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THE RETURN OF THE STRANGLER? CASE REPORT OF A FATAL CASE OF DIPHTHERIA

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ABSTRACT:

This article is a case report of a case of diphtheria which presented as diphtheritic tonsillitis in stridor and finally succumbed to diphtheritic myocarditis. Here we describe the case presentation, the treatment modalities undertaken, and the fatal course of events followed by an elaborate discussion on diphtheria.

INTRODUCTION: 1,6

No bacterial disease of humans has been as successfully studied as diphtheria. Its history dates back to the times of Hippocrates, who first clinically described it in reference to the disease in ancient Syria and Egypt in the 17th century. By the 18th century, diphtheria reached epidemic proportions in Europe and America. It came to be known as “El Garatillo” meaning “the strangler” in Spain and “the gullet disease” in Italy and Sicily. More relevantly to us, there seems to be a quiet resurgence of diphtheria in the last few years in our country, with cases in India, far outnumbering those of any other country in the world, according to a report by the WHO. So are we seeing “The Return of The Strangler” ??

CASE REPORT:

An 18 years old married female patient Valli, hailing from Kanchipuram, was brought by her mother, brother and husband to Stanley General Hospital casualty on 30/11/2011 at 12:51am in a state of stridor. On quickly assessing

the situation, the medical officers on duty at the causality that night, made an immediate admission and issued a call over to the ENT department for further management of the patient. On probing into the details, the patient's relatives gave a history of fever and throat pain for 10 days, and breathlessness for 2 days. The patient had 1st been taken to other hospitals and had finally been referred to us for further management. On examining the patient, we found her to be febrile, toxic and in severe stridor. An examination of the oral cavity revealed trismus, an edematous uvula and enlarged, congested tonsils covered by a dirty greyish yellow membrane which was more on the right side and extending onto the soft palate as well. Removal of this membrane provoked bleeding. The rest of the oropharynx could not be visualized.



The patient's neck was suggestive of Bullneck.



An xray neck AP view of the patient showed findings suspicious of a Steeple's sign with possible narrowing of the larynx at the region of the subglottis and proximal tracheal narrowing.



The patient's relatives did not know about the immunization status of the patient. The patient was admitted, given intravenous fluids, parenteral antibiotics and a dose of intravenous steroids in an effort to control the infection and the laryngeal edema which could have set in. After doing the basic investigations and taking necessary pre-operative preparations, the patient was shifted to the emergency operation theatre for emergency tracheostomy under local anaesthesia. After infiltrating the skin with a premixed solution of 2% solution xylocaine with 1 in 80,000 adrenaline, a midline incision was made below the cricoids cartilage in the Jackson's triangle. Tracheostomy was proceeded with in the usual way, separating the skin and subcutaneous fascia, retracting the strap muscles and issthmus of thyroid. Finally the pre-tracheal fascia was incised and the trachea identified. A tracheal stoma was created by removing a tracheal cartilage and a portex cuffed tracheostomy tube inserted to secure the airway with stay sutures holding it in place. After ensuring complete heamostasis and an adequate airway, the patient was shifted to the ENT ward for observation and further care. The patient who was initially stable, started developing symptoms and signs suggestive of diphtheritic myocarditis induced heart block in the next couple of hours with chest pain and a declining pulse rate and blood pressure. Despite our best efforts to revive her, she succumbed to it, and was declared dead on 30/11/2011 at 5 10am. Since the suspicion of a diphtheritic etiology was held strongly, the operation theatre was closed down for the next 12 hours and properly re-sterilized. The anaesthetists, surgeons, staff and workers who had thus been exposed to a possible infectious case of diphtheria were given off for the next 5 days in an endeavour at isolation, the membrane that has been described previously, had been scraped on the operating table and sent for histopathological and microbiological examination for arriving at a diagnosis and the causative agent. Our worst fears came true when a report of *Corynebacterium diphtheriae-gravis* type was issued.

DISCUSSION:

A BRIEF RUN THROUGH HISTORY:¹

The bacterium was first identified by Koch in 1883, and cultivated by Loeffler in 1884.

Roux and Yersin discovered the soluble exotoxin in 1888, while Von Behring and Kitasato came up with the antitoxin in 1890.

In 1909, Theobald and Smith identified the toxin-antitoxin complex, while the Schick test came into practice in 1913.

In 1924, Ramon stumbled onto a means to prepare the non-toxic antigenic equivalent of the diphtheria toxin(TOXOID), by treating it with formaldehyde.

Freeman in 1951, described the lysogenic nature of the pathogenic (toxigenic) strains of *Corynebacterium diphtheria*.

EPIDEMIOLOGY: ^{3,1,13,6,5}

Under the 2012 ICD-10-CM diagnosis codes, diphtheritic tonsillitis comes under code A36.0, which is applicable to diphtheritic membranous angina and tonsillar diphtheria.

Diphtheria is a contagious disease that can be contracted through direct physical contact, by breathing in the aerosolised secretions of infected individuals, and by consuming the milk of infected cows. In endemic areas, it is mainly a disease of childhood. It is rare in the first year of life, due to passive immunity received from the mother, reaches a peak between 2-5 years of age and then gradually declines in its incidence. Asymptomatic carriers are the most important source of infection. Once considered to be a dreaded disease, it has now been brought well under control largely due to active efforts at mass immunization coverage. This is well reflected by the statistical data of countries worldwide. For example, if we take the United States, there were 150,000 cases and 13,000 deaths due to diphtheria in the 1920s. Vigorous immunization brought down this rate to 19,000 in the 1945. There were 196 cases/year between 1970-1979. However between 1980-2004, there were just 57 cases of diphtheria. An outbreak of diphtheria occurred in Russia during the early 1990s with 50,425 cases reported in 1995, at a yearly rate of 17.3 cases/100,000 persons. Mass immunization, early identification and appropriate treatment of these cases, has reduced this rate to 0.6 cases/100,000 persons since 1999. There were 3978 reported cases to the WHO in 2006. However the recent trend in the Indian statistics has been alarming. According to the National Health Profiles released by the Central Bureau of Health Intelligence under the Directorate General of Health Services, the total number of diphtheria cases in India in 2006 was 2834, 3354 in 2007 and 6081 in 2008 (with 65 deaths). Even as recent as the WHO's Health Statistics, 2009, India ranks highest in the world with respect to the number of diphtheria cases. The problem seems to lie in inadequate immunization coverage with the triple antigen DPT, which is only 50-60%. It needs to become a 100% to achieve disease eradication.

THE TAXONOMICAL POSITION OF THE DIPHTHERIA BACILLUS: ³

Kingdom: Bacteria

Phylum: Actinobacteria

Order: Actinomycetales

Sub-order: Corynebacterineae

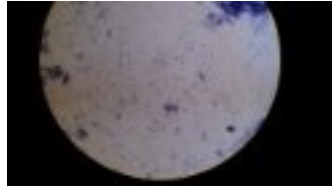
Family: Corynebacteriaceae

Genus: Corynebacterium

Species: diphtheria

CORYNEBACTERIUM DIPHTHERIA: 3,

The name is derived from the tough leathery pseudomembrane formed in the disease. (diphtheros, meaning leather). These are slender rods (bacilli) with a tendency to clubbing at one or both ends. They are non sporing, nonmotile and non capsulated, Gram positive bacilli.



Metachromatic granules (*volutin or Babes Ernst granules*) composed of polymetaphosphate are seen in the cells, which are more gram positive than the rest of the bacterial cell. They are often situated at the poles of the bacilli and hence called *polar bodies*. They can be demonstrated clearly with special stains such as *Albert's, Neisser's and Ponder's*. the bacilli are arranged in a characteristic *Chinese letter or Cuneiform pattern* in smears due to incomplete separation on daughter cells after binary fission. This is an Albert's stain stained microscopic picture of the diphtheria bacillus.



Media commonly used for cultivation are Loeffler's serum slope and tellurite blood agar. Diphtheria bacilli grow very rapidly on Loeffler's serum slope, and colonies can be seen in 6-8 hours. Tellurite(0.04%) inhibits the growth of most other bacteria, acting as a selective agent. Diphtheria bacilli reduce tellurite to metallic tellurium giving the colonies a grey or black colour. Based on the colonial morphology on tellurite medium and other properties, *McLeod* classified diphtheria bacilli into 3 types- *gravis, intermedius and mitis*, of which *gravis* causes the most severe form of disease, *mitis* the mildest and *intermedius*, a disease of intermediate severity. The *gravis* and *intermedius* types are associated with high case fatality rates(5-

10%), reaching upto 20% fatality rate in the age groups less than 5 years and more than 40 years. Only the gravis types is positive for glycogen and starch fermentation.

Virulent strains of diphtheria produce a very powerful exotoxin(protein). The pathogenic effects of the bacilli are due to the exotoxin. It consists of two fragments, A & B. All the enzymatic activity is present on fragment A, while fragment B is responsible for binding the toxin to the cell. The toxigenicity depends on the presence of *corynephages*. The toxigenicity remains only as long as the bacilli is lysogenic. The diphtheria toxin acts by inhibiting protein synthesis. Specifically, fragment A inhibits polypeptide chain elongation in the presence of NAD, by inactivating the elongation factor EF2.

PATHOGENECITY:^{2,3,5,7,14}

The incubation period is commonly 3-4 days. The site of infection may be 1. Faucial, 2. Laryngeal, 3.nasal, 4.otitic, 5.conjunctival, 6. Genital- vulval, vaginal or prepucial, 7. Cutaneous. Faucial diphtheria is the commonest type. According to clinical severity, diphtheria may be classified as 1. **Malignant or hypertoxic**, with marked adenitis(bullneck), where death is due to acute circulatory failure,2. **Septic** and 3. **Haemorrhagic**. The common complications are asphyxia, acute circulatory failure, post diphtheritic paralysis (palatine and ciliary but not papillary, where spontaneous recovery is the rule) and sepsis (pneumonia and otitis media). On an anatomical basis and in an ascending order of severity from mild to severe, clinical types can be arranged as follows:

Nasal- involvement of the anterior nares- little toxin absorption.

Tonsillar- membrane on one or both tonsils- moderate tonsil absorption.

Pharyngeal- membrane on the posterior wall or fauces- moderately severe toxin absorption.

Nasopharyngeal- involvement of the mucous membrane of the posterior nares, upper pharynx and tonsils- toxin absorption severe.

Laryngeal- (three types):

Primary- sole involvement of the larynx- toxin absorption minimal.

Tracheobronchial- involvement of the trachea,bronchi, smaller bronchioles and occasionally alveoli- toxin absorption moderate.

Mixed- involvement of the larynx plus extension downwards and upwards to involve the other structures as well. Toxin absorption will depend upon the extent of involvement of non-laryngeal structures.

Diphtheritic tonsillitis differs from acute follicular tonsillitis in that it occurs in unimmunized individuals, causing low grade fever, severe toxic symptoms, bullneck, neurological deficits and albuminuria. The organism will be demonstrable by special stains.

The Steeple sign and tracheal narrowing seen in this patient's X-ray neck AP view, re-establishes the fact that though croup(acute laryngotracheobronchitis) is the primary diagnosis to be considered in patients with such radiological findings,other differential diagnoses such as epiglottitis, bacterial tracheitis, foreign body, diphtheria, retropharyngeal abscess, peritonsillar abscess and asthma should also be borne in mind while evaluating such patients.

DIPHTHERITIC MYOCARDITIS:^{8,9,10,11,12,13.}

diphtheritic myocarditis has an associated mortality rate of 60%, and it accounts for majority of the deaths related to diphtheria. Diphtheria causes disturbances in impulse formation and conduction. The diphtheria toxin causes severe acute myocarditis leading onto cardiac damage. Risk factors for cardiac involvement in diphtheria: older age, low socio-economic status, extensive involvement of the respiratory tract. A study by Nalmas et al, states that the risk of cardiac damage is higher in patients with fever, toxic disease and membranous disease. The ECG findings associated with diphtheritic myocarditis include PR interval prolongation and T wave changes in asymptomatic individuals, and intraventricular blocks and AV blocks in symptomatic patients. A complete AV block is the most ominous ECG finding. The pointers for a bad prognosis in diphtheritic myocarditis: ventricular ectopics on presentation, WBC count >25,000 cells/microL, aspartate transaminase > 80U/L (serum transaminase levels provide valuable diagnostic and prognostic information in diphtheritic myocarditis) and membrane extending to atleast 2 anatomical sites. Minh Dung et al have conducted a study to assess the usefulness of temporary insertion of a cardiac pacemaker in the treatment of severe diphtheritic myocarditis and found that it helped to improve the outcome even in the face of complete heart block.

TREATMENT:^{3,14}

A patient with suspected or confirmed diphtheria, should be hospitalized immediately, isolated and hydrated adequately with intravenous fluids. The recommended duration of isolation for patients with diphtheria is about 7-10 days. The exceptions being the nasopharyngeal and laryngeal forms, in which case, the patient should be hospitalized for a minimum duration of 42 days. This stay can be appropriately extended depending on the course of the disease and any complications that the patient may develop. Contacts may be isolated for a period corresponding to the incubation period of the disease. Antitoxin should be administered as early as possible. It forms the main anchor of treatment for diphtheria. The dictum still holds good that the prognosis in diphtheria depends largely on the first day the antitoxin is administered. This is because the antitoxin can neutralize only the circulating toxin. It becomes useless once the toxin gets fixed to the tissues. Of the total dose of antitoxin being administered, half should be given by intravenous route, and the other half by intramuscular route. The recommended dose of antitoxin for the various forms of diphtheria are as follows:

Nasal – 10,000 to 20,000 units

Laryngeal/Pharyngeal – 20,000 to 40,000 units.

Tonsillar – 15,000 to 25,000 units.

Combined type/delayed diagnosis – 40,000 to 60,000 units.

Severe disease (extensive disease/ more than 3 days duration/ neck edema/ collapse/breathlessness) – 80,000 to 100,000 units.

Carrier/Contact – not required.

Though they cannot replace the role of the antitoxin, antibiotics are necessary and useful adjuncts in the treatment of diphtheria. They can be used to for patients as well s carriers in an attempt to eradicate the diphtheria bacillus and prevent its transmission. The recommended antibiotics are:

- a) Procaine Penicillin G given intramuscularly for 14 days.
- b) Erythromycin (in dose of 40mg/kg with a maximum of 2g/day) given orally for 14days.

In case of allergy to Penicillin and Erythromycin,Rifampicin or Clindamycin can be used.

Carnitine 100mg/kg/day BD for 4 days may help prevent myocarditis.a

In case of complications in the form of airway obstruction, tracheostomy or intubation may be considered appropriate to the situation and disease presentation.

PROPHYLAXIS:^{3,4,14,15,16}

Diphtheria vaccine for children is combined with tetanus and acellular pertussis and given as a triple vaccine known as DTaP (diphtheria, tetanus, acellular pertussis). DTaP should be given at two, four and six months of age,next at 15 to 18 months, and finally between four and six years.The guidelines given in the Indian National Immunization Schedule direct the primary course of DPT vaccine (containing whole cell pertussis component) to be given at 6,10 and 14 weeks of age, a booster dose between 16-24 months, DT at 5-6 years and lastly TT at 10 and 16 years.

In 2005, a new vaccine was approved as single booster vaccination for adolescents and adults called Tdap (tetanus, diphtheria and acellular pertussis). The recommended age for Tdap vaccination is 11 to 12 years. Td (tetanus and diphtheria) vaccine can also be used as booster dose in adolescents and adults. It does not contain the pertussis component.

Adults aged between 19 and 64 years should receive a single dose of Tdap to replace a single dose of Td for active booster vaccination if they received their last dose of Td more than ten years earlier. Thereafter, Td should be given every ten years to maintain immunity.

Persons who have been exposed to patients with diphtheria, may be given vaccine prophylaxis depending on their immunization status: booster vaccine if they have already completed the primary course of diphtheria vaccine, or the full primary course of 3 vaccine doses if they have not been immunized previously, apart from appropriate anti-microbial prophylaxis. In fact it has also been recommended that the patients themselves receive diphtheria prophylaxis in the convalescence period, as the disease is not known to give life-long immunity.

A recent article by the Advisory Committee on Immunization Practices (ACIP) on the Immunization of Health-Care Professionals has recommended that all Health-Care Professionals receive a single dose of

Tdap as soon as feasible, if they have not previously received it, regardless of age (as pre-exposure prophylaxis).

Recommended Principles of post-exposure prophylaxis for Health-Care Professionals: (based on a 'Exposure Management Infectious Diseases: Healthcare Personnel (Hep)' policy adopted by the University of Toledo last year)

1. Nasopharyngeal cultures will be obtained from exposed personnel. These HCP will be monitored for signs and symptoms of diphtheria for seven (7) days after exposure.
2. Antimicrobial prophylaxis will be administered to personnel who have contact with respiratory droplets or cutaneous lesions of patients infected with diphtheria.
3. Previously immunized exposed personnel will be immunized with Tdap.
4. Exposed personnel will have nasopharyngeal cultures repeated at least two (2) weeks after completion of antimicrobial therapy. Those who remain culture positive will receive repeat antimicrobial therapy.

CONCLUSION:

This incident is a wake up call for us to sit up and take notice of this re-emerging dangerous disease, and take appropriate steps to bring the situation under control. Widespread complete immunization coverage should be the modus operandi as it greatly helps in nipping the problem in the bud. There are lessons to be learnt and technological/medical advancements to be made in the early identification and management of diphtheritic myocarditis. Public awareness is another area to be addressed, so that they identify the symptoms and seek medical attention as early as possible. Efforts should be taken to ensure that the necessary treatment methods and preventive measures are available at every level of the health care delivery system, as, this disease, though highly contagious and threatening on one hand, is highly amenable to control and eradication if we act quickly and consistently.

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