CASE REPORT

Respiratory Diphtheria in Two Children Presenting to A Tertiary Hospital in South–East Nigeria

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ABSTRACT

Respiratory diphtheria is an acute and infectious disease that can progress to cardiac and neurological complications ultimately resulting in increased morbidity and mortality in affected individuals. Diagnosis was made in line with the WHO clinical case definition for Diphtheria. This is a report of two probable cases of complicated respiratory diphtheria presenting within 3 weeks of each other to the Paediatrics Department of Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, Anambra state, South-East Nigeria.

The first patient was a 5-year-old female who presented on referral with a history of fever, throat pain, noisy breathing and facial fullness, in whom bull neck appearance and membrane in the throat was observed. She was tachycardic, in respiratory distress, had elevated jugular venous pulse (JVP), soft tender liver and a greyish membrane in the throat. She was managed as a case of Diphtheric Carditis and discharged after 17 days on admission in stable condition.

The second patient was also a 5-year-old, male, who presented with a history of fever, difficulty in swallowing, change of voice (progressing from hoarseness to whispers), cough and staggering gait. Onset of the illness was associated with membrane in the throat, bull neck and stridor. Examination revealed cranial nerve deficits, aphonia, hypotonia and staggering gait. CSF analysis was within normal. He was managed as a case of Diphtheric Neuropathy and was discharged home in stable condition after 16 days on admission. *C. diphtheria* IGG done 2 weeks post discharge was 0.19 IU/ml.

The cases suggest that respiratory diphtheria still occurs in children in our environment. A high index of suspicion is needed to diagnose and properly nurse these children back to health.

Keywords: *Corynbacterium diphtheriae, Paediatric Pulmonology*

INTRODUCTION

Diphtheria is an acute, toxin mediated and vaccine preventable disease caused by the aerobic gram positive bacteria *Corynebacterium diphtheriae* and manifests as either upper respiratory tract or cutaneous infection.[1] *C. diphtheriae* causes both endemic and epidemic diseases and was first described by Hippocrates in the 5th century BC.[1] The infection is spread from person to person through close contact with discharges from an infected person's eyes, nose, throat or skin.[2] In more than 90% of paediatric patients, the primary foci for diphtheria infection are the tonsils or pharynx; the nose and larynx are the next most common sites.[3]

Symptoms of respiratory diphtheria would include sore throat, hoarseness of the voice, malaise, low–grade fever, muscle weakness, loss of appetite, enlarged lymph nodes in the neck (giving the bull-neck appearance), respiratory distress manifesting as stridor, wheezing, cyanosis, accessory muscle use with retractions.[1,2,3,4] A greyish coloured pseudo-membrane may form over the nose, throat and tonsils making it difficult to breathe or swallow.[1,2] Respiratory diphtheria can quickly progress to respiratory failure following airway obstruction or aspiration of the pseudomembrane.[1] Attempts at scrapping this membrane usually results in bleeding.[1,4] Since the widespread use of diphtheria antitoxin, incidence of diphtheria has declined.[4]

The heart and nervous system can significantly be affected by diphtheria toxin.[4] Toxic cardiomyopathy occurs in 10–25% of paediatric patients with respiratory diphtheria and is responsible for 50–60% of deaths.[3,4] Cardiac toxicity usually manifests in the 2nd–3rd week of illness as pharyngeal disease improves but can occur anytime between the 1st–6th week of illness.[4] Cardiac toxicity results in myocarditis (with or without endocarditis).[1] It manifests as tachycardia (usually disproportionate to the fever and can be as a result of autonomic dysregulation), prolonged PR and ST–T segment changes, dysrhythmia, heart block (1st, 2nd or 3rd) and cardiac failure.[1,4] Recovery from this toxic cardiomyopathy is usually complete although survivors of severe dysrhythmia can have permanent conduction deficits.[4]

Toxic neuropathy occurs within the 2nd–3rd week of pharyngeal disease and are usually multiphasic.[4] It manifests with local paralysis of the soft palate; weakness of the post pharyngeal, laryngeal and facial nerves may follow causing a nasal quality to the voice and difficulty in swallowing.[3,4] Cranial neuropathy occurs in the 5th week and causes oculomotor and ciliary paralysis which result in strabismus, blurred vision or difficulty with accommodation.[3,4] Symmetric polyneuropathy has its onset 10 days to 3 months of oropharyngeal infection causing motor deficits and reduced deep tendon reflexes (DTRs).[3,4] Distal muscle weakness with proximal progression is more common but the reverse can be the case; clinical and cerebrospinal fluid (CSF) findings maybe indistinguishable from Guillan–Barre syndrome in the former.[4] Diaphragmatic paralysis can occur.[3,4] Stock–glove neuropathy can also be a manifestation of neuropathy.[1] Complete neurologic recovery is common but vasomotor centre dysfunction can rarely occur 2–3weeks after onset of illness resulting in hypotension and cardiac failure.[4]

Severity of cardiac and neurologic complications of diphtheria relate directly to

severity of pharyngeal disease.[1,4] Recovery is often slow but complete.[4] Corticosteroids do not reduce these complications and are not recommended.[4]

A case of diphtheria can be classified as a 'probable case' if it meets the clinical description and a 'confirmed case' – which is a probable case with laboratory confirmation or a probable case linked to a laboratory confirmed case.[5] Our case reports are two probable cases of complicated respiratory diphtheria.

Diphtheria is caused by lack of immunization, incomplete immunization, waning immunity (which occurs over time), nil booster doses, low herd immunity, low socioeconomic class, poor health system, overcrowding, among others.[1,3] Complications result in high mortality especially in individuals less than 5years and above 40years.[1] Antitoxin is the mainstay of treatment and is given based on clinical diagnosis as it neutralizes only free toxin.[1,3,4] Antibiotics like penicillin or erythromycin is given to halt toxin production.[1,3,4] Primary prevention is by vaccination.[4,5]

Sporadic cases of diphtheria have been reported in Nigeria.[6,7,8] A 13 year old Nigerian girl reported to have diphtheria with cardiac and neurologic complications, died of complete heart block.[8] In Vietnam, 20.8% of children clinically diagnosed with diphtheria had diphtheric cardiomyopathy while 5% had diphtheric neuropathy.[9] All patients with fatal cases from that report died of diphtheric cardiomyopathy.[9] Sadoh *et al.* reported a mortality rate of 33.3% among children managed for diphtheria in University of Benin Teaching Hospital, Nigeria. [10]

An outbreak of diphtheria was reported in Northeast Nigeria in 2011; 98% of the cases were never immunized for diphtheria.[11] In a rural community in South West Nigeria, 29.5% had full immunization and 53.8% had completed this immunization by 12 months in line with the National Programme for Immunization in Nigeria.[12,13,14] Lack of booster doses for diphtheria could result in waning immunity and overall lower herd immunity.

This is supported by the report by Henry *et al.* that found up to 29.9% of both mothers and their newborns having no protection from diphtheria (antibody titre <0.01IU/ml).[15] Protection against serious disease is assumed at diphtheria antitoxin levels of 0.01–0.10 IU/ml.[4] Paediatric Association of Nigeria (PAN) has a recommendation for complete immunization in Nigerian children[16]; this is yet to be adhered to.

Management challenges abound in the care of children with diphtheria and its complications in Nigeria.[6,7,8,10.11] Diagnostic challenges in the absence of confirmatory diagnosis would result in missed cases. This report was deemed necessary to draw attention to this.

CASE REPORTS

Case 1

O.K., a 5-year-old female referred to Nnamdi Azikiwe University Teaching Hospital(NAUTH) Nnewi from a private health care institution with a history of fever of 2 weeks, throat pain of 11 days, abdominal pain of a week, facial puffiness of 2 days and 2 episodes of vomiting. She was managed at a private facility at the onset of the illness for a febrile illness associated with sore throat, stridor and neck swelling -

'bull neck' associated with a membrane in the throat. She was said to be vaccinated in infancy though immunization card was not tendered.

On presentation, she was restless, centrally cyanosed and in marked respiratory distress with a respiratory rate of 64cycles per minute and the presence of intercostal and subcostal recessions. She had bilateral submandibular and cervical lymphadenopathy and bilateral pitting leg oedema. With respect to the cardiovascular system, the apex beat was displaced and located at the 6th intercostal space. The pulse was faint and she had a grade III pansystolic murmur maximal at the apex. She still had a residual whitish membrane in the throat. There was also soft and tender hepatomegaly with ascites.

A diagnosis of post diphtheric myocarditis with possible pericardial effusion and congestive cardiac failure was made. Chest radiograph showed bilateral pleural effusion while abdominopelvic ultrasonography revealed enlarged hepatic veins and inferior vena cava, ascites, bilateral pleural effusion and pericardial effusion. ECG showed sinus tachycardia. The requested 2D-chocardiography and other investigations were turned down by the mother who cited financial constraints.

Treatment with intravenous crystalline penicillin was commenced. Intranasal oxygen, intravenous frusemide and oral lisinopril were also administered. She made remarkable progress and was discharged 17 days after admission with no residual deficits. Sustained recovery was affirmed via phone conversation as patient did not return for scheduled follow up visits.

Case 2

O.L., a 5-year-old boy presented via a referral from a private health care institution with a month history of recurrent fever, difficulty in swallowing, voice change (progressing from hoarseness to whispers), cough and 5-day history of staggering gait. A whitish membrane was said to have been observed in the throat. He was treated for fever, sore throat and diffuse neck swelling (associated with noisy breathing worse during sleep) at a private facility before referral. He was said to have completed the primary immunization series in infancy; no immunization card was provided.

On examination, he was conscious and obeyed commands with normal mentation. He had dysphonia with ataxic gait and right lower motor facial nerve palsy. Power and tone were symmetrically reduced in both lower limbs but normal in the upper limbs. Yellowish exudates were noticed on moderately enlarged tonsils with a hyperaemic pharyngeal wall. The cardiovascular system examination was essentially normal.

A diagnosis of post diphtheric polyneuropathy was made and investigations requested for included full blood count, pharyngeal swab microscopy and culture for *C. diphtheria,* cranial CT with contrast, CSF analysis and neck x–ray. Culture for *C. diphtheria* was not done due to unavailability of reagents; CSF chemistry was normal, culture yielded no growth and neck x – ray was normal.

He was placed on intravenous ampicillin, sulbactam and oral azithromycin. He made good progress and was discharged after 16 days on admission. At 2 weeks follow up, he was noted to still fall occasionally while playing. Sample was collected for *C.*

diphtheria immunoglobulin G at that time and found to be 0.19IU/ml. Patient presently has made full recovery.

DISCUSSION

Diphtheria is an infectious disease caused by the exotoxin produced by *Corynebacterium diphtheriae*.[1] Respiratory diphtheria is one of the two types of diphtheria and is defined as an upper respiratory tract infection with fever, sore throat and adherent pseudo membrane of the pharynx, tonsils, larynx and nose.[17] It is sometimes associated with complications involving the cardiovascular and neurologic systems.[1,3,4,17]

The two patients presented within 3 weeks of each other (but having no common epidemiologic contact) with a history of upper respiratory tract infection associated with membrane in the throat. A diagnosis of diphtheria was made in both cases based on the WHO definition for probable diphtheria as an illness characterized by pharyngitis, nasopharyngitis, tonsillitis or laryngitis with an adherent membrane of the pharynx, tonsils, larynx and/or nose.[5] Culture of *C. diphtheriae* and confirmation of the toxigenicity of the isolate by Elek test is the gold standard for diagnosis. However, it was not done in the above patients because they presented after they had been treated to an extent, and secondly because of unavailability of reagents. Blood sample for serology was analysed for diphtheric antibody in one of the cases in a laboratory in South Africa. This is however a nonspecific test as the result does not distinguish between infection and being vaccinated against diphtheria.

It was also observed that the two patients did not receive diphtheria antitoxin at presentation. This may be due to delay in making a diagnosis, late presentation and unavailability of diphtheria antitoxin. It is recommended that diphtheria antitoxin be administered immediately diphtheria is suspected with prompt commencement of antibiotics.[1,3,4] This is because the antitoxin neutralises the circulating toxins and prevents the worsening of symptoms.[1,3,4]

The emergence of the reported cases may be due to poor immunization coverage and inadequate immunity. Although the patients were immunized in infancy, booster doses are needed to ensure continued protection.[4] It has been advocated that after completion of the primary series, booster doses should be administered to older children and adults.[1,4]

A high index of suspicion is always needed in any case of diphtheria. We recommend that healthcare professionals be sensitized to probable cases of diphtheria and possible complications. There is the need to stock diphtheric antitoxin in our pharmacies as well as equip our laboratories to confirm cases of diphtheria.

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