A DIPHTHERIA OUTBREAK IN ASSAM, INDIA

Lahari Saikia[1], Reema Nath[1], Naba Jyoti Saikia[2], Gargi Choudhury[1] and Mili Sarkar[1]

[1]Department of Microbiology, [2]Department of Eyes, Noses and Throats,
Assam Medical College, Dibrugarh, Assam, India

Abstract. Between May and July 2009 there was a small outbreak of diphtheria in adults in Assam, India, with 13 confirmed cases, 8 males and 5 females. The mean age of the confirmed patients was 21.8 ±10.5 years. Common signs and symptoms of these patients included low grade fever, sore throat and pseudomembranes on the tonsils. The case fatality rate was 30.8%. Neurological complications were observed in one case. None of the patients received antidiphtheric serum (ADS) since none was available.

INTRODUCTION

Following the introduction of immunization with diphtheria toxoid and Diphtheria-Pertussis-Tetanus (DPT) vaccines, the incidence of diphtheria has declined dramatically and some developed countries have virtually eliminated the disease over the last three decades. In developing countries, with increasing immunization coverage, the incidence of the disease has also declined (Vitek and Wenger, 1998). Data regarding the incidence of diphtheria in some developing countries is not available, where it account for 80-90% of the global burden of diphtheria cases (Vitek and Wenger, 1998).

In addition to reduction in incidence, a change in the epidemiological profile of the disease has also been seen (Khuri-Bulos *et al*, 1988; Galazka and Robertson, 1995; Eskola *et al*, 1998).

The incidence of the disease has declined in India over the years because of wider vaccination coverage in the children below five years of age with only 2,817 cases being reported in 1997 (Anonymous, 2008). The details regarding the age distribution, immunization status, disease severity and outcomes of these cases are not available. No large outbreaks of diphtheria have been reported in recent times from India. In this paper we review a small outbreak of diphtheria in Barbaruah, Dibrugarh District, Assam, India, where adults were primarily affected.

Correspondence: Dr L Saikia, Department of Microbiology, Assam Medical College, Dibrugarh-786002, Assam, India.
E-mail: lahari.saikia@yahoo.com

MATERIALS AND METHODS

Dibrugarh, one of the eastern districts of Assam, has a subtropical monsoon climate with a mild winter and a warm, humid summer. It experiences uneven rainfall in various parts. It is famous for its oil and tea industry. It has a population of 12,31,412 (2001 census) distributed in 6 towns, 7 blocks, 1326 villages and has 146 tea plantations.

The diagnosis of diptheria infections was based on clinical manifestations with bacteriological confirmation. Definitions used during the outbreak investigation were:

Suspected case: Patient of any age with upper respiratory tract disease (pharynx, larynx, tonsils, nose), characterized by

throat pain, mild fever, with adhering pharyngeal membrane and/or difficulty in swallowing or breathing.

Confirmed case: A symptomatic or asymptomatic case confirmed by isolation of toxigenic *Corynebacterium diphtheriae*, or any suspected case that has an epidemiological link with a laboratory-confirmed case.

Contact: Any person living with a confirmed case, or frequenting his/her household or having some link (occupational, academic, or social) with a confirmed case.

RESULTS

In 2009, an outbreak of diphtheria occurred in Barbaruah, a rural area of Dibrugarh District between 27 May and 20 July with 13 confirmed cases. The first reported case, a 45 year-old female from Patra goan of Jamira village, came to Assam Medical College and Hospital with a 4 day history of fever, throat pain and difficulty in swallowing and breathing. Throat examination showed a grayish-white membrane over the tonsils, uvula, and adjacent soft palate. Even though trecheostomy was done on 31 May, the membrane extended to the trachea and ultimately the patient died on 2 June due to respiratory obstruction. A throat swab was sent for culture, but *C. diphtheria* was not isolated from the sample.

During the next 45 days (referred to in this report as "the first period") 5 additional cases occurred, three of whom also died, with essentially the same signs and symptoms. The signs and symptoms included fever (11 cases), throat pain (11 cases) and membranes on the tonsils (11 cases). None of these cases received antidiphtheria serum (ADS) since it was not available.

A bacteriological study of 64 cases who consulted health services spontaneously, and who had direct on indirect contact with suspected or confirmed cases of diphtheria, was carried out. *C.diphtheriae* was isolated in 14.1% (9) of the cases. All the cases, except two, occurred in persons who were either household contacts with bacteriologically confirmed diphtheria cases or with fatal cases, this occurred during the first part of the outbreak. One bacteriologically confirmed case died. The age group above 15 years was the most group most affected by the outbreak (69.2%). The cases were scattered over 5 villages in Barbaruah Block. No single focus of outbreak was identified, which implies there were multiple sources of infection. The characteristic features of the confirmed cases are depicted in Table 1.

Of the 13 confirmed cases, there were 8 male cases and 5 female cases.

The case-fatality rate of the outbreak was 30.8% (4/13). One patient developed neurological complications with palatal palsy and polyneuritis. The age groups of patients were: 7.7% (1/13) in the 5-9 year old group, 23.1% (3/13) in the 10-14 year old group, and 69.2% (9/13) in the 15-45 year old group (Table 1). No confirmed cases were found in children less than 5 years old.

Interventions

A plan with 5 strategic lines of action was designed: 1) intensive vaccination of risk groups; 2) monitoring and reporting of suspected cases; 3) review and adaptation of the case management protocol; 4) mass education campaign; 5) interinstitutional and intersectoral coordination for case management and adequate procurement of supplies (among them anti diphtheria serum). All symptomatic cases and carriers were treated with erythromycin and immediate immunization of dropout

cases was done. One booster dose of DT was given to all previously immunized children within 2 years, and 2 doses of DT were given at a 4 week interval to children up to 15 years of age whose immunization status was not known. Strict surveillance continued after the plan of operation concluded and no new case have been reported since August 2009.

During investigation, difficulties included delays in identifying the outbreak due to lack of laboratory confirmation and non-availability of ADS. The very high case fatality rate was attributed to delay in diagnosis and non-availability of antitoxin. Delay in laboratory confirmation may be due to poor specimen handling and prior treatment with antibiotics. The toxigenicity test of isolated *C. diphtheriae* could not be done due lack of laboratory facilities.

DISCUSSION

The children of Assam had consistently low rates of childhood immunization (Phukon and Barman, 2009). Although no outbreaks had been reported in recent years from Assam, in May 2005, over a two weeks period, five children aged $1^1/_2$-8 years, from rural areas of neighboring districts of Dibrugarh, presented to Assam Medical College and Hospital with diphtheria (unpublished data). Except for one case, all the children were either unimmunized (1) or partially immunized (3) and died. *C. diphtheriae* was isolated from 3 out of 5 patients. These cases may not give a true picture of the disease burden in the community since we do not know how many subclinical, asymptomatic and undiagnosed cases there were.

The unusual feature of this outbreak was the age distribution of those affected, the majority of whom were older than 10 years. To the best of our knowledge, no published data of diphtheria outbreaks in adults have been reported from India. A few hospital based retrospective studies from various parts of the country have revealed an increased incidence of diphtheria cases in adults. In a case series of 616 cases over a period of 5 years (1989-1993) from West Bengal, 40% of cases occurred above age of 5 years (Ray *et al*, 1998). An earlier study from a south Indian district hospital also discovered a similar age shift, with the occurrence of 45% of cases in children >5 years old (Havaldar, 1992). A recent study from Malegoan and Dhole in Maharastra also demonstrated a shift in age with 88.1% of cases occurring in those >5 years old (Dravid and Joshi, 2008). In a retrospective case analysis of 101 cases from Assam, 59% of cases were in those >5 years old (Nandi *et al*, 2003). This outbreak indicates the changing epidemiology of diphtheria and the lack of protective antibodies against diphtheria in adults in this part of the country. To prevent recurrence of diphtheria lifelong immunity is necessary. In the prevaccine era, when the circulation of *C. diphtheriae* organisms was common and the prevalence of diphtheria cases was high, natural immunity was acquired by overt or subclinical infection. After introduction of mass immunization with diphtheria toxoid and Diphtheria-Tetanus-Pertussis (DTP) vaccines, the circulation of toxigenic strains in the community has resulted in decreased opportunity to acquire immunity (Galaska and Robertson, 1995; Eskola *et al*, 1998). Serological studies in many countries have revealed in the absence of adult vaccination and natural immunity a high proportion of adults become susceptible to diphtheria (Nakajima *et al*, 2008). The potential for outbreaks of diphtheria in the community may be enhanced when there are

Table 1
Characteristics of confirmed diphtheria cases.

Age in years	Sex	Immunization status	Duration of illness	Contact history	Symptoms	Signs	Complications	Microbiology	Treatment	Outcome
10	F	Unknown	5 days	-	Fever, difficulty in swallowing, swelling of the neck.	Bull neck, membrane over tonsils.	Respiratory failure.	Smear and culture positive for *C. diphtheriae*.	Antibiotics and cardio-respiratory support.	Expired on 3rd day.
8.4	M	Unknown	5 days	Household contact of cases no.1	Fever, difficulty in swallowing, swelling of the neck.	Bulls neck, membrane over tonsils.	Respiratory failure.	Not done.	None.	Expired on the way to hospital.
32	M	Immunized	4 days	Neighbor of case no. 7	Fever, pain in the throat, difficulty in swallowing.	Membrane over tonsils, cervical lymphadenopathy.	-	Smear and culture positive for *C. diphtheriae*.	Antibiotics and cardio-respiratory support.	Discharged after 2 weeks.
30	F	Immunized	2 days	Household contact of case no. 3	Pain in the throat.	Inflammed and enlarged tonsils.	-	Smear and culture positive for *C. diphtheriae*.	Antibiotics.	Discharged after 2 weeks.
22	M	Unknown	3 days	Household contact of case no. 7	Fever, pain in the throat.	Inflammed and enlarged tonsils with membrane in the throat.	-	Smear and culture positive for *C. diphtheriae*.	Antibiotics.	Discharged after 2 weeks.
21	M	Imminized	3 days	House hold contact of case no. 7	Fever, pain in the throat.	Inflammed and enlarged tonsils with membrane in the throat.	-	Smear and culture positive for *C. diphtheriae*.	Antibiotics.	Discharged after 2 weeks.
20	M	Unknown	2 days	-	Fever, pain in the throat, difficulty in swallowing.	Membrane over tonsils and soft palate, cervical lymphadenopathy and enlarged tonsils.	Septicemia and acute myocarditis.	Smear and culture positive for *C. diphtheriae*.	Antibiotics and cardio-respiratory support.	Expired on 6th day.

25	F	Unknown	3 days	Neighbor of case no. 7.	Fever, pain in the throat, difficulty in swallowing.	Membrane over tonsils and soft palate, cervical lymphadenopathy and enlarged tonsils.	Palatal palsy and peripheral neuritis.	Smear and culture positive for *C. diphtheriae*.	Antibiotics, cardiores-piratory support.	Discharged on 6th day.
14	M	Unknown	3 days	Household contact of case no. 10.	Pain in the throat.	Inflammed and enlarged tonsils with membrane in the throat.	-	Smear and culture positive for *C. diphtheriae*.	Antibiotics	Discharged after 2 weeks.
45	F	Unknown	4 days	-	Fever, pain in the throat, difficulty with swallowing and respirations.	Enlarged tonsils with extensive membrane in the throat that extended to the larynx and trachea after tracheostomy, cervical lympha-denopathy.	Septicemia and respiratory obstruction.	Smear and culture positive for *C. diphtheriae*.	Mechanical ventilation, tracheostomy, antibiotics.	Expired on 7th day.
28	M	Unknown	3 days	Neighbor of case no. 7.	Fever, pain in the throat.	Inflammed and enlarged tonsils.	-	Smear and culture positive for *C. diphtheriae*.	Antibiotics	Discharged after 2 weeks.
20	F	Immunized	4 days	-	Fever, pain in the throat.	Inflammed and enlarged tonsils with membrane on the right tonsil.	-	Smear and culture positive for *C. diphtheriae*.	Antibiotics	Discharged after 2 weeks.
10	M	Partial	3 days	-	Fever, pain in the throat, difficulty in swallowing.	Inflammed and enlarged tonsils with membrane in the throat.	-	Smear and culture positive for *C. diphtheriae*.	Antibiotics	Discharged after 2 weeks.

susceptible adults and unimmunized children in the same community (Vitek and Wenger, 1998). Recent epidemics of diphtheria in the Ukraine, Russian Federation, and other countries of the former Soviet Union are examples of resurgence due to ineffectively maintained immunization programs (Vitek and Wharton, 1998).

Diphtheria is a resurgent problem in our region affecting both children and adults. The rising number of diphtheria cases in adults in the country with low rates of routine immunization is a matter of concern for public health officials. Priority should be given to reach a high coverage rate with a primary series of DPT vaccine in infants and a 1st and 2nd booster dose in preschool children. At the same time it is also essential to establish a good surveillance system with improved laboratory services with modern laboratory techniques to detect diphtheria as early as possible. There is an urgent need to maintain diphtheria antitoxin in district level hospitals to reduce morbidity and mortality. The implications of the changes in age distribution of diphtheria cases should be further studied by screening for immunity against the disease in the community and if necessary adults should be vaccinated with Td rather than Diphtheria and Tetanus Toxoid (DT) since the side effects with the higher doses of diphtheria toxoid present in DT are more common in older children and adults (CDC, 1991).

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