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CASE REPORT

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Diphtheria in a 13 year old adolescent girl: Management challenges

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Abstract: ***Background:*** Diphtheria is an acute toxic infection which is associated with a high morbidity and mortality and can pose management challenges especially in the absence of proper diagnostic and therapeutic facilities.
Case report: A.S. was a 13 year old girl who presented with fever of five days duration, dysphagia and neck swelling of 4 days duration and sore throat and hoarse voice of 3days duration. Her illness started a day after returning from a 4-day holiday youth camp. She received only oral polio vaccine immunization in childhood. Significant physical examination findings included a swollen neck, a greyish membrane covering the soft palate and uvula with haemorrhagic spots. The pharynx, anterior nares and the nasal turbinates were inflamed and erythematous.
A working diagnosis of respiratory diphtheria was made. Throat swab microscopy showed club shaped Gram positive baccilli. Appropriate culture medium for C. diphtheria was not available.
She received intravenous crystalline penicillin and metronidazole and lateroral erythromycin in an isolated ward. On the 6th day of admission she developed cardiac and neurologic complications– bradycardia (PR=40bpm), hypotension (BP=70/40mmHg), drooling of saliva and paraparesis. Electrocardiography confirmed a complete heart block. She died on the 11th day of admission while efforts were being made to raise funds for a cardiac pace maker.
Conclusion: Management of this vaccine preventable disease requires a high index of suspicion and diphtheria antitoxin should be made readily available.

Introduction

Diphtheria is an acute toxic infection caused by *Corynebacterium* species, typically *Corynebacterium diphtheriae* and rarely toxigenic strains of *Corynebacterium ulcerans*[1,2,3]. The classic disease affects the upper respiratory tract with the formation of an adherent gray-white pseudomembrane in the infected place followed by systemic symptoms caused by elaboration of an exotoxin produced by the bacillus[1,4]. The disease progresses rapidly with a case fatality rate as high as >20% in acute disease states if there is no sufficient diagnostic procedure and therapy option[1]. Therefore it requires a high index of suspicion. The most dominant factor causing death is myocarditis and diphtheria myocarditis incidences related to nasopharyngeal diphtheria is 10-20% with a death rate as high as 50-60%[5].

The emergence of immunization program changed the epidemiology of the disease and reduced its prevalence worldwide. In the Western world, diphtheria is near eradication level in most countries[6]. Also, in many African countries with a high diphtheria immunization coverage rate, the incidence of diphtheria has decreased by >95% across the region in the past 10 years[6]. In Nigeria also, reported cases of diphtheria has been declining even with just low to moderate coverage with DPT3.[7] Accordingly, there has been no reported case from Our centre in the past 10 years.

However, recently there are pockets of sporadic cases being reported in Nigeria. Sadoh et al[8] reported nine cases of diphtheria in children who were aged between 11months and 10years in the University of Benin Teaching Hospital (UBTH) between 2008 and 2010, while Oyeyemi et al[9] reported ten cases of diphtheria in children aged 3-13years in the Federal Medical Centre Katsina on two clusters of diphtheria outbreak between 2009 and 2010 involving three contiguous local government area in Katsina State. In this case we report a 13 year old girl who died from probable diphtheria myocarditis and the diagnostic and management challenges encountered.

Case Report

AS was a 13 year old girl who presented at the Children Out Patient Clinic of the University of Port Harcourt

Teaching Hospital with complaints of fever of five days duration, dysphagia and neck swelling of four days duration, sore throat and hoarse voice of three days duration. Her illness started a day after returning from a four-day holiday youth camp. She received amoxicillin capsules before presentation. She had never been immunized except for Oral Polio Vaccines which she received on National Immunization Days (NIDs).

Physical examination revealed a lethargic child in painful distress with a bull neck, hoarse voice, and drooling saliva. Throat inspection showed a thick greyish membrane covering most part of the soft palate and hanging down over the uvula with areas of haemorrhagic spots. The pharynx was erythematous, the anterior nares and the nasal turbinates were inflamed and plugged with blood crusts. (Fig 1) She had a good volume and regular pulse with a rate of 82 beats per minute, a blood pressure of 100/70mmhg and normal heart sounds. She had no neurological deficits.

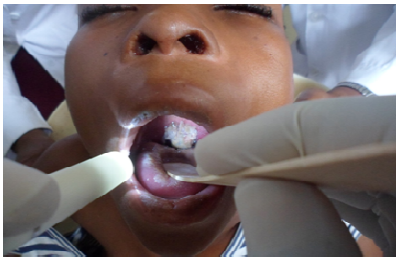

Fig 1: Greyish adherent membrane in the soft palate and uvula, and the haemorrhagic exudates in the nostrils

A diagnosis of probable respiratory diphtheria was made. Microscopy of the throat swab and swab of the anterior nares showed club shaped Gram positive rods. Culture using Tellurite salt agar could not be done as this was not available. She was reviewed by the Otorhinolaryngologist while the State Disease Surveillance and Notification (DSN) unit was notified.

She was nursed in an isolation room, received intravenous crystalline penicillin at 0.4MU/kg/day in 4 divided doses, intravenous Metronidazole at 8mg/kg/dose every 8hours, intra venous fluid, oral toileting with saline water and bed rest. All close contacts were counseled especially on the need to immunize all under-5 children whose last DPT dose was more than 12 months ago and were placed on Tablets Erythromycin – 500mg qds for two weeks.

By the 6th day of admission, she developed cardiovascular complications – bradycardia (PR=40bpm) and hypotension (BP=70/40Hg). She received 20mls/kg of normal saline over 30minutes, intravenous hydrocortisone and Atropine with no apparent clinical improvement. Her condition deteriorated and by the 7th day of admission her pulse rate dropped further down to 24bpm and the power in the lower limbs was reduced to grade two. A diagnosis of Diphtheria Toxic cardiomyopathy (Heart Block) and neuropathy (Para paresis) was made. An electrocardiogram confirmed a Complete Heart Block. (Fig 2) Parents were counselled on the need for an urgent pacemaker. Efforts were ongoing to raise fund for a pacemaker before she died on the 11th day of admission.

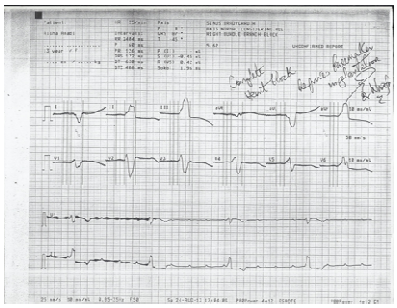

Fig 2: ECG tracing of AS showing complete dissociation of the p wave and QRS complex which are widened (172ms), idioventricular rhythm with rate of 25/mm and a giant T wave inversion

Discussion

Diphtheria is an acute toxic infection caused by *Corynebacterium diphtheriae*, an aerobic, non-encapsulated, Gram positive bacillus.[1] *C. diphtheriae* is an exclusive inhabitant of human mucous membranes and skin. It spreads primarily by airborne respiratory droplets, direct contact with respiratory secretions or exudates from infected skin lesion. Incidence peaks during the dry season with majority of the cases occurring in unimmunized children below 15 years of age. Diphtheria occurs by entry of C. diphtheriae into the nose or mouth. After a 2-4 day incubation period, toxins are secreted which leads to toxin-mediated tissue necrosis. This coupled with local inflammatory response produces patchy exudates which later forms fibrinous exudates and a tough adherent membrane.[4] Respiratory embarrassment may follow extension of disease into larynx or tracheobronchial tree.

Our patient never had DPT vaccine and hadjust returned from a crowded youth camp. These are strong risk factors for respiratory diphtheria. She also presented with features typical of probable respiratory diphtheria like sore throat and dysphagia, progressive neck swelling, haemorrhagic and inflamed nasal turbinates and an adherent greyish white membrane hanging down the pharynx. The early presentation and short duration of these symptoms confirms the short incubation period and rapid progression of the disease as this child at presentation within five days of disease onset was already very ill and lethargic.

Complications remain the greatest cause of morbidity and mortality following infection with diphtheria. Complications secondary to the elaborated diphtheria toxin are the most common. Toxic cardiomyopathy most commonly occur in the second week of the disease but can appear as early as the first or as late as the sixth week of illness[1,10]. Toxic cardiomyopathy occurs in 10–25% of patients with respiratory diphtheria and is responsible for 50–60% of deaths[1]. Neurologic complications appear after a variable latent period, are predominantly bilateral and are motor rather than sensory and usually resolve completely. Paralysis of the soft palate is common and generally appears in the third week. Our patient developed features of myocarditis by the second week of disease onset and bilateral motor weakness of the lower limbs by the third week which is in line with disease

progression. This early onset of cardiac manifestation is associated with rapid disease progression and is a poor prognostic feature as was the case of our patient. Drooling of saliva and hoarse voice in this patient may be due to sore throat and dysphagia or to paralysis of the soft palate.

A diagnosis of diphtheria may be described as "probable" or "confirmed". It is probable if the case meets the clinical description or confirmed if a probable case is laboratory confirmed or linked epidemiologically to a laboratory confirmed case. A clinical description is an illness characterized by laryngitis or pharyngitis or tonsillitis, and an adherent membrane on the tonsils, pharynx and/or nose. However, persons with positive *C. diphtheriae* cultures and not meeting the clinical description (i.e. asymptomatic carriers) should not be reported as probable or confirmed diphtheria cases. Our patient met the criteria for probable diphtheria but could not be confirmed. Our centre and many others in Nigeria lack the appropriate capacity and skills for the isolation of this organism and this does have several deleterious effects on the management and surveillance of this vaccine preventable disease.

A lot of challenges were encountered in the management of this patient. Once diphtheria is suspected, management entails isolation of the patient, use of specific antitoxin and antibiotics, management of complications, supportive care and chemoprophylaxis for close contacts of patient. The first management challenge was lack of specific diphtheria antitoxin. The use of specific antitoxin is vital in halting disease progression. Antitoxin can neutralize circulating toxin or toxin that is absorbed to cells but is ineffective once cell penetration has occurred. Specific antitoxin is the main stay of therapy and should be administered as early as possible by intravenous route and in a dosage sufficient to neutralize the free toxin. Unfortunately as important as this is in the treatment of patient with diphtheria this anti toxin is unavailable in the country. Only a probable diagnosis could be made in this case as it could not be bacteriologically confirmed by the appropriate culture medium. This challenge may not be limited to our centre as many other centres contacted to assist with the culture also admitted not having the culture medium.

Antibiotics are indicated to clear the causative organism and thereby halt toxin production, and prevent transmission of organisms to contacts. Our patient received intra venous crystalline penicilline and metronidazole which have very good coverage for diphtheria but did not respond to it. This was probably because the disease has reached an advanced stage before presentation and elaborated toxins may have fixed to tissues which are not affected by antibiotics. Management of complications was also challenging. Our case developed both cardiac and neurologic complications both of which may have contributed to the mortality. Although she was diagnosed of having complete heart block, lack of funds and unavailability of the pacemaker made this management option not available

Primary prevention in form of active immunization as DPT vaccine at 6,10, 14 weeks of age and booster dose at 15-18 months and again between 4-6 years of age is recommended. The National Programme on Immunization (NPI) presently does not provide booster doses but a high coverage rate in infancy provides significant disease protection. Unfortunately, our case received neither the primary vaccine nor booster dose. This buttresses the need to reinforce and ensure full coverage of primary immunization by checking immunization cards as a requirement for school enrolment.

All household contacts and those who have had intimate physical contact with a patient are closely monitored for illness through the 7-day incubation period. Antibiotic prophylaxis is given, regardless of immunization status using erythromycin (40-50 mg/kg/day) for 7-14 days or a single injection of benzathine penicillin.[1] This was done for all close contacts of our patient including the managing team. Unfortunately, it was not possible to trace the asymptomatic carrier from whom our patient contracted the disease, neither was it possible to trace other adolescents that participated in the youth camp for possible development of symptoms.

Conclusion

In conclusion, diphtheria, a vaccine preventable disease (VPD) is a disease with rapid progression and requires a high index of suspicion. Facilities necessary for the diagnosis and treatment of this disease especially diphtheria specific antitoxin should be made readily available in Nigeria. Parents and caregivers of children should utilize the opportunity of free immunizations to vaccinate their children, for indeed, prevention is better than cure.

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