculated onto chocolate agar and on Blood Tellurite Agar (BTA) and was incubated at 37°C under aerobic conditions. Small black colonies were obtained on BTA after 48 hours of aerobic incubation. On chocolate agar circular small whitish colonies appeared. Gram and Albert stained smears were prepared from these colonies, which again revealed the presence of pleomorphic gram positive bacilli arranged in palisades manner. Green coloured bacilli with bluish-black metachromatic granules were noticed in Albert smear [Table/Fig-4]. Urease test was negative which differentiates between *C. diphtheriae* and *C.ulcerans* and *C.pseudotuberculosis* which are urease positive [1]. Finally, the isolate was confirmed as *C. diphtheriae* using MALDI-TOF-MS system (Bruker Daltonics, Bremen, Germany) with an identification score of 1.9.



[Table/Fig-1]: Shows greyish white patch over the both sides of uvula (Blue arrows).
[Table/Fig-2]: Gram stain showing slender gram positive bacilli in direct throat smear under 100X. (Images from left to right)



[Table/Fig-3]: Albert stain showing green coloured bacilli with bluish-black metachromatictic granule from direct throat smear under 100X.
[Table/Fig-4]: Albert stain showing green coloured bacilli with metachromatic granules after culture under 100 X. (Images from left to right)

The physician was informed after the first microscopic examination, keeping the possibility of faucial diphtheria the patient was administered 50,000 units of Diphtheria Antitoxin (DAT) to prevent

S. No.	Study	Year	Case/Outbreaks	Region/State	Age	Sex	Immunisation status	Treatment/outcome
1.	Loganathan T and Mohamed PY [5]	2018	Case	Malaysia	29-year-old	Male	Partially immunised	i.v. Erythromyc in Outcome- Recovered
2.	Swarna SR et al., [6]	2020	Case	NAD	28-year-old	Female	Fully Immunised	i.v. crystalline penicillin 20 lac IU i.v. metrogyl 500 mg Tab Erythromycin for 3 days Outcome- Recovered
3.	Sangal L et al., [7]	2017	Outbreak	Kerala	≥18 years	Females	Partially immunised	Treatment Not specified Outcome- Recovered
4.	Das PP et al., [8]	2016	Case	Assam	18-year-old	Male	No record of vaccination	Tab Erythromycin Outcome- Recovered
5.	Krishnan S et al., [9]	2018	Outbreak	Malappuram	16 and 20 years	Female	Partially immunised	i.v. Azithromycin, Ceftriaxone, Nafcillin, and Steroids Outcome- Died
6.	Lurie P [10]	2003	Case	Pennsylvania	63-year-old	Male	Non immunised	i.v. Azithromycin, Ceftriaxone, Nafcillin, and Steroids Outcome- Died
7.	Present case	2021	Case	Chandigarh	24-year-old	male	No record of vaccination	Treatment- Inj. amoxicillin and clavulanic acid 1 gm BD for 5 days Outcome- Recovered

[Table/Fig-5]: Recently published case/outbreaks on Adult Diptheria from India [5-10].
NAD: Non availability of data

any systemic complications. After culture reports the patient was put on inj. amoxicillin and clavulanic acid 1 gm BD (twice a day) for five days and later was shifted to oral doses of the same for another 10 days along with other symptomatic measures. The patient recovered uneventfully and on follow-up after 10 days and was asymptomatic.

DISCUSSION

Diphtheria is a potentially fatal acute infectious disease of childhood caused by toxigenic strains of *Corynebacterium diphtheriae*. The pathogenesis involves the ability of a given strain of *C. diphtheriae* to colonise within the oropharyngeal cavity from where it can spread to adjacent structures including the larynx leading to laryngeal diphtheria and its ability to produce diphtheria toxin. The determinants involved in the colonisation of the host are encoded by the bacteria, and the toxins are encoded by the corynebacteriophage [2].

According to the data given by the Government of India to World Health Organisation (WHO) during 1980-2008 on vaccine-preventable diseases, diphtheria continues to persist in small pockets without much decline over the last 25 years [3]. Despite fully functional Universal Immunisation Program (UIP) in India, there are reports of recent re-emergence of cases of diphtheria in adults indicating two main possibilities of this shifting paradigm, one is failure to undergo immunisation during childhood and second is the waning of vaccine-induced immunity which results in a decrease in the level of protective antibodies over time. Other than these two possibilities, it is also found that some Indian states especially in Hyderabad the incidence of diphtheria was found to be three times higher among Muslims (27 per 100,000) as compared to non Muslim community (9 per 100,000). Poor immunisation coverage and failure to take boosters along with the infecting dose, virulence of the diphtheria bacilli, overcrowding, increase in the migrant population and low awareness among parents, late recognition of the epidemic and an irregular supply of vaccines could be associated possible reasons for the rise in cases of adult diphtheria in India [4].

In present case after taking due consent from the patient to present the case, the contact tracing of his family was also done. All members were asymptomatic which suggested the possibility of infection being acquired from community. No immunisation record was available for present case and it is likely due to failure to undergo vaccination in early childhood.

Authors have mentioned few reports of published cases/outbreaks on Adult Diphtheria from India in the past few years, thus concluding shifting paradigm in the occurrence of diphtheria from children to adolescents as mentioned in [Table/Fig-5] [5-10].

It is known that immunity conferred by diphtheria vaccination wanes with time, UIP offers two booster doses at 18 months and 56 to 72 months age in addition to the routine doses given at 6, 10, and 14 weeks of age [11]. The data from WHO says that in India 10 states namely Kerala, Assam, Delhi, Gujarat, Haryana, Karnataka, Nagaland, Maharashtra, Rajasthan and West Bengal, accounted for 84% of these cases [12]. Serological studies suggest that for long-term protection the level of anti diphtheria toxoid IgG (Immunoglobulin G) antibody should be >1.0 IU/mL and a titer below this is not protective therefore the importance of booster doses of tetanus-diphtheria toxoid, for adults particularly at school leaving age, pregnancy, and after the age of 18 years have been recommended [13,14]. The extent of cases of adult diphtheria does not reflect the true picture in a community because of sub clinical and asymptomatic infections and undiagnosed cases therefore, clinicians should maintain a high suspicion of adult diphtheria while keeping in mind other differential diagnoses.

CONCLUSION(S)

The present case shows that the existence of diphtheria amongst adults is associated with failure to undergo immunisation during childhood therefore, implementation of public health measures is essential along with an enhanced surveillance to find the source of infection in adult population. Also, the provision of antidiphtheritic serum within the key hospitals should be made available to prevent complications and to reduce mortality in case of adult diphtheria. Raising public awareness and emphasising the benefits of childhood vaccination along with booster doses every 10 years should be done in future to prevent resurgence of vaccine preventable disease.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 02, 2021
- Manual Googling: Aug 16, 2021
- iThenticate Software: Aug 16, 2021 (7%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 30, 2021**
Date of Peer Review: **May 14, 2021**
Date of Acceptance: **Aug 18, 2021**
Date of Publishing: **Sep 01, 2021**