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Diphtheria Tonsil with Bullneck and Allergy to Anti-Diphtheria Serum

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ABSTRACT

Diphtheria is an acute, highly contagious, vaccine-preventable disease that mainly affects children. Anti-diphtheria serum (ADS) should be administered as soon as a case is declared a probable case based on clinical diagnosis without waiting for laboratory diagnosis. This case report aims to further explore the diagnosis of diphtheria and the management of allergic anti-diphtheria serum given to children. In this case report we discuss a 14-year-old male patient who was diagnosed with diphtheria of the tonsils with bullneck with the main complaints of fever, painful swallowing, and pseudomembranes on the left and right tonsils of greyish-white colour, difficult to remove and diffuse swelling of the neck. Patient's lab work showed leucocytosis and gram-stained morphology suitable for Corynebacterium diphteriae which then followed by administering antibiotics and ADS. Electrocardiography was performed periodically to observe cardiac complication. Soon after ADS was administered, the child complained of coughing and itching of the body and limbs, and extensive urticaria was found on the body and extremities. Anti-Diphtheria Serum administration was then continued with desentisation technique (besredka) until the complete ADS dose was given and there were no complaints in the patient. The child was treated for 14 days and then controlled at the outpatient clinic.

Keywords: *diphtheria; allergy; anti diphtheria serum; bullneck*

INTRODUCTION

Diphtheria is a highly contagious acute disease caused by Corynebacterium diphtheriae (C. diphtheriae) that can produce exotoxin when infected by Corynephage carrying the diphtheria toxin (dtx) gene. The disease is characterised by the formation of pseudomembranes that generally form in the tonsil area, pharynx, larynx, and can even extend to the trachea and bronchi. Pseudomembranes can cause oedema in the underlying mucosal tissue, which can lead to airway obstruction and death in patients with respiratory diphtheria. In addition, severe systemic effects caused by exotoxins from diphtheria can cause myocarditis, neuritis, and kidney damage.[1,2]
From 2000 to 2015, diphtheria cases in the Asian region were the highest in the world. Indonesia is the country with the second highest incidence of diphtheria compared to other countries in the Asian region, namely India. The number of diphtheria cases reported in Indonesia from 2011-2015 was 3,203 cases, while India still has the highest number of diphtheria cases with 18,350 cases.[3,4] Of all the diphtheria cases, 51% of them did not get vaccinated.[5]
Late diagnosis and treatment can increase the mortality rate up to 20 times higher than the normal mortality rate.[6] The overall case fatality rate of diphtheria is 5-10%, with higher mortality rates (up to 20%) in the under-five age group and the elderly over 40 years of age.[1,7,8] Factors influencing the

high mortality rate of diphtheria patients include: inadequate immunisation, socio-economic conditions, population density, delayed treatment, and absence or delayed administration of antitoxin.[9,10] And immunisation is the most significant and most influential factor.[8]

This case report aims to further explore the diagnosis of diphtheria and the management of allergic diphtheria serum given to children.

CASE PRESENTATION

A boy, aged 14 years, with chief complaint of fever since 2 days before admission. Swallowing pain and decreased appetite since 1 day ago. Usually the child eats 2-3 times a day, half an adult portion. During the illness, the child only wanted to eat 1-2 times a day and only consumed 2-3 tablespoons each time. Swelling of the neck was noticed by the parents since 1 day ago. There is no cough, shortness of breath, runny nose, nausea and vomiting. Urination of normal amount and frequency. Bowel movements of normal colour and consistency. No complaints of chest pain and chest palpitations. There was no history of allergy in the patient. The child is fully immunised with no booster. The child eats 2-3 times/day, usual amount with less varied protein menu.

The patient appeared moderately ill, fully conscious, blood pressure 100/70 mmHg, pulse 96 x/min, respiratory rate 18 x/min, body temperature 36.5oC. The patient's body weight (BW) was 34 kg and the body height (BH) was 155 cm. BW/Age 59%, BH/Age 92%, BW/BH 75.5%, with the impression of undernutrition. The skin was warm. The head was round, symmetrical, head circumference 53 cm, normocephalic according to Nellhaus standard. There was diffuse swelling on both sides of the neck, no pain, no redness. Dark hair, not prone to shedding. Conjunctiva not anemic. Ears are not abnormal. Nose no abnormality. Tonsils T2-T2 hyperemic, crypts dilated, detritus present, pseudomembranes on the left and right tonsils greyish white, difficult to lift. Normal chest shape, symmetrical chest movement, no retraction, vesicular breath sounds. Heart rhythm is regular, no murmur. Abdomen not distended, supple, hepatic and splenic not palpable, tympanic percussion, bowel sound was normal. Warm Acral limbs, good capillary refilling time.

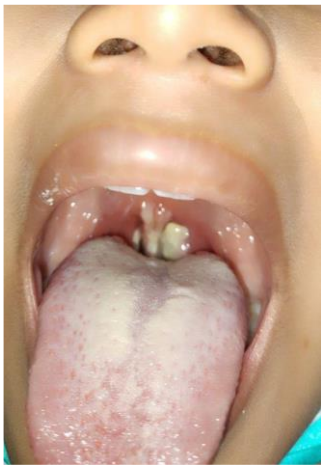

Figure 1: Pseudomembranes on the patient's tonsils

Laboratory examination showed haemoglobin 14.6 g/dL, leucocytes 11,370/mm3, erythrocytes 5,460,000/mm3, haematocrit 44%, platelets 183,000/mm3, reticulocytes 1.2% type count 0/0/3/82/14/1, with an impression of leucocytosis with neutrophilia shift to the right. Based on the results of history, physical examination and support, the patient was diagnosed with Tonsillar Diphtheria with Bullneck and Undernourished. The patient underwent further examination of the throat swab with samples taken from the tissue under or around the pseudomembrane. Gram stain and culture of the throat swab samples on Amies media were performed. Electrocardiogram (ECG) results showed sinus rhythm.

The child was given 6 x 300 cc liquid diet, Penicillin procaine 1 x 1,500,000 IU IM, ADS 1 x 80,000 IU IV, Paracetamol 3 x 350 mg per oral and periodic ECG checks were performed. The patient had a skin test before ADS administration, with the results of no itching, no redness, and no induration (negative). When ADS administration was started, the patient complained of itching all over the body and coughing, without

shortness of breath. Previously, the patient had no history of drug allergy. Vital signs were within normal limits. Skin urticaria was found on the body and extremities. The patient with suspected ADS allergy was given Dexamethason and Diphenhydramine IV. Furthermore, ADS administration was carried out by Besredka with prior informed consent. During the administration of ADS by besredka until completion, no signs of allergy were found again in the patient.

Procain penicillin was administered for 14 days, with neck swelling gradually reducing, and pseudomembranes disappearing by the 7th day of treatment. During regular monitoring, ECG showed sinus rhythm. Microbiological examination (Gram stain of throat swab specimen): Gram (+) rod bacteria were found arranged as palisades with granules at both ends of the cells. The morphology is suitable for C. diphteriae. Results of Culture Examination with amies transport media: negative C. diphteriae. Results of Throat Swab Examination on day 14 before the patient was discharged were No bacteria matching the morphology of C. diphtheria were found.

DISCUSSION

The diagnosis of diphtheria tonsil in this patient was based on history taking, physical examination, and laboratory examination. Based on anamnesis, the patient had complaints of fever for 2 days ago, not high, continuous, no sweating, no chills. Swallowing pain for 1 day ago, initially the throat looked red and appeared white patches that gradually increased in both tonsils. There was no cough, runny nose and shortness of breath. On physical examination, the child was found to have a temperature of 37.5ºC, pseudomembranes on both tonsils, and diffuse swelling of the neck. These findings are in accordance with the literature, where during the incubation period patients rarely have a high fever that exceeds 38.9º C. In addition, the clinical findings in this patient are also in accordance with the results of a study in Surabaya which found that 99.3% of diphtheria patients had fever and 62.2% had swallowing pain. The study also found that pseudomembranes were found on both sides of the tonsils in 84.4% of patients.[11] Diffuse swelling of the patient's neck is also known as bullneck, which is an oedema of the submandibular area and anterior coli followed by diffuse lymphadenopathy. The finding of a bullneck indicates that the diphtheria case is severe.[2,7,11]

The Child received complete basic immunisation, but never received a booster. Poor immunisation status (never received basic immunisation or booster) is the most important factor that significantly affects the incidence, spread and mortality rate of diphtheria cases.[8–10,12] Based on research conducted by Lestari KS et al, incomplete immunisation status has a risk of 1.142 times greater for diphtheria than complete immunisation status.[12] Meanwhile, based on other literature, it was stated that children who did not receive Diphtheria, Pertusis and Tetanus (DPT) vaccine had a 5-fold higher risk of diphtheria infection compared to children who received DPT immunisation.[13] Giving three doses of DPT vaccine in infancy can provide immunity to diphtheria for several years.[10,14,15] However, booster immunisation is still important, as the duration of immunity after primary diphtheria immunisation can vary significantly from one individual to another. Booster immunisation is needed so that a person can maintain their immunity to diphtheria for up to a lifetime. Based on the literature, booster immunisation every 10 years is recommended to avoid diphtheria.[16] In Indonesia, a fourth dose of DPT vaccine at the end of the second year of life and a dose of Diphtheria and Tetanus (DT) vaccine at the start of school are the most commonly chosen options.[14,15] The absence of diphtheria booster immunisation in this patient makes the patient vulnerable to C. diphtheriae infection. This is in accordance with the results of Fitriansyah A's study, which found that the majority of diphtheria patients did not receive repeat

immunisation, either DPT-Hepatitis B-Haemophilus Influenzae type B (Hib) booster vaccine, DT, or Tetanus diphtheria (Td). Based on this study, it is concluded that the completeness of 7 doses of diphtheria immunisation plays an important role in the incidence of diphtheria, especially in repeat diphtheria immunisation.[13] Furthermore, patients are advised to get booster immunisation 1 week later.

The physical examination also showed an impression of malnutrition. Poor nutritional status is one of the factors that affect the incidence of diphtheria.[1,9] Based on research conducted in Sidoarjo in 2012, it was found that children with poor nutrition had a 1.787 times greater risk of diphtheria than children with good nutritional status.[12]

The throat showed hyperemic T2-T2 tonsils, non-dilated crypts, detritus present, grey-white pseudomembranes in both tonsils that were difficult to remove. This is in accordance with the clinical manifestations of diphtheria tonsils.[1,2]

The results of microbiological examination by Gram stain found Gram (+) rod bacteria arranged like palisades with granules at both ends of the cells, where the morphology is suitable for C. diphteriae. Impression: C. diphteriae (+)/positive. This result is in accordance with the literature, where on Gram staining, germs can appear in palisade arrays, L or V shapes, or in clusters with Chinese letter-like formations.[7,17]

Meanwhile, culture examination of this patient's throat swab specimen showed negative results. Based on the literature, culture examination can also give negative results (in 40% of cases) or show the presence of other organisms that develop in the culture medium.[18] Research conducted by Dhinata KS et al, also found that there were only 23.9% of diphtheria patients who showed positive culture results.[8] In addition, another study by Puspitasari D et al, also found that there were only 22.9% of diphtheria patients who showed positive culture results.[11] These negative culture results can be caused by several factors, one of which is due to indirect sample delivery (within 2 hours) and samples stored without a special container.

The aim of treating diphtheria patients is to inactivate toxins that have not entered the cells as soon as possible, prevent and strive for minimal complications, eliminate C. diphteriae to prevent transmission and treat co-infections and diphtheria complications. Management of diphtheria patients includes the administration of ADS, antibiotics, and corticosteroids in certain conditions.[2] Antibiotics are given not as a substitute for antitoxins but to kill bacteria, stop toxin production, and to prevent transmission.[2,19] Procaine penicillin 50,000-100,000 IU/kgBW/day (divided dose every 12 hours IM) for 10 days, if there is a history of penicillin hypersensitivity, erythromycin 40 mg/kgBB/day (divided dose every 6 hours PO or IV, maximum 2 grams per day).[2,20]

Management of patients with ADS should be administered immediately after throat swab sampling without waiting for results from the microbiology laboratory and only based on clinical diagnosis, considering that antitoxins can only neutralise freely circulating toxins before infiltration into cells. Delaying treatment will increase the mortality rate up to 20 times higher than the normal mortality rate.[1,7,10] ADS is given 80,000 IU to neutralise the toxin circulating in the body so that it does not damage other organs, the dose given in diphtheria with bullneck is 80,000-120,000 IU. Before starting the administration of ADS, a skin test was performed with the results of no itching, no redness, and no induration. However, urticaria appeared after starting intravenous administration of ADS in this patient. Therefore, ADS administration was continued by desensitisation (besredka). The desensitisation process can usually be done in two ways, intravenously and non-intravenously, as shown in the table 1 and 2.

Table 1. Desensitised administration of ADS via Intravenous (IV) Route[19,21]

Dose Number*	Dilution of DAT in Normal Saline	Amount of Injection (cc)
1	1:1,000**	0.1
2	1:1,000	0.3
3	1:1,000	0.6
4	1:100**	0.1
5	1:100	0.3
6	1:100	0.6
7	1:10**	0.1
8	1:10	0.3
9	1:10	0.6
10	undiluted	0.1
11	undiluted	0.2
12	undiluted	0.6
13	undiluted	1.0

* Administer at 15 minute intervals.

**1 ml (antitoxin) + 9.0 ml of saline = 1:10 dilution
1 ml (1:10 dilution) + 9.0 ml of saline = 1:100 dilution
0.1 ml (1:10 dilution) + 9.9 ml saline = 1:1000 dilution
[1 ml (1:100 dilution) + 9 ml saline = 1:1000 dilution]

Table 2. Desensitised ADS Administration via Intradermal, Subcutaneous, or Intramuscular Routes[19,21]

Dose Number*	Route of Administration	Dilution of DAT in Normal Saline	Amount of Injection (cc)
1	ID	1:1,000**	0.1
2	ID	1:1,000	0.3
3	SC	1:1,000	0.6
4	SC	1:100**	0.1
5	SC	1:100	0.3
6	SC	1:100	0.6
7	SC	1:10**	0.1
8	SC	1:10	0.3
9	SC	1:10	0.6
10	SC	undiluted	0.1
11	SC	undiluted	0.2
12	IM	undiluted	0.6
13	IM	undiluted	1.0

*Administer at 15-minute intervals.

**1 ml (antitoxin) + 9.0 ml of saline = 1:10 dilution
1 ml (1:10 dilution) + 9.0 ml of saline = 1:100 dilution
0.2 ml (1:10 dilution) + 9.9 ml saline = 1:1000 dilution
[1 ml (1:100 dilution) + 9 ml saline = 1:1000 dilution]

Corticosteroids are recommended in diphtheria cases with symptoms of upper airway obstruction (with or without bullneck); and if there is a complication of myocarditis.[2,20] Prednisone 2 mg/kgBW/day for 2 weeks and then reduce the dose gradually.[2]

The negative results obtained from the previous skin test contradict the urticaria experienced by the patient after ADS was started intravenously. This is in accordance with the literature which states that a negative skin test result is not an absolute guarantee that the patient will not experience a sensitivity reaction. Thus, ADS should still be administered with caution even in individuals with negative skin test results. After ADS administration is complete, the patient should also be closely monitored for at least 30 minutes for the presence or absence of anaphylaxis symptoms.[19]

The patient was also given procaine penicillin 1,500,000 IU for 14 days. Based on the literature, procaine penicillin is given at a dose of 50,000-100,000 IU/kgBW/day for 10 days.[2,20] Another source states that procaine penicillin G can be given intramuscularly for 14 days.[6,7,19,22] The administration of Penicillin Procaine aims to kill C. diphtheriae so that it does not produce toxins and prevent the spread of organisms to uninfected contacts. This patient was given procaine penicillin for 14 days, after which a throat swab staining test was performed once with negative results. The child was then discharged.

The most common and severe complication of diphtheria is myocarditis. Myocarditis usually occurs within 10-14 days, with neural manifestations generally occurring after 3-7 weeks. Surveillance of cardiac disorders is through serial ECG examinations on days 1, 3, 7, and 14 which are assessed for arrhythmia, sinus tachycardia, ST-T wave changes and block. In this case, no abnormalities were found on the ECG examination. The patient was also advised to have regular weekly controls for 4 to 6 weeks after discharge to detect any possible complications of myocarditis as early as possible.[10,23]

The prognosis of diphtheria after the discovery of ADS and antibiotics is better than before. However, in Indonesia, in areas that have not been touched by immunisation, severe diphtheria cases with poor prognosis can still be found.[2] Late diagnosis and treatment can increase the mortality rate up to 20 times higher than the normal mortality rate.[10] According to Krugman, sudden death in diphtheria cases can be caused by (1) sudden airway obstruction caused by the detachment of diphtheria membranes, (2) the presence of myocarditis and heart failure, (3) diaphragm paralysis as a result of neuritis of the nephric nerve. Children who have had myocarditis or neuritis as a complication of diphtheria will generally recover completely without sequelae; however, persistent heart defects have been reported.[2] However, other studies suggest that the incidence of diphtheria myocarditis associated with nasopharyngeal diphtheria is 10-20% with a mortality rate of 50-60%. Approximately 50% of diphtheria myocarditis patients have severe conduction problems associated with fatal outcomes.[10]

CONCLUSION

Diphtheria is an acute, highly contagious, vaccine-preventable disease that mainly affects children. Late diagnosis and treatment can increase the mortality. Immunisation is the most significant and most influential factor in diphtheria case. Management of diphtheria patients includes the administration of ADS, antibiotics, and corticosteroids in certain conditions. Even if the patient is allergic to ADS, we can still give it through the Besredka method.

Declaration by Authors

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