CASE REPORT

FATAL DIPHTHERIA IN A THAI ADULT

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Diphtheria was recognized as early as the 4th century BC. In 1884, Friedrich Loeffler proved that its etiologic agent was a bacillus. The incidence of diphtheria declined markedly following extensive use of diphtheria toxoid. Now it is considered a rare disease in developed and in most developing countries. However, the case-fatality is still approximately 5% to 10% (Fedson *et al,* 1990). In populations with a high rate of immunization, the improved coverage in children has led to a shift in the age distribution of diphtheria patients to unimmunized or poorly immunized adults (Fedson *et al,* 1990; Feigin, 1992; Tongsonjit *et al,* 1979; Loevinsohn, 1990). We encountered a sporadic case of diphtheria in an adult who lived in Bangkok, an area with a high rate of primary immunization (Busabong, 1992).

A mentally retarded 31-year-old Thai female initially presented with a 3-day history of fever and productive cough. Her immunization record was unknown. On physical examination, she was slightly tachypneic. Her temperature was 38.5°C, blood pressure 100/60 mmHg, heart rate 120 beats/minute and respiratory rate 32/minute. A gray-white patch was found over her injected oropharynx. There were no abnormal cardiopulmonary, abdominal, neurological or cutaneous finding. A complete blood count revealed a hemoglobin of 12 g/dl and a white blood cell count of $33 \times 10^9/l$ with 94% neutrophils and 6% lymphocytes. A gram stain of the pharyngeal patch revealed numerous mixed gram positive coccobacilli and gram negative bacilli. Her chest x-ray showed bilateral diffuse interstitial infiltrations. Three hours after admission, she was noted to have dyspnea and cyanosis. She was intubated and assisted ventilation was started with 100% oxygen. During intubation, the pharyngeal pseudomembrane was found to extend beyond the larynx. Penicillin G sodium 1 million units every 4 hours and a single dose of diphtheria antitoxin 20,000 units were given intravenously. Severe hypoxia could not be corrected by breathing 100% oxygen and her blood pressure dropped. Bilateral pneumothorax was suspected and bilateral intercostal drainage was performed immediately. Severe hypoxia and hypotension persisted and she expired 10 hours after admission. A culture of pseudomembrane revealed moderated growth of toxin producing *Corynebacterium diphtheriae.* At autopsy, the epiglottis and tracheobronchial tree revealed severe inflammation and sloughing of mucosa in the form of a gray-white membrane. Inflammation extended into the small bronchi (Fig 1, 2).

Corynebacterium diphtheriae is a non-motile pleomorphic gram positive bacillus. It is a non-invasive organism and produces an exotoxin which depends on the presence of a lysogenic B phage. The human is the only reservior. Silent carriers of the organism on the skin and in the pharynx are responsible for outbreaks of the disease (Macgregor, 1990; Halsey, 1992).

C. diphtheriae usually causes local infection in the respiratory tract and skin as seen in our case. The pharyngeal infection may extend to laryngeal and trachiobronchial involvement (Feigin, 1992; Halsey, 1992). Mucosal edema and sloughing can embarrass the airway. However complete obstruction is less common in adults due to the larger airway (Halsey, 1992).

After a presumptive diagnosis of diphtheria, administration of a single dose of diphtheria antitoxin intravenously after skin testing is the cornerstone of treatment. The dose of antitoxin depends on the location, the extent of the pseudomembrane and the duration of illness before treatment (Thisyakorn *et al,* 1984). Recommended antibiotics are penicillin and erythromycin given for 14 days. Corticosteroids have no place in treatment of

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diphtheria (Macgregor, 1990). Isolation and supportive care are important. Airway obstruction is the major cause of death and occurs early in the course of the disease. Tracheostomy or endotracheal intubation and removal of pseudomembrane as early as possible are mandatory (Macgregor, 1990).

Diphtheria can be successfully prevented by immunization with formalin inactivated toxin as part of routine childhood immunization. Three doses are given in the first year of life and booster doses at age 18 months and 4-6 years. Moreover, natural immunity may be also important (Limsuwan *et al,* 1978).

In our case, the patient whose immunization history was unknown developed fatal diphtheria in Bangkok where this disease has been controlled by high immunization coverage of children (Busabong, 1992). We know that the reappearance of diphtheria in a population with high rate of immunization occurs almost entirely in patients with diphtheria antibody levels below 0.01 international unit/ml. (Feigin, 1992; Macgregor, 1990). Studies show that the level of antibody increases with the numbers of dose and decreases with age and duration since the last dose. At least 50% of adults are thought to be susceptible to diphtheria especially women and the elderly (Fedson *et al,* 1990; Galazka and Keja, 1988; Karzon and Edward, 1988; Gardner and Schaffner, 1993). Recent outbreaks of the disease in areas with vaccination coverage involved older patients, alcoholics and so call "street people". (Fedson *et al,* 1990; Feigin, 1992; Thongsomjit *et al,* 1979; Loevinsohn, 1990). The susceptibility of adults also reflects diminished natural exposure to subclinical diphtheria infection because of the effect of mass immunization and inadequate compliance with recommendations to complete the childhood vaccination program and receive booster doses of diphtheria toxoid (Macgregor, 1990; Galazka and Keja, 1988). In the United States, it has been shown that almost all cases of adult diphtheria occur in patients who never completed a primary immunization series (Gardner and Schaffner).

There may be a real need for review of the schedule of diphtheria immunization in adults in areas where diphtheria has been controlled by high immunization coverage in children. To avoid diphtheria outbreaks, better compliance with childhood booster dose regimens and perhaps even revaccination should be encouraged. The combined tetanus and diphtheria toxoid (dT), adsorbed, is the preparation of choice for active tetanus and diphtheria immunization of adults (Fedson *et al,* 1990; Macgregor, 1990; Halsey, 1992; Gardner and Schaffner, 1993). Adults should be immunized every ten years or whenever tetanus toxoid is indicated, *eg* in treatment of wounds in an emergency room or when traveling into an endemic area (Fedson *et al,* 1990; Macgregor, 1990; Galazka and Keja, 1988; Garder and Schaffner, 1988; Kjeldsen *et al,* 1985; Gardner and Schaffner, 1993). Most such vaccinations in Thai emergency rooms unfortunately still use only tetanus toxoid and not the combinded product.

ACKNOWLEDGEMENTS

We thank Prof Henry Wilde for reviewing our manuscript.

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