Section: Pediatrics

Case Report

A CASE OF DIPHTHERIA IN AN UNDER IMMUNIZED CHILD IN CENTRAL INDIA

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Abstract

Diphtheria is an acute infectious disease caused by Corynebacterium diphtheriae, marked by toxin production. Despite the global decrease in incidence due to effective vaccination, cases still occur among children and adolescents in various states in India, even with the implementation of a comprehensive Universal Immunization Program. Here, we report a case of diphtheria in a 4-year-old male child from the Wardha district of Maharashtra, who missed getting the booster dose of the vaccine because of COVID-19 pandemic. This highlights the importance of raising awareness about the disease and emphasizes the crucial role of regular vaccination visits in preventing its resurgence.

INTRODUCTION

Diphtheria is a sudden-onset infectious illness resulting from Corynebacterium diphtheriae, a bacteria strain associated with respiratory and skin infections. Additionally, it can present as an asymptomatic carrier state. Common symptoms encompass cervical lymphadenopathy, a sore throat, fever, and a sense of malaise.[1] Diphtheria is a dangerous infectious disease in children, potentially leading to fatality, caused by Corynebacterium diphtheriae. It has the potential to create obstructive pseudomembranes in the upper respiratory tract.[2]
Cyanosis, dyspnea, and a swollen neck (referred to as "bull neck") are additional indicators of diphtheria, suggesting a potentially more severe case. Corynebacterium diphtheriae can release toxins, leading to complications arising from toxin-mediated tissue damage. These complications may include myocarditis, heart block, and respiratory failure, with a notably higher mortality rate observed in children.[3]
Despite the implementation of India's Universal Immunization Programme (UIP), providing three doses of the Diphtheria, Pertussis, and Tetanus (DPT) vaccine starting at 6 weeks of age, there have been reports of the reemergence or persistence of diphtheria in various Indian states over the last 5 to 10 years.[4-7]
Nevertheless, there are currently no published records of diphtheria in the Central Indian population of eastern Maharashtra in recent years. We now present a verified case of diphtheria from this region, underscoring the looming possibility of the infection's reemergence.

CASE PRESENTATION

A 4-year-old male child, previously in good health, sought care from a local primary care practitioner due to a two-day history of high-grade fever. The fever was intermittent, without chills and accompanied by a non-productive cough that exhibited no diurnal variation. The child also presented with mild neck swelling. The local practitioner-initiated treatment with a broad-spectrum antibiotic. However, as the high-grade fever persisted, the child was referred from the primary care setting to the district government hospital and subsequently to a tertiary care rural medical hospital in Central India for further evaluation. Upon arrival, a thorough history of the presenting illness was obtained, focusing on fever, cold, cough, and neck edema. There was no previous hospitalization for other emergencies, and no significant family history was reported. Antenatal, natal, and postnatal events were uneventful, and there were no indications of developmental delay. However, the child's immunization records indicates that vaccination administered only upto the age of 9 months and there were no subsequent booster shots or follow up. The diphtheria booster was not received due to the COVID-19 pandemic.
In terms of anthropometry examination, the child was classified as Grade II protein-energy malnutrition (PEM) with mild wasting and 1st-degree wasting.

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During the examination of vital parameters, the child presented with a fever of 103°F, a pulse rate of 110 beats per minute, a respiratory rate of 36 breaths per minute, and a blood oxygen saturation level (SpO2) of 97%. In the general physical examination, bilateral cervical lymphadenopathy, mouth breathing, and significant halitosis were observed. During the oral examination, the tonsils were found to be congested, partially covered with a grayish-white membrane, and notably tender.

Table 1

Parameters	Observed	Expected	Inference
Weight	11 Kg	16.3 Kg	< -3 SD
Height	94 Cm	103 Cm	-3 SD to -2 SD
Head Circumference	47 Cm	50.2 Cm	-3 SD to -2 SD

*Kg, Kilogram; Cm, Centimeter; SD, Standard Deviation
Mid Upper Arm Circumference (MUAC) – 14 Cms

The presence of a whitish membrane over the tonsils marked as A & B was observed.

Systemic examination revealed findings in the respiratory system, specifically bilateral rhonchi, and wheeze. In other systems, including cardiovascular, abdomen, and central nervous system, no abnormalities were detected, and tone, deep tendon, and plantar reflexes were intact.

Following the examination, a provisional diagnosis of Wheeze Associated Lower Respiratory Tract Infection (WALRI) with a consideration of diphtheria infection was made. The child was admitted to the Intensive Care Unit (ICU) for one day due to tachypnea and signs of dehydration. Intravenous broad-spectrum antibiotics were initiated. Routine blood investigations, peripheral smear, arterial blood gas (ABG) analysis, throat swab, and blood culture were sent for further evaluation.

The blood examinations revealed several findings: an indication of infection with a C-reactive protein (CRP) level of 22.09 mg/L, anemia with a hemoglobin (Hb) level of 10.9 gm%, leukocytosis with a white blood cell count (WBC) of 18.6 x 103/µL, and a peripheral smear indicating microcytic hypochromic red blood cells. Neutrophil leucocytosis was observed in the WBCs. The chest radiograph displayed pulmonary plethora. Arterial blood gas (ABG) analysis revealed respiratory acidosis with hyponatremia.

Results from the throat swab obtained in the microbiology lab showed Gram-positive cocci in pairs on gram stain, along with slender Gram-positive bacilli with clubbed ends morphologically resembling Corynebacterium diphtheriae. Albert stain revealed bacilli with metachromatic granules. Antimicrobial susceptibility testing (AST) was not performed due to the limitations of automated methods and demanding AST techniques.To confirm the virulence of strain, Department of microbiology did the toxin detection test by Elek's gel precipitation but could not succeed in that.Since the guinea pig was unavailable microbiology department could not perform the animal pathogenicity testing.The throat swab strains were sent to a WHO surveillance project for follow-up and record-keeping. The organism demonstrated sensitivity to several drugs, including Ciprofloxacin, Erythromycin, Gentamicin, Linezolid, Penicillin G, and Tetracycline.

Figure 1: Shows Growth on potassium tellurite medium after 48 hours of incubation. The colony morphology was 'frog's egg appearance.

The nasal swab analysis showed an absence of pus cells, with scattered Gram-positive cocci and Gram-negative bacilli observed. There was a moderate growth of Non A Non B Streptococcus species, and these organisms exhibited sensitivity to Trimethoprim, Penicillin G, and Erythromycin.

Additionally, the blood culture conducted using the BacT/Alert system showed no growth within the initial 48 hours of incubation. However, the culture bottle was continued for a total duration of 5 days, and still, no growth was detected.

Considering the array of symptoms, test results, and drug sensitivity, and after consultation with the Chief Pediatric Consultant, the decision was made to initiate treatment for the patient. The prescribed regimen included thrice-daily injections of Dexamethasone for three days and twice-daily injections of Azithromycin for a 14-day period. The patient's response to this treatment plan was closely monitored, revealing a significant improvement in symptoms. Tachypnea normalized, and there was a reduction in tonsillar swelling. Follow-up consultations were scheduled to assess the ongoing

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effectiveness of the treatment and monitor the patient's overall condition. During these follow-up visits, the patient consistently exhibited improvement and stability, indicating a positive response to the prescribed treatment regimen.

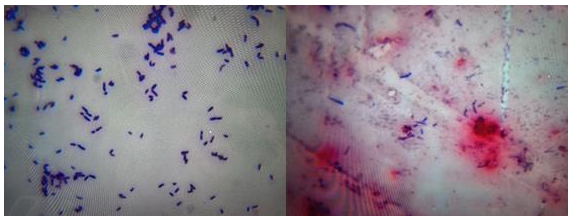

Figure 2: Gram Stain of Corynebacterium diphtheriae in Throat Swab Sample

This Gram stain image highlights the characteristic slender, Gram-positive bacilli with clubbed ends, indicative of Corynebacterium diphtheriae, as observed from the throat swab sample

DISCUSSION

Diphtheria can manifest as either an upper respiratory tract or cutaneous infection, with faucial diphtheria being the most common presentation.[8] During the primary assessment of a patient suspected of having diphtheria, a thorough examination of the airway is essential to ensure its integrity, given that the pseudomembrane associated with the infection can expand and potentially obstruct the airway. Strict adherence to contact and droplet precautions is crucial to prevent additional exposure, especially to vulnerable populations and individuals with incomplete immunity to the disease. Without proper treatment, patients are at risk of respiratory complications, as the tonsils, uvula, lymph nodes, and pseudomembrane may enlarge and obstruct the airway, posing danger to small children. Additionally, patients may experience cardiological, renal, and neurological symptoms as complications when systemic toxins from the bacteria are present.[9] The definitive test for diagnosing toxigenic C. diphtheriae is the detection of the lethal and potent exotoxin produced by the causative organism.[10] In this particular case, while we successfully identified C. diphtheriae, we were unable to conduct an analysis for toxin production. There is a growing number of case reports highlighting the potential resurgence of diphtheria in India, despite the implementation of multiple national immunization programs such as "Mission Indradhanush" (MI) and "Intensified Mission Indradhanush" (IMI), which represent significant efforts toward achieving a diphtheria-free nation. India adheres to the universal immunization program (UIP), recommending three doses, four weeks apart, followed by two booster doses. However, the average coverage for the diphtheria-tetanus-pertussis (DPT) vaccine stands at only 84%.[11] Diphtheria Antitoxin (DAT) was not easily accessible in our rural medical college. However, given the patient's significant improvement with no emergent complications in this case, the urgent requirement for DAT did not arise. The availability of DAT is not consistent across all health facilities, and its production is limited. The scarcity of DAT is attributed to a potential lack of awareness regarding the reemergence of the disease and a false sense of security regarding immunization coverage. Community-based screening of antibody titers against diphtheria has not been evaluated, further contributing to this unavailability.[12] Laboratory support for vaccine-preventable diseases plays a crucial role in enhancing outcomes and offering real-time information on the prevalence of diphtheria. The inclusion of requisitions for Diphtheria Antitoxin (DAT) alongside laboratory confirmation can facilitate a swift response.[13] Changes in the Antibiotic Susceptibility Testing (AST) breakpoints for penicillin-susceptible C. diphtheriae by the Clinical and Laboratory Standards Institute (CLSI) may cause concern for microbiologists and clinicians. Some strains previously classified as penicillin-susceptible could now fall into the penicillin intermediate category, marking a shift in the interpretation of susceptibility.[14] Furthermore, the absence of disc diffusion standards and the challenges associated with broth dilution methods restrict the availability of Antibiotic Susceptibility Testing (AST) for C. diphtheriae in laboratories throughout India. Consequently, it is recommended to consider the implementation of molecular tests that detect the rpoB and tox genes in endemic or high-risk areas. This approach aims to reduce the response time for Diphtheria Antitoxin (DAT) administration.[15] Swift diagnosis and treatment of diphtheria lead to a notable reduction in the recovery period from the disease. In our case, prompt diagnosis was facilitated by immediate reporting from our microbiology laboratory's throat swab, and the patient responded positively to the administered sensitive antibiotic. The median incubation period for diphtheria is 1.4 days. When antibiotics are used appropriately, the median time for an individual to no longer be infectious is 5.9 days, a significant improvement compared to the 18.5 days without antibiotic intervention.[16]

Establishing national surveillance is a crucial measure in comprehending the prevalence of diphtheria in India, with only limited regional studies conducted thus far. Additionally, there have been documented instances of penicillin-resistant C. diphtheriae, raising significant concerns due to the imperative need for laboratory intervention in such cases.[7,17]

India faces a substantial challenge, but with each documented case and policy briefing, there is potential for improved control of this lethal, vaccine-preventable ailment. This case underscores the importance of maintaining a heightened clinical suspicion for diphtheria and exercising vigilance in the laboratory when managing patients with membranous tonsillitis. Given that antibiotic therapy

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can eliminate the infection but not reverse the effects of the diphtheria toxin, ensuring the availability of diphtheria antitoxin in healthcare centers is imperative. Adequate immunization, with a focus on administering missed booster doses due to COVID-19 pandemic as seen in this case, coupled with the generation of high-quality data on DPT vaccination coverage in line with the Universal Immunization Program (UIP), will significantly contribute to the eradication of this dreaded infectious disease.

CONCLUSION

While diphtheria has been largely eliminated in the developed countries and highly preventable in developing countries such as India, healthcare professionals must remain vigilant regarding the potential for infection, considering symptoms like cervical lymphadenopathy and difficulty breathing in cases of respiratory diphtheria, alongside the patient's immunization history. Prompt treatment initiation is crucial, as it correlates with the duration of recovery. This case emphasizes the significance of administering booster doses during childhood immunizations to prevent vaccine-preventable diseases.

Reflection by Dr. Vaibhav Pradip Deshmukh:

"Diphtheria is a vaccine-preventable disease. Although we have successfully introduced new combination vaccines like the pentavalent vaccine, a portion of the pediatric population still misses out on immunization. Diagnosing and reporting such cases will help reinforce immunization coverage, especially during pandemics like COVID-19, as demonstrated by this case. Vaccination remains a simple and highly effective measure for preventing fatal diseases like diphtheria."

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