

Paediatric Patient with Diphtheria Presenting With Bullneck in Vaccinated Era: A Case Report and Review

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Abstract

Background: Diphtheria is a fatal infectious disease of the respiration tract. Although vaccination is available and already reach a high coverage, Indonesia still has reported cases of outbreaks and deaths on the past few years. Thus, it is important to understand that the disease hasn't completely disappeared in this vaccination era, and early treatment should be administered following prompt diagnosis to prevent disease progression and complications.

Case Presentation: A 10-year old boy was admitted to the ER due to dysphagia. Upon admission bull neck and pseudomembrane were found, and throat swab was performed. Upon positive findings, antibiotic and anti-diphtheria serum (ADS) was administered. Patient was hospitalized for 10 days, no shortness of breath and complications were observed during the admission.

Summary: Although vaccination is available and already reaches a high coverage, the disease hasn't completely disappeared in this vaccination era such as reported in this case. Early treatment should be administered following prompt diagnosis to prevent disease progression and complications.

Keywords: Diphtheria; Bullneck; Tonsilopharyngitis; Vaccination

1. Introduction

Diphtheria is a fatal infectious disease of the respiration tract. Although vaccination is available and already reach a high coverage, Indonesia still have reported cases of outbreaks and deaths on the past few years. Thus, it is important to understand that the disease hasn't completely disappeared in this vaccination era, and early treatment should be administered following prompt diagnosis to prevent disease progression and complications.

2. Case report

A 10-year-old boy was taken to the ER at Ngudi Waluyo Wlingi Hospital, Blitar, with the main symptoms of dysphagia for 4 days. It was accompanied by intermittent fever for 2 days. Patient also complaint of difficulty in swallowing food and drink because of the pain. Other symptoms were denied. Similar symptoms have never been occurred before. Patient had completed his vaccinations. His mother administered oral paracetamol, chlorphenamine maleate, and metamizole at home, but they didn't alleviate his symptoms.

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During pregnancy, his mother had routine antenatal care with a midwife. The pregnancy was normal without any history of bleeding, hypertension, diabetes mellitus, or infection. Patient was born pervaginam with no history of cyanosis or jaundice. Nutritional status were normal.

Patient was compos mentis but lethargic during the admission. Blood pressure was 115/87 mmHg, pulse rate 120 times per minute, respiratory rate 24 times per minute, and SpO₂ is 99%, weight 25 kg. He was also subfebrile, with the temperature of 36,8°C. There were no signs of cyanosis, icterus, and dyspnea. On examination of the pharynx it was shown to be erythematous, edematous tonsil, and white membrane was visible on the tonsil. Bull neck was also present. Cervical lymphadenopathy was present. Mallampati score was 3. Bilateral vesicular breath sounds were found upon thorax examination, there were no rhonchi or wheezing. Heart sound was regular with neither murmurs nor gallops. On abdominal examination, abdomen was soft, abdominal sound was present normally, tenderness was not present. Patient's extremities were warm and capillary refill time was <2 seconds with normal turgor.



Figure 1 Chest X-Ray on October 4th 2023 CXR showing patchy infiltrate on the bottom lobe of the right lung



Figure 2 Visible White Membrane on the Tonsils

Thorax x-ray was performed on the day of admission (October 4th 2023). On CXR, patchy infiltrate was found on the bottom lobe of the right lung. Complete laboratory results were also performed and are shown on **Table 1** below. Throat swab was performed and *Corynebacterium diphtheriae* with metachromatic granules were found with Neisser's staining.

Patient was diagnosed with diphtheria. Patient was hospitalized. No shortness of breath was present during the admission. In the ER, patient received IVFD therapy of normal saline + 5% dextrose 1500 cc/24 hours, accompanied by 20 mg Omeprazole and 250 mg Paracetamol injection. During the admission he received IVFD normal saline + 5%

dextrose 1500 cc/24 hours, 250 mg of intravenous Paracetamol four times a day, 20 mg of Omeprazole injection (0.5 – 1 mg/kgBW/24 hours), 60.000 IU of anti-diphtheria serum (ADS), and intramuscular injection of 700.000 IU (25.000 – 50.000 IU) penicillin procaine injection for 10 days. Oral medication included 10 mg of Cetirizine, 5 mL of Sucralfat given 3 times a day (40 – 80 mg/kgBW/24 hours), and multivitamin syrup. Patient received soft diet 3 x ½ portion with milk given 3 x 200 mL.

Table 1 Complete blood count and electrolyte serum.

Parameter	04/10/23	09/10/23	10/10/23	15/10/23	17/10/23	Unit	Normal Value
Complete Blood Count							
Hemoglobin	15.9		11.6	11.6	10.5	g/dL	12 – 17
Leukocyte	12.93		12.52	9.04	8.99	X10 ³ µL	4,5 – 11
Hematocrit	45.0		34.2	33.4	31.2	%	38 – 51
Thrombocytet	346		335	343	351	X10 ³ µL	150 – 450
Electrolyte Serum							
K+	4.16	4.16				mmol/L	3,4 – 5,3
Na+	133.6	135.1				mmol/L	135 – 150
Calcium ion	1.25	1.23				mmol/L	1,00 – 1,40
Chloride	99.9	99.2				mmol/L	98 – 107/ 96 – 114

3. Discussion

Diphtheria is known to be one of the most contagious infectious disease caused by *Corynebacterium* genus from the toxigenic strain, including *C. diphtheria* and rarely those related such as *C. ulcerans* and *C. pseudotuberculosis*. Human is the only known reservoir of this bacteria. Transmission happens through droplets from coughing, sneezing, vomiting, food utensils, or close contact through skin lesion. Even though the rate has been decreasing rapidly due to increasing vaccination coverage, diphtheria occurrence is still reported each year. On 2022, there were 9,802 cases reported throughout the world, 3,985 of which (1,9 per 1,000,000 total population) were reported from South East Asia region according to WHO [1].

Without prior immunization and treatment, this disease has a mortality rate reach to 50%, and decreased to 10% with treatment. Mortality rate for pediatrics bellow the age of 5 is 5 – 10%, and is 20% on adults above 40 years of age. Indonesia has been administering DPT immunization (diphtheria, pertussis, and Tetanus) since 1976 for three doses on babies age 2, 3, and 4 months as recommended by WHO. Then another DT immunization is administered in BIAS program (Bulan Imunisasi Anak Sekolah, or School Immunization Month) since 1984. To increase diphtheria prevention, a regiment of DPT-HB-Hib is also registered as routine immunization for 18 months old pediatrics since 2001, and since 2011, Td immunization (tetanus diphtheria) replaces TT immunization (tetanus toxoid) in BIAS immunization program. In Indonesia itself, even though vaccination coverage has reached 50 – 79% of the population, 1,026 cases of diphtheria were still reported in 2018 [2,3]. A study of 87 children with diphtheria in India shows that 54% of the patients were unimmunized and 21% of the patients were partially immunized. Majority of the cases also shown pediatrics in the age lower than 5 years, which probably is due to an inadequate coverage of vaccination. Only 19% of them are adequately immunized in the same study [4,5]. However, in Kalimantan, it was shown that children who had diphtheria mostly has been immunized against DPT, similar to the patient in this case [6].

Aside from vaccination rate other risk factors might affect pediatrics' vulnerability to diphtheria such as nutritional status. Nutritional and immune deficiencies reduce body's response to vaccines, as shown in a study of diphtheria in Situbondo [7]. Mobility of respondents (travel history to area with high cases of diphtheria) is also shown to be related to incidence rate [6]. However, within this case report, patient doesn't have any history of travel and has a normal nutrition status.

Diphtheria sign and symptoms might be started with lethargy, dysphagia, and flu, similar to other lower respiratory infections. These symptoms will then develop to hoarseness, cough, and children might also drool. On severe cases

stridor and shortness of breath may be present with or without fever. A study shows that 98% of the patient have fever, 90% with dysphagia, 63% with cough, 58% presented with throat pain, 35% with difficulty in breathing, 34% with bull neck, 20% with hoarseness of voice, 6% with bleeding, and 2% with seizures [4]. Within this case is a 10-year-old boy which is presented with dysphagia and complaint of throat pain. Shortness of breath is not found in this case; however, bull-neck was already present during the admission.

Diagnosis can be made through clinical and laboratory investigation. Clinical diagnosis is made through clinical presentation especially pharyngitis, tonsillitis, laryngitis, tracheitis or some form of combinations of the above, might be accompanied by sub febrile fever and grayish white pseudo-membrane which might bleed when scratched or manipulated in some sort of way. The membrane might be initially white and glossy, however it might develop into green or black patchy necrosis, the extension of the membrane is also correlated with the disease severity. Clinical warning signs includes stridor, fast respiratory rate, chest in-drawing, restlessness or lethargy, bull neck, delayed capillary refill, fast heart rate and cold extremities, along with central cyanosis [2,8]. The suspicion of diphtheria in this case rises from the existence of pseudo-membrane which bleed upon examination in the emergency department and the presence of a clinical warning sign, bullneck.

Laboratory diagnosis is performed by diphtheria bacteria culture from throat swab specimen. Swabbing can be obtained through the edges of mucosal lesions, which then is placed in Amies or Stuart media in ice packs, or dry swabs in silica gel sachets. Then it should be followed by inoculation onto tellurite-containing media (for example Tinsdale media) and blood agar. The modified Elek immunoprecipitation test can be used to detect toxins in suspected colonies; this standard assay takes 24 to 48 hours to complete. The etiologic diagnosis is confirmed by a positive culture with *C. diphtheriae*, the toxin-producing bacteria [9].

Diphtheria medication should be performed as soon as the symptoms were visible to avoid complication and mortality. Medication regiments includes antibiotic to kill the bacteria and anti-diphtheria serum (ADS) to neutralize the exotoxin from diphtheria bacteria. Below (Table 2) is the dose needed for each type of diphtheria. ADS dose do not differ between pediatrics and adults [2].

Table 2 ADS Dose for Each Type of Diphtheria

Diphtheria Type	ADS dose (IU)	Route
Tonsil diphtheria	40.000	Intravenous
Pharyngeal diphtheria	40.000	Intravenous
Laryngeal diphtheria	40.000	Intravenous
Combination of upper location, without the involvement of nose/ nasal	80.000	Intravenous
Diphtheria + comorbidities and/ or bullneck is found	80.000 – 100.000	Intravenous
Late administration of medication (>72 hours), wherever is the location of the infection	80.000 – 100.000	Intravenous

Antibiotic treatment should also be performed for probable and confirmed cases as soon as possible. Intravenous or intramuscular preparation can be administered for patients whom cannot swallow or are critically ill. There are three options for severely ill patients according to WHO Operational Protocol for Clinical Management of Diphtheria: Intravenous Procaine benzyl penicillin (Penicillin G) IM (50 mg/kg once daily with maximum dose of 1,2 grams a day) for 14 days; Intramuscular or slow intravenous Aqueous benzyl penicillin (penicillin G) 100,000 units/kg/day administered in divided dose of 25.000 IU/kg for every 6 hours with 4 MIU or 2,4 grams per day as the maximum dose; and intravenous Erythromycin 40-50 mg/kg/day (maximum 2 mg/day) in divided dose, 10-15 mg/kg every 6 hours, maximum 500 mg per dose for 14 days [9].

Once patient's condition improves clinically, a stepdown to oral antimicrobials can be performed. Oral therapy can be used for less sick patients who is able to swallow. Oral antibiotics of choices includes: oral Phenoxymethylpenicilin V 50 mg/kg/day in divided dose 10-15 mg/kg/dose administered every 6 hours, maximum 500 mg per dose for 14 days; Oral Erythromycin 40-50 mg/kg/day (maximum 2 mg/day) in divided dose, 10-15 mg/kg every 6 hours, maximum 500 mg per dose for 14 days; and oral Azythromycin 10-12 mg/kg once daily, maximum 500 mg/day for 14 days (however there is still not enough data to support the exact duration of the required azithromycin) [9].

Follow up is needed to evaluate possible complications including myocarditis, neurological paralysis (palatal palsy, pharyngeal palsy, motor weakness, etc), or motor weakness [10]. During follow up to the outpatient department, patient have no complaints and complications were not found.

4. Conclusion

Although vaccination is available and already reach a high coverage, the disease hasn't completely disappeared in this vaccination era such as reported in this case. Early treatment should be administered following prompt diagnosis to prevent disease progression and complications.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from individual included in this study.

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