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Diphtheria in the current era of universal vaccination

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Abstract

Diphtheria is a vaccination preventable infectious disease with local and systemic complications predominantly affecting upper respiratory tract in younger (<5-year age) children. Its virulence is due to its ability to produce toxin which can cause fatal complications such as myocarditis and permanent damage in form of peripheral neuropathy. Diagnosis of diphtheria is primarily clinical supported by demonstration of toxin producing bacteria by culture. Early diagnosis and management with diphtheria anti-toxin can prevent mortality and morbidity. Here we present a case of 16-year-old boy managed with azithromycin, amoxycillin-clavulanic acid and diphtheria anti-toxin with complete recovery.

This case brings out the importance of recognising the re-emergence of diphtheria in older age groups. Lacunae in the universal immunisation process, rumours on vaccination effects and poor living conditions for refugee population are likely reasons in Asia and Europe. Universal immunisation, early diagnosis, prophylaxis and adequate supportive care are measures to prevent it.

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Case presentation

A 16-year-old male resident of a remote village in Haryana was referred to our medical emergency for progressive dyspnoea of one day. He presented with complaints of fever with chills, progressive neck swelling and drooling of saliva for three days duration. The parents could not recall vaccination history, BCG scar was also absent suggesting unvaccinated status. Examination of the oral cavity revealed an off whitish raised membrane, adherent to the posterior pharyngeal wall with surrounding redness and edema [Figure-1A]. On general physical examination he had; tachycardia, tachypnoea and neck swelling [Figure-1B]. He was suspected of having diphtheria and a throat swab was sent immediately for albert/gram staining in the emergency laboratory. Investigations showed Hb -11.8gm/dl (12-18gm/dl), TLC-13300/µL (4000-11000/ µL), neutrophils-76% (40-75%), lymphocytes-12% (20-45%), monocytes-10% (2-10%) and eosinophils-2% (1-6%) with borderline (27 U/L) raised Creatine kinase-MB enzyme (CK-MB) (5-25 U/L). Throat swab gram stain [Figure 2A] and albert stain [Figure 2B] were positive for diphtheriae like bacteria; confirming the diagnosis of diphtheria.

He was transferred to an isolation room, and diphtheria anti toxin (100,000 units) was infused over one hour. He was started on intravenous azithromycin (500mg q24hrly) and amoxycillin clavulanate (1.2 gm q8hrly) due to the local unavailability of intravenous (IV) procaine penicillin and IV erythromycin. He was monitored daily for the development of complications like myocarditis, stridor or neuropathic symptoms. The culture of the throat swab in Hoyle's tellurite blood agar showed black coloured growth of corynebacterium diphtheriae [Figure-2C]. Parents and all health care workers who came in contact were given oral erythromycin as prophylaxis. His fever subsided and tachypnoea improved. On the fifth day of admission, the patient was able to take liquids orally and was later discharged on oral amoxycillin and erythromycin for a total duration of fourteen days. On follow up; he was completely asymptomatic and his whole family was vaccinated with the tdap vaccine. This patient belonged to a poor rural family; he was born at home and did not have any prior hospital admission. His family was unaware of the vaccination status of his siblings also, showing a lack of awareness about vaccination in rural India.

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Figure 1A Pseudo-membrane visualized at the posterior pharyngeal wall

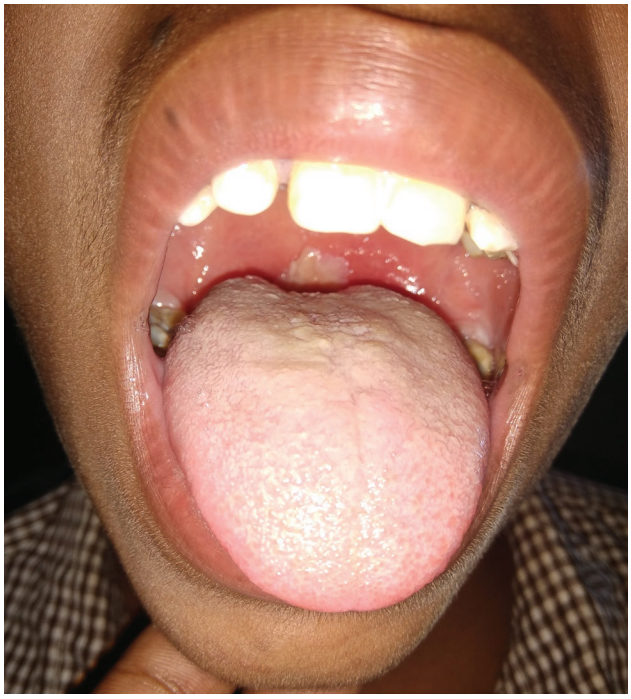
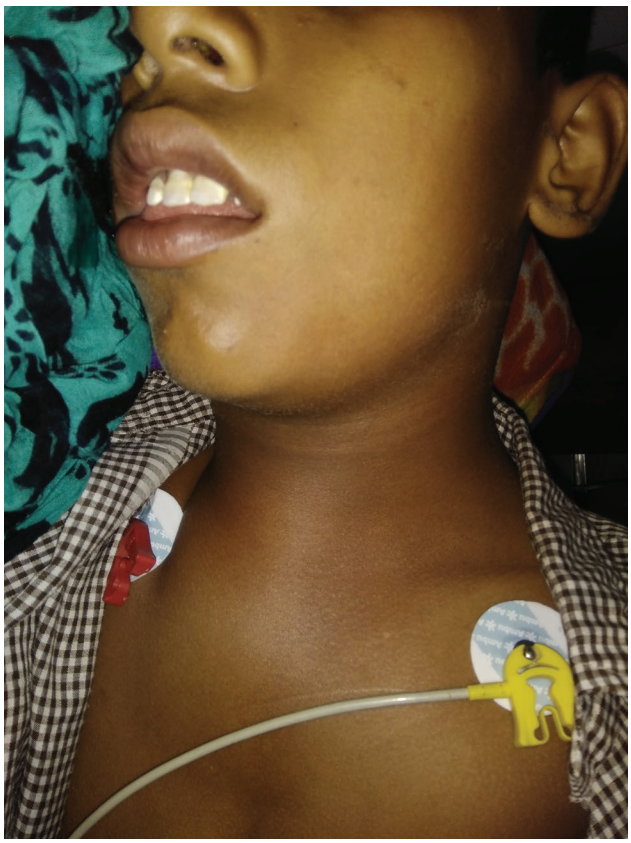


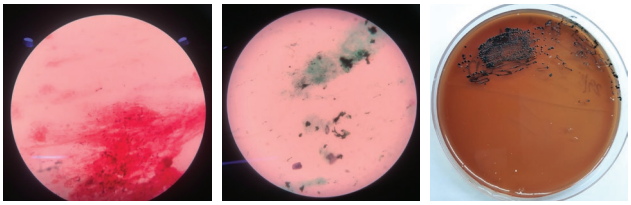
Figure 1B Bull neck like swelling with cervical lymphadenopathy



Discussion

Diphtheria is an acute infection predominantly localised to the throat and associated with multiple systemic manifestations caused by the toxin producing corynebacterium diphtheriae

Figure 2
A Gram stain showing gram positive club-shaped bacillus
B Albert stain showing the Chinese letter pattern of Corynebacterium diphtheriae
C Tellurite blood agar showing black colored colonies of Corynebacterium diphtheriae



A B C

and sometimes corynebacterium ulcerans with an incubation period of two to five days.[1] Its major virulence lies in the bacteria's ability to produce potent polypeptide exotoxin which inhibits protein synthesis.[2] The severity of infection is determined by the site of infection, the immunisation status of the patient, and the extent of systemic involvement. Mucosal bleeding, bull neck, airway obstruction requiring tracheostomy, larger pseudo-membrane size, cardiogenic shock, raised CK-MB, ventricular arrhythmias and acute kidney injury are poor prognostic markers.[3] The diagnosis of diphtheria remains mainly clinical; supported by careful visualisation of the pseudo membrane and microbiological demonstration of corynebacterium by albert stain, and confirmation by positive culture. However, microbiological confirmation is rare.[4] Staining is a highly sensitive investigation which can be rapidly obtained in a high quality microbiological laboratory.

Upper airway obstruction is the most common complication, but diphtheria can cause myocarditis, peripheral neuropathy, and acute kidney injury.[3] Airway obstruction is managed conservatively and may require tracheostomy in case of stridor. Intubation is difficult due to swelling with the risk of membrane dislodgement and airway obstruction.[5] Myocarditis and neuropathy are delayed complications and can be prevented by the early administration of diphtheria antitoxin.[3] Intravenous penicillin G or erythromycin (oral/intravenous) is the treatment of choice.[3] However, in the absence of intravenous penicillin G and erythromycin; treatment should be started with intravenous amoxycillin, clindamycin or azithromycin.[2]

In this era of vaccines, there has been an epidemiological shift of diphtheria affecting older age groups (>5 years) with a higher mortality.[6,7] This can be attributed to a reduction in vaccination coverage during childhood, waning adult immunity, lack of booster vaccine dosage, large scale population movements, disruptions in health services, and inadequate supplies of vaccine and antitoxin.[5] Mortality is higher in extremes of age, severe disease, unimmunised children and delayed administration of antitoxin.[3]

There has been re-emergence of diphtheria cases lately in India and Europe.[1,4,8] In India, coverage of the diphtheria

vaccination is less than 80%, leading to lesser herd immunity and a decrease in immunity in the school going children.[1] Also low awareness among caregivers about the utility of vaccination, vaccination schedules, and vaccine preventable diseases could be another contributory factor leading to poor immunisation.[7] In contrast to poor vaccination coverage being the main reason in India; refugee and migrant populations are the predominant cause of the re-emergence of diphtheria in Europe.[8] A rising number of incompletely vaccinated or unvaccinated individuals, an increase in lifespan, and growing vaccine scepticism in Europe are other reasons.[8]

Conclusion

Lately diphtheria has been seen in older age groups; a high index of suspicion is warranted. Early diagnosis with specific microbiological stains and early administration of diphtheria antitoxin leads to a favourable prognosis to a disease which can otherwise lead to significant morbidity or mortality. To prevent the spread of disease all persons who come into contact with a proven case of diphtheria should receive chemoprophylaxis with oral erythromycin (250-500 mg q6 hourly) and adequate vaccination coverage should be ensured in the society.[4]

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