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Diptheria-Case series: Importance of early diagnosis and treatment

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Abstract
Diphtheria is infectious disease caused by toxigenic Cornybacterium diphtheriae. Despite widespread mass immunization still outbreaks are frequently encountered in our country. Here we report case series of 4 clinically suspected cases with diphtheria from which three survived and one died reflecting importance of Microbiological diagnosis on the basis of clinical suspicion along with prompt treatment of patient leading to significant decrease in morbidity & mortality.

Keywords: ADS (Anti diptheric serum), Nasopharyngeal diptheria, Sentinel surveillance

Case series

Case 1

A male 8 years old, resident of Boruti village (Border area Maharashtra & Karnataka), was admitted to the Pediatric department of our hospital, with the chief complain of high grade fever, difficulty in breathing for past 3-4 days, swelling was seen on the neck region. On asking about the immunization history parents mentioned that patient has taken one vaccine at the time of birth, no further vaccination was given to the patient. Patient did not have any significant past history or family history. There was no evidence of any membrane on the tonsillar region. Since crepitation & rales were heard on chest auscultation LRTI was suspected. Patient was alert, conscious and talkative. Patient was started on Inj Ceftriaxone 1.2 mg I.V. BD, Inj Gentamicin 60 mg I.V. BD. Patients laboratory parameters were normal, however patient's condition worsened on second day of admission, patient appeared toxic, irritable and lethargic, unable to open mouth and complained of difficulty in breathing, O/E greyish patch was seen on the tonsillar pillars, throat swab was sent to Microbiology department for Gram stain, Albert's stain and Culture. Gram stain of throat swab showed evidence of pus cells with gram positive bacilli in V and L forms (Chinese pattern) morphologically suggestive of *Cornybacterium diptheriae*. Albert stain showed evidence of bacilli appearing green in colour with granules stained dark blue to black in colour at each pole of the bacilli suggestive of metachromatic granules suggestive of *Cornybacterium diptheriae*. The reports were immediately conveyed telephonically. The findings were later confirmed by black colour colonies on Potassium tellurite agar and Elks gel test for toxin production. ADS (Anti diptheric serum) was administered along with supportive and symptomatic treatment to the patient on the basis of provisional report. Patient's condition improved after 1 day and patient was discharged after 1 week of hospitalization. Patient was advised for follow up in OPD, now the patient is healthy with no complication and has recovered fully. Prophylactic treatment was given to other members at home (T. Erythromycin according to weight).

Case 2

A female 11 years old, resident of Dodne (border area of Maharashtra & Karnataka), was admitted to the Pediatric ward with fever since 4 days, difficulty in swallowing from 3 days, difficulty in breathing for 3 days which was progressive in nature. On admission patient appeared restless and toxic, patient was not able to swallow even liquids. Patient did not have any significant past history or family history. Child was accompanied with the mother, on enquiring about the child immunization status, she told that child was given few vaccines, about which she didn't knew exact details. On Examination patient had bull neck, grey colour membrane bilaterally on the tonsils extending to hypopharynx and posterior pharngyeal wall. Patient was in extreme distress for which oxygen support was given. Throat swab was sent for Gram stain, Albert's stain and Culture to Microbiology department. The report of Gram stain for throat swab showed evidence of pus cells with gram positive bacilli in V and L forms (Chinese pattern) morphologically suggestive of *Cornybacterium diptheriae*. Albert stain showed evidence of bacilli appearing green in colour with granules stained dark blue to black in colour at each pole of the bacilli suggestive of metachromatic granules morphology suggestive of *Cornybacterium diptheriae*. The reports were immediately conveyed telephonically, unfortunately patient's condition worsened and patient collapsed within a short span of time. The findings were later confirmed by inoculation on blood agar, Mac conkey agar and selective media Potassium tellurite medium. Black colour colonies were seen on potassium tellurite agar and Elks gel test was done confirmation of toxin production. However the patient died within 1 hour of admission and ADS (Anti diptheric serum) could not be

administered.

Case 3

A male patient 10 years of age resident of Hili village (border area of Maharashtra & Karnataka), was admitted to the Pediatric ward with the low grade fever since 3 days, breathing difficulty since 2-3 days, swelling, pain in throat since 2-3 days, body ache since 2-3 days. Patient was brought by his father, as per the father there was no significant past history or family history but the child's immunization was not complete. All other laboratory parameters were normal. On examination there was swelling over the neck region along with greyish patches on the right tonsillar area was seen. Throat swab was send to Microbiology department for Gram stain, Albert's stain and Culture. The reports of Gram stain for throat swab showed evidence of pus cells with gram positive bacilli in V and L forms (Chinese pattern) morphologically suggestive of *Cornybacterium diptheriae*. Albert stain showed evidence of bacilli appearing green in colour with granules stained dark blue to black in colour at each pole of the bacilli suggestive of metachromatic granules morphology suggestive of *Cornybacterium diptheriae*. The reports were immediately conveyed telephonically. The findings were later confirmed by black colour colonies on potassium tellurite agar however Elks gel test for did not show toxin production. Due to strong clinical suspicion ADS (Anti diptheric serum) was administered along Inj Ceftriaxone 1 gm I.V. BD, Inj Gentamicin 50 mg I.V. BD, Inj Meropenem 200 mg I.V. TDS, Inj Neomol 2 cc I.V. BD, Inj Metro 200 mg I.V. TDS, Inj Ondem 1 cc BD, Vit K 50 mg OD. Patient's condition improved within 2 days of admission and was discharged from the hospital on day 8. Patient's was called for follow up, in which patient was fine and completely recovered. Prophylactic treatment was given to other members at home (T. Erythromycin according to weight).

Case 4

A 3 year old male patient resident of Mandargi (border area Maharashtra & Karnataka)was admitted to the Pediatric department with complain of fever with cough since 1 week, difficulty in breathing since 3 days, Patient was brought by his mother, as per the mother child was unimmunized. On examination patient was weak lethargic but awake and conscious with cold clammy extremities. Patient pulse was 120/minute, respiratory rate was 24/minute rest other laboratory parameters were in normal range. The next day early morning patient's condition detoriated, patient complained of difficulty in swallowing even own saliva, neck region showed swelling, dyspnea worsened. On examination both the tonsils were enlarged with greyish patches present over both the tonsils. Throat swab was send to Microbiology department for Gram stain, Albert's stain and Culture. The reports Gram stain of throat swab showed evidence of pus cells with gram positive bacilli in V and L forms (Chinese pattern) morphologically suggestive of *Cornybacterium diptheriae*. Albert stain showed evidence of bacilli appearing green in colour with granules stained dark blue to black in colour at each pole of the bacilli suggestive of metachromatic granules and morphology suggestive of *Cornybacterium diptheriae*. The reports were immediately conveyed telephonically. The findings were later confirmed by black colour colonies on potassium tellurite agar and Elks gel test for toxin production. ADS (Anti diptheric serum) was administered along Inj Ceftriaxone 1 gm I.V. BD, Inj Gentamicin 50 mg I.V. BD, Inj Meropenem 200 mg I.V. TDS, Inj Metro 200 mg I.V. TDS, Inj Ondem 1 cc BD, Vit K 50 mg OD. Patient's condition improved within 3 days of admission and was discharged from the hospital on day 8. Patient's was called for follow up, in which patient was fine and completely recovered. Prophylactic treatment was given to other members at home (T. Erythromycin according to weight).

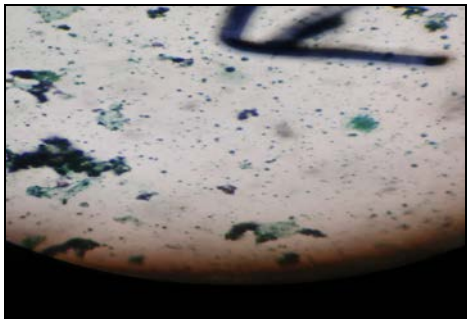

Fig 1: Albert stain shows bacilli with metachromatic granules

Fig 2: Black colour colonies on Potassium tellurite medium

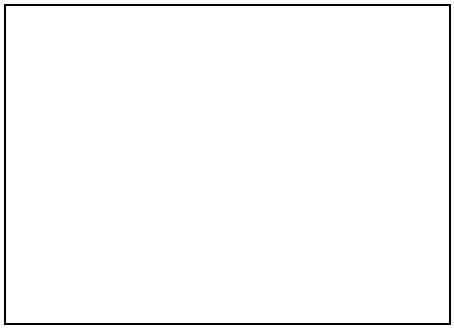

Fig 3: Gram Positive bacilli showing Chinese pattern (V & L Forms)

Discussion

Cornybacterium diptheriae is gram positive bacilli that exists in 4 biotypes (gravis, intermedius, mitis and belfanti). Severe disease is associated with gravis biotype but any strain can produce toxin. Major virulence factor of *C. diptheriae* is potent exotoxin that inhibits protein synthesis [2].

Although diphtheria has been eliminated from many developed countries by effective immunization, still it

continues to be endemic in India and it is leading cause of morbidity and mortality especially border area between two states [3]. The present case series points out cases of diphtheria that were reported from border area of Maharashtra and Karnataka and were referred to our hospital which in tertiary care hospital located in Solapur. This case series points out that endemic focus of diphtheria is present at border region between Maharashtra & Karnataka. Many cases have been reported from this area. There is need to have active surveillance in this area to prevent outbreak of diphtheria.

Hospital based sentinel surveillance as well as outbreaks published in last 20 years (1996-2016) shows that diphtheria cases have been reported most commonly in school going children and adolescents. As per National level health surveys coverage of three doses of diphtheria vaccine is about 80% during 2015-2016, however the information about booster doses is scares. So there is also need to form policies to keep track of booster doses as this may lead to decrease in the prevalence of diphtheria. As per CBHI 41,672 cases were reported between 2005 to 2014 with 899 deaths (CFR 2.2%) [4]. Ten Indian states Andhra Pradesh, Assam, Delhi, Gujarat, Haryana, Kolkata, Nagaland, Maharashtra, Rajasthan, West Bengal accounts for 84% of cases reported. Majority of cases were unimmunized or incomplete immunization. There is need to focus on improving coverage of primary and booster dose of diphtheria vaccine as a part of universal immunization practice and introduction of diphtheria vaccine to school going children age group [4].

Diphtheria if not detected early and promptly treated can lead to significant morbidity and mortality due to life threatening complications. A suspected patient should be isolated to minimize risk of transmission of infection to others [5]. Prompt anti diptheric serum administration is mainstay treatment along with other symptomatic and supportive care. Apart from management of index case there is need to assess risk and management of contacts to reduce transmission of the disease. Recent trends suggests that there has been shift of age group affected from preschool children to school going children and even adolescents which clearly points out importance of immunization among susceptible population, as the disease is vaccine preventable. In adolescents tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine is recommended (CDC 2011).

Conclusion

Diphtheria is a fatal disease most likely to occur in partially immunized and non-immunized cases, so this signifies importance of immunization, we must encourage high uptake of scheduled immunization by increasing awareness among population. Clinical suspicion along with Microbiological confirmation will affect outcome of cases and lead to decrease morbidity and mortality. Thus Microbiology reports play pivotal role in early detection of infection as well as tp prevent outbreaks.

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