Case Report

Is Diphtheria Back?

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Abstract

Diphtheria is a nearly eradicated disease in Sri Lanka. After introduction of EPI vaccination program in 1978 childhood diphtheria has been eradicated. However sporadic cases of adult diphtheria have been reported among the non-immunised adult population. Classical presentation of active severe exudative pharyngitis, and cervical adenitis associated with acute neurological deficit with clinical response to anti-diphtheria toxin makes adult diphtheria a probable clinical diagnosis in the patient. However, isolation of Corynebacterium diphtheriae from the throat of a patient is required for definitive diagnosis. The need for a prepared laboratory system is discussed.

Introduction

Mr. YMP is a 48 year old farmer from Ethimale, Monaragala. He was born in Gala-uda in the Badulla district and moved to his present home at the age of 22 years. He had been apparently healthy in the past and gave no history of any major infectious or non–infectious medical problems. He did not give a history of recurrent sore throats and was unaware of his vaccination status. He presented to the medical unit of District General Hospital, Monaragala on the evening of 03.09.2008 with a one day history of mild fever, sore throat, dysphagia, odynophagia, difficulty in opening eyes and paresthesia of both hands and feet. He was conscious and rational but was drooling saliva and looked very ill on admission. He had four vaccination scars on his left upper arm (a large scar from small pox vaccination and three BCG vaccination scars). He had shotty cervical lymphadenopathy, but no “Bull-Neck”. His sinuses were non-tender, lungs were clear, and he was maintaining his peripheral oxygen saturation at 98% on room air with a normal hemodynamic status. His throat could not be visualized on admission. Neurological examination revealed bilateral partial ptosis and complete ophthalmoplegia with pupillary sparing (Figure 1). Palatal movements were normal, there

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was no nasal regurgitation and he did not have any objective sensory loss or diminished reflexes.

His full blood count on admission showed a WBC count of 7,700/mm$^3$ with 70% neutrophils, a haemoglobin of 13.6g% and a platelet count of 275,000/mm$^3$. His blood picture showed a mild neutrophil leukocytosis with cytoplasmic vacuoles suggestive of a bacterial infection. His serum sodium was 135meq/L, potassium 3.5meq/l, blood urea 21mg% and creatinine 0.7mg%.

His ECG on admission showed no abnormalities. Random blood sugar on admission was 90mg% and fasting blood sugar on the following day was 95mg%. His AST and ALT were 27 U/L and 14 U/L respectively. Laboratory facilities to process nasal/throat swabs and blood cultures were not immediately available. However, nasal/throat swabs were taken the following day, after administration of 3 doses of antibiotics (penicillin and erythromycin). A significant growth of Klebsiella spp. was obtained from these sites.

He was immediately transferred to the isolation room of the ICU for reverse barrier nursing and IV C Penicillin 2 MU 6 hourly and Erythromycin 500mg 6 hourly was commenced. He was kept on oxygen via a variable face mask and a nasogastric tube was inserted for feeding. He was given a regular dose of Paracetamol for fever. As there was a high suspicion of diphtheria from the beginning and as his throat could not be visualized properly to find a cause for the dysphagia and odynophagia, it was decided to inspect the throat with an upper gastrointestinal endoscope. Endoscopy showed severe exudative pseudomembranous pharyngitis suggestive of diphtheria (Figure 2). For the next two days he was in the ICU on antibiotics and became afebrile. However, his neurological status and dysphagia remained the same. His level of consciousness, blood pressure and heart rate remained stable and sequential ECGs were all normal. Throughout the illness his renal function was normal.

As he had already developed neurotoxicity, on the 3rd day following admission 80,000U of diphtheria anti-toxin was given. At 24 hours his neurological deficits began to improve. He was fully recovered neurologically and was able to drink at 48 hours. He was transferred back to the ward and was discharged (after seven days of hospital stay) on oral penicillin 500mg
6 hourly and erythromycin 500mg 6 hourly for seven days. He was given a dose of adult Diphtheria Toxoid (aTd) (diluted ten times) on discharge.

During his hospital stay the regional epidemiologist was notified. Close contacts were identified for follow up. There have been no further cases suspicious of diphtheria from within the hospital or from his home town of Ethimale.

**Discussion:**

Even though very rare in present day clinical practice, the classical presentation of active severe exudative pharyngitis and cervical adenitis associated with acute neurological deficit made adult diphtheria the most likely diagnosis from the outset. Since he was born before the EPI vaccination era, it is likely that the patient was not vaccinated and therefore susceptible to diphtheria. The complete and dramatic resolution of his neurological deficit and exudative pharyngitis after administration of diphtheria anti-toxin was also suggestive of the diagnosis. Isolation of *C. diphtheriae* from the throat of a suspected patient requires a prepared laboratory. Swabs collected prior to antibiotic treatment should be transferred using a transport medium (Loeffler agar) and inoculated on to selective tellurite containing media. The transport of ordinary swabs to a distant laboratory (Monaragala to Colombo in this instance - 244km) and plating on non selective media could result in isolation of organisms such as *Klebsiella* species which are likely to colonize the throat of patients on antibiotics. In conclusion our patient is a clinically probable but unconfirmed case of pharyngeal diphtheria.

**Diphtheria:**

Diphtheria is a nearly eradicated disease in Sri Lanka. After the introduction of the EPI vaccination program in 1978 childhood diphtheria has disappeared. However sporadic cases of adult diphtheria have been reported until 1985 among the non-immunized adult population (Figure 1).

Diphtheria is a disease caused by *Corynebacterium diphtheriae*. The sites of infection are respiratory tract or skin. Rarely, other toxogenic Corynebacteria, like *C. ulcerans* and *C. pseudotuberculosis* can also cause a similar respiratory illness. The disease spreads by droplets, direct contact of secretions, skin or rarely by fomites.

The usual incubation period is 2-5 days and initial symptoms are a mild sore throat, malaise and low grade fever. The hallmark of diphtheria is a grayish-white pseudo membrane on the pharynx, larynx and the tonsils. This membrane formation can extend into the larynx causing airway obstruction and death. The absorbed toxin can cause cardiac, neuro and nephro-toxicity in some cases. These complications may persist for months even if the respiratory diphtheria resolves within a few days. Overall case mortality rate is about 10%.
Diagnostic tests used to confirm infection include isolation of *C. diphtheriae* and toxigenicity testing. Although no other tests for diagnosing diphtheria are commercially available polymerase chain reaction (PCR) tests on clinical specimens to confirm infection with a toxigenic strain can be done. The PCR assay allows for detection of the regulatory gene for toxin production (dtxR) and the diphtheria toxin gene (tox). PCR is useful if nonviable *C. diphtheriae* organisms are present in clinical specimens that are obtained after antibiotic therapy has been initiated. However toxigenicity testing using the Elek test should be done to determine whether the organisms produce diphtheria toxin. Demonstration of toxin production is required to classify a case as confirmed diphtheria. PCR does not demonstrate production of diphtheria toxin but only detects the diphtheria toxin gene. A positive PCR test in the absence of a positive culture does not meet the laboratory requirement for classifying a case as confirmed diphtheria.

The mainstay of treatment of a case of suspected diphtheria is prompt administration of diphtheria antitoxin. This should be given without waiting for laboratory confirmation of the diagnosis. The recommended dosage and route of administration depend on the extent and duration of disease. Persons with suspected diphtheria should also receive antibiotics to eradicate carriage of *C. diphtheriae* to limit transmission and to prevent further production of diphtheria toxin. Treatment with erythromycin or penicillin is administered as a 14-day course. **Because the disease does not always confer immunity, an age-appropriate vaccine**
Containing diphtheria toxoid should be administered during convalescence. The disease should be notified and close contacts should be immediately tracked and given prophylaxis with aTd/DT (for adults and children >5yrs respectively) vaccine and antibiotics before the short incubation period of 2-5 days.6,7,8

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