CASE REPORT

Adult Diphteria: Possible Transmission of *Corynebacterium diphtheriae* from Unvaccinated Child?

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ABSTRACT

A case of a toxigenic strain of *Corynebacterium diphtheriae* in an immunocompetent adult is presented, with the possibility of the adult acquiring the infection from her unvaccinated child. The abovementioned adult is a 29-year-old housewife who was previously immunised with diphtheria, tetanus, and pertussis (DTaP) vaccination in childhood, who presented fever, cough, sore throat, hoarseness of voice, odynophagia, and bilaterally enlarged tonsils. A throat swab confirmed the presence of toxigenic *Corynebacterium diphtheriae*. The patient was given 80,000 international units (IU) dose of diphtheria antitoxin (DAT) and treated with 2.4 million units (MU) QID intravenous penicillin and oral erythromycin 800 mg twice daily for two weeks. The patient responded well to the treatment and recovered with no cardiovascular or neurotoxicity.

Keywords: *Corynebacterium diphtheriae*; Diphtheria, Tetanus and Pertussis (DTaP); Elek Test; Diphtheria Antitoxin

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INTRODUCTION

Diphtheria is a vaccine-preventable illness due to *Corynebacterium diphtheriae*. Pharyngeal diphtheria is caused by the toxigenic strains of *Corynebacterium diphtheriae* (1). In the early 1950s, immunisation against diphtheria in industrialised countries became widespread, which reduced the occurrence of diphtheria. The reduced occurrence of toxigenic *Corynebacterium diphtheriae* led to reduced levels of natural boosting antibodies among adults. During the 1990s, diphtheria cases are on the rise in European countries, with many cases in adults (2). There is a low awareness of the benefits of immunisation in adults, despite the increase in vaccine-preventable diseases and more *Corynebacterium diphtheriae* infections that are seen among unvaccinated individuals compared with vaccinated individuals.

CASE REPORT

A 29-year-old woman presented cough and sore throat for four days, as well as hoarseness of voice and odynophagia. There was no history of travel or contact with sick people. She is married with five children aged between two and nine years old. Her youngest child had missed several vaccinations, including DTaP at 18 months due to logistics issues. Her children are all healthy and well.

During examination, the patient was conscious and alert. Her throat was injected. Intraoral examination revealed erythematous and boggy in the right peritonsillar region. Slough was seen in her right peritonsillar region, but there was no bleeding. Her uvula was oedematous, covered with slough, and deviated to the left. Grade 2 bilateral tonsils were seen, as shown in Figure 1. The patient was seen by a medical and an ear, nose, and throat (ENT) team, and was started on IV penicillin 2.4 MU stat and QID. Incision and drainage of the peritonsillar region were done, and the patient's throat swab was sent for culture.

The specimen was cultured on Blood Agar (BA), MacConkey Agar (MAC), and Potassium Tellurite Agar (PTA), which was incubated aerobically. The Gram stain of the throat swab sample showed numerous Gram-positive rods with Chinese character arrangement, as shown in Figure 2. The blood agar showed a mixed growth of three types of organisms: alpha lysis, beta lysis, and grey colonies. Figure 3 shows blackish colonies were observed on the PTA. The Gram stain of the black colonies showed Gram-positive rods, where the Albert stain was positive with metachromatic granules, as shown in Figure 4.

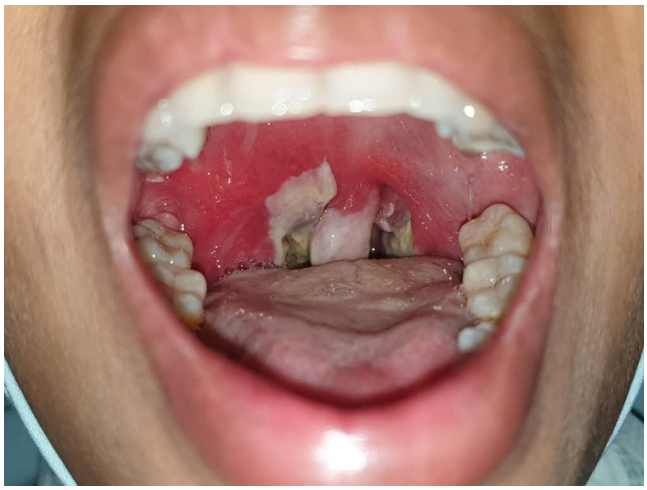

Figure 1: Findings of intraoral examination

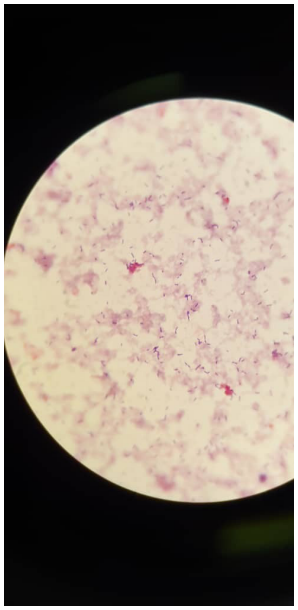

Figure 2: Gram Positive Rods with Chinese characters. Magnification x100

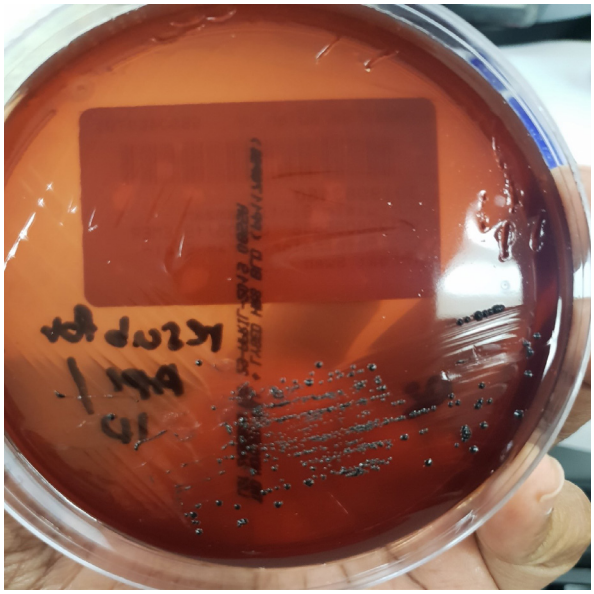

Figure 3: Black colonies on Potassium Tellurite Agar (PTA)

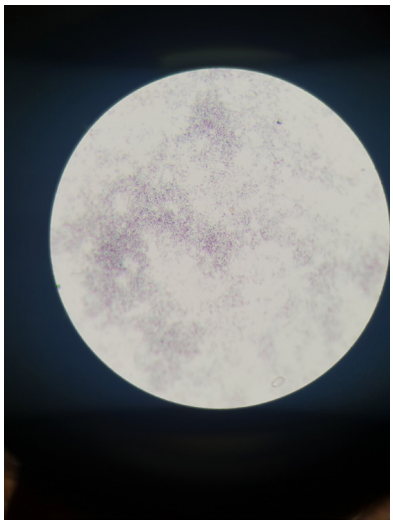

Figure 4: Gram Positive Rods with Positive Albert Stain. Magnification x100

The patient's renal profile, coagulation studies, liver function test, and troponin T were normal. The blood culture for aerobes and anaerobes revealed no growth after five days of incubation. The C-reactive protein level was elevated and the full blood count showed neutrophilic leukocytosis. Otherwise, haemoglobin and platelet counts were normal.

The patient continued to have a persistent spike in temperature despite being on IV penicillin for more than 48 hours. Hence, the managing team decided to discontinue penicillin and start her on 1.2 g Augmentin intravenous thrice daily. Diphtheria antitoxin was given (80,000 IU concentration), mixed with one pint of normal saline in a slow infusion over four hours.

After a few days of admission, patchy consolidations were seen in the middle and lower zones of the patient's right lung from her chest X-ray. She was prescribed with 500 mg of Azithromycin oral daily to cover atypical infections. After a week, the final throat swab culture confirmed *Corynebacterium diphtheriae*, which is sensitive to penicillin, gentamicin, vancomycin, and erythromycin.

Therefore, intravenous penicillin was restarted and parenteral Augmentin was discontinued. The bacteria isolate was subcultured on BA and sent for an Elek test to the Institute for Medical Research (IMR), Malaysia, which later reported as positive.

Subsequently, the throat swab culture was repeated twice and tested was negative for *Corynebacterium diphtheriae*. The patient became progressively better, with no cardio or neurotoxicity and a subsided fever. Thus, she was discharged after two weeks of admission and prescribed with 800 mg of erythromycin oral twice daily for 14 days. She was given an appointment for follow-up and catch-up vaccination for her children.

DISCUSSION

Diphtheria cases in Malaysia have fluctuated substantially in recent years, with cases increasing from 1998 to 2017, ending at 32 cases in 2017. In 2016, 31 confirmed cases of diphtheria were reported in Malaysia. Meanwhile, the World Data databases reported only 18 diphtheria cases in Malaysia in 2018. Although diphtheria cases in Malaysia have varied noticeably in recent years, the number increased from 1999 to 2018, ending at 18 in 2018. A molecular characterisation study using multilocus sequence typing (MLST) was done on several isolates, which revealed new clones of *Corynebacterium diphtheriae* in Malaysia since then. This case had probably led to the increasing numbers of diphtheria cases in 2017 (3).

One case of adult diphtheria was reported in Malaysia in 2016. The patient was a 28-year-old gentleman who had a previous history of a missed booster dose of diphtheria vaccine. He presented respiratory distress and was then admitted to the intensive care unit (ICU) and given diphtheria antitoxin and intravenous antibiotics. Toxigenic *Corynebacterium diphtheriae* was isolated from the patient's throat swab and patient was quarantined for seven days until two consecutive cultures showed negative results after the completion of his antibiotics. The patient was discharged well (4). There are several factors that lead to the emergence of this disease among adults; firstly, the reduced immunisation coverage among children due to anti-vaccine parents. Hence, the herd immunity is affected. The second reason is the waning immunity among adults, as the booster dose of diphtheria toxin only lasts for 10 years (5). Adults, especially those in the high-risk group, should be encouraged to receive a booster dose for combatting this disease. The third is the great entry of foreign workers, whose vaccination status against diphtheria is unknown. These foreign workers may have an increased the incidence of adult diphtheria cases in Malaysia. Another factor is the late recognition of the epidemic, as several laboratory investigations are still needed to confirm diphtheria cases. Both clinical suspicion and laboratory results must be proven to confirm the diagnosis.

In Malaysia, diphtheria vaccination is compulsory at two, three, and five months of life, and a booster dose must be administered at seven years old. The Centers of Disease Control and Prevention (CDC) recommended that an adult vaccination consists of one dose of Tdap, then a Td booster every 10 years. However, there may be an irregular supply of vaccines due to cost factor in certain areas, whereby the supply for adults may be hampered. Consequently, this leads to inadequate vaccination supply in the adult group, and eventually, an infection.

The complications of diphtheria in patients can be prevented via immunisation with a formalin-inactivated toxin ("toxoid"). Since antitoxin levels decline slowly over time after immunisation, tetanus and diphtheria toxoids [Td] booster doses should be administered at 10-year intervals to maintain protective antitoxin levels. People that have had close contact with those with incomplete or unclear immunisation status should promptly receive a dose of toxoids appropriate for their age. They must also complete the proper series of immunisations and receive prophylactic treatment with erythromycin or penicillin. According to the National Antibiotic Guideline 2014, the treatment for diphtheria is antitoxin and erythromycin or benzylpenicillin.
With proper antibiotic, antitoxin, and toxoid immunisation, the cases of adult diphtheria can be curbed.

In the case of the abovementioned patient, the source of infection is unknown. It could be that the infection had come from her youngest daughter, who was not fully vaccinated. The child could be colonised by *Corynebacterium diphtheriae*. Transmission may still occur in vaccinated individuals because these individuals may be colonised and possibly transmit the infection, as vaccination can only reduce the transmission of this disease by 28% (5). Therefore, it is also possible that the patient could have been infected by carriers vaccinated with diphtheria. As for this patient, her child was not fully vaccinated and did not have any clinical symptoms; hence, the risk of transmission is higher, as no precautionary measures had been taken.

Crowding could also contribute to increased diphtheria infections in adults. This patient lives with her husband and five children in a flat, which is considered a crowded living condition. A throat swab should also be done for the youngest daughter to confirm the colonisation of *Corynebacterium diphtheriae*. Due to the absence of a swab test, contact prophylaxis is a must for all the family members in contact. In this case, no contact prophylaxis was observed. The child was given a memo to visit a nearby government clinic solely for a catch-up vaccination schedule.

Other reasons for infection could be due to reduced antibody levels in adults, as the waning antibodies during adulthood could lead to infection due to this bacterium. Insufficient antibody protection leads to susceptibility to the infection. Although inadequate, the presence of an antibody against diphtheria and the immediate antitoxin administration prevented further worsening complications, such as cardiological and neurological complications and invasive diphtheria complications.
The patient should be kept under isolation and refrained from contact with others due to high risk of infection. Antibiotics and antitoxins should be administered adequately. The antibiotics reduce the duration of infection, while the antitoxins work to limit morbidity (5).

CONCLUSION

Clinical suspicion and accurate diagnosis of diphtheria cases are crucial for rapid implementation of control measures, especially in adults, due to the reemerging of the disease. The benefits of Tdap vaccine administration should be propagated for the protection of young adults and the elderly.

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