DIPHTHERIA: MAY BE NOT!

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We report a case of *Arcanobacterium haemolyticum* infection in which diphtheria was clinically suspected requiring appropriate medical and public health management until bacteriological results became available.

Diphtheria, an acute illness caused by toxigenic strains of *Corynebacterium diphtheriae*, primarily affects the upper respiratory tract. It is characterized by an inflammatory exudate which forms a greyish membrane and can cause acute obstruction. A toxin produced by the organism can result in neuropathy, cardiomyopathy and death. The introduction of diphtheria antitoxin in the 1890's reduced the death rate to about 10%, but the mortality has not been reduced further by the use of antibiotics and other modern treatments. Symptoms similar to diphtheria may occasionally be caused by microorganisms other than *C. diphtheriae*.

Case Report

A 33 year old man from central Queensland was reviewed by an ear, nose and throat surgeon following acute onset of an extremely sore throat with fever and systemic symptoms. He experienced difficulty swallowing even liquids. Examination revealed a greyish membrane involving the right tonsil but also extending up over the soft palate. His white cell count was elevated at 20.2×10^3 / uL with a left shift (89.9% neutrophils). Heterophile antibody was negative. His ESR was 13 mm / hr. Urgent gram strain of a throat swab showed moderate numbers of leucocytes and gram positive cocci and small numbers of gram positive bacilli. Although not considered characteristic of *C. diphtheriae* this diagnosis could not be excluded. Liver function was mildly abnormal with an aspartate transaminase of 51 U / L and an alanine transaminase of 77 U / L.

The patient reported receiving routine childhood immunisations but no recent boosters for either diphtheria or tetanus. His wife subsequently also developed a sore throat, although 2 and 5 year old sons, both of whom had been vaccinated, remained well. He had not ingested unpasteurized milk, nor had prolonged direct contact with animals. Neither he nor any family members had travelled overseas. Both the patient and his wife had attended a trade exhibition involving many overseas delegates, in the week prior to onset.

The throat swab was inoculated onto tellurite agar, Loefflers slope (and subcultured after 1 day to tellurite agar) as well as blood agar containing a mupirocin disc at the junction of the primary and secondary streaks. All plates were incubated at 35-37°C aerobically.

In view of the clinical suspicion of diphtheria, diphtheria antitoxin was administered prior to bacteriological results becoming available and following consultation with an infectious diseases physician at Fairfield Hospital in Melbourne. Diphtheria antitoxin, which is derived from horse serum, can contain foreign protein and may provoke acute allergic reactions or serum sickness. Therefore the patient was transferred to an intensive care unit for administration of the antitoxin. A test dose and subsequently the full recommended dose was administered without adverse effect. Following this and the administration of high doses of intravenous penicillin and a cephalosporin followed by erythromycin, the patient made a full recovery.

Screening and prophylactic treatment of close contacts was coordinated by the Central Queensland Public Health Unit and carried out by several general practioners in Bundaberg. Nasopharyngeal swabs and throat swabs were collected from nine contacts and prophylactic erythromycin was prescribed prior to culture results becoming available. Subsequently throat swabs from the patient grew *A. haemolyticum* in heavy growth. His wife was found to have a Group A beta haemolytic *Streptococcus*. No screening cultures grew *C. diphtheriae*. Diphtheria toxoid IgG (EIA) performed at the time of onset of his illness demonstrated a low positive result, consistent with past vaccination.

Discussion

This case has been reported to heighten awareness of the potential for a resurgence of diphtheria, a disease with which many practitioners may have become unfamiliar. Diphtheria has become rare in Australia, unlike other vaccine preventable diseases such as rubella, pertussis and measles that have occurred at epidemic levels recently. Following the introduction of immunisation in the 1940s the number of cases has dropped dramatically. A single case of diphtheria was notified in 1993, 14 cases in 1992 and 8 cases were notified in 1991[1]. It is uncertain if these notified cases represent clinical cases of diphtheria. Patel *et al* report the isolation of 63 (24 toxigenic and 39 nontoxigenic) isolates of *C. diphtheriae* from predominantly Aborigi-

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nal patients over a 10 year period[2]. Only two had signs of faucal diphtheria.

Since 1990, however, there has been a major resurgence of diphtheria in Europe, centred mostly in Russia and Ukraine[3]. The outbreak in the Russian Federation is the largest outbreak in the developed world in recent years and has been the focus of global concern. Increasing international travel, migration from Eastern Europe and the emergence of epidemic clones means that accurate epidemiologic surveillance, reliable laboratory screening and clinical awareness are necessary. Although the reasons for the diphtheria epidemic are not fully understood, the presence of large numbers of susceptible children and adults has enabled the introduction or re-emergence of toxigenic strains of *C. diphtheriae*. Spread of the organism may have been facilitated by crowding and population migration resulting from the dissolution of the Soviet Union. In addition, adequate control measures were not implemented during the early phase of the epidemic.

Since many of the cases in Russia have been in young adults, waning vaccine induced immunity without the opportunity for natural boosting from exposure to the disease may have contributed to the resurgence. This highlights the importance of decennial booster vaccinations (in conjunction with tetanus) throughout adulthood for maintenance of immunity to diphtheria. A high primary vaccination rate must also be maintained. Routine cultures on throat swabs are unlikely to detect the presence of *C. diphtheriae* and if suspected, the laboratory should be alerted so that appropriate culture techniques can be performed[4].

This case is also reported to increase awareness of *A. haemolyticum* as a potential cause of bacterial pharyngitis in the community. Its commonest presentation is with a patchy follicular exudative pharyngitis often with a scarlatiniform rash (33-64%). Adolescents and young adults are more likely to be infected. Less commonly, it may cause a diphtheria like illness with the formation of a pseudo diphtheric membrane, a septicaemic illness or peritonsillar abscess[5-7]. It is likely to be more common than previously realised. Over a one year period one laboratory isolated the organism from 0.8% of throat swabs cultured[8]. In the 15-25 years age group, the isolation rate was 2.5%, which was just under half as frequent as Group A *Streptococcus* in this age group. One investigator has estimated that *A. haemolyticum* is almost as likely as Group A *Streptococcus* to cause pharyngitis, if a rash is present, in the 11-20 years age group[9].

Previously known as *Corynebacterium haemolyticum*, this organism may be misidentified as either a diphtheroid organism of *Corynebacterium* spp or dismissed as a contaminant or 'normal flora'. Characteristic haemolysis around the bacterial colonies does not develop until 48 hours or more after incubation when plates may have been discarded. This may contribute to the low rate of reported isolation. The current antibiotic treatment recommendation is erythromycin. Although the organism is sensitive to penicillin, antimicrobial tolerance with clinical relapses has been described[10].

References

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National Health and Medical Research Council recommendations on diphtheria immunisation[1]

- Diphtheria vaccine in the form of diphtheria tetanus pertussis vaccine (DTP) should be given to all infants and children according to the Standard Childhood Vaccination Schedule at the ages of 2 months, 4 months, 6 months, 18 months and prior to school entry (4-5 years).
- Older individuals who have not received diphtheria vaccination should receive a primary course. These individuals are also likely to have missed vaccination against tetanus and, in the case of children, pertussis.

  Prior to the 8th birthday a primary course is three doses of DTP at intervals of two months.

  After the 8th birthday primary vaccination is 3 doses of adsorbed diphtheria tetanus vaccine (ADT) at intervals of 2 months.
- Protective antibody levels wane with age and booster doses should be given in the form of ADT at 10 year intervals.
- Diphtheria can be a significant risk for travellers in some countries so international travellers should ensure that their diphtheria vaccination is current.

Based on: National Health and Medical Research Council. *The Australian immunisation procedures handbook, fifth edition*. Canberra: Australian Government Publishing Service, 1995.

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