Suspected diphtheria

An 8-month-old previously well infant was referred from a secondary hospital to Red Cross Children's Hospital in Cape Town (Western Cape Province) on 13 August 2013 with an initial diagnosis of croup. There was a three-day history of fever, cough, tachypnoea, 'sores in the mouth' and poor feeding. The child was resident in Western Cape Province and there was no history of recent travel. Clinically, the child had a barking cough, excessive salivation and stridor with rapidly progressive respiratory distress that was unresponsive to adrenaline nebulisation and necessitated intubation. On examination of the mouth and throat, there was marked halitosis, redness of the uvula and normal tonsils, but no associated lymphadenopathy. During intubation under anaesthesia, a necrotic appearance of laryngeal structures, cords and subglottic area was noted, and swabs were taken; these samples were submitted to the bacteriology laboratory for routine microscopy and culture as well as culture on selective media for *Corynebacterium diphtheriae*. Ampicillin, gentamycin, fluconazole and aciclovir were administered to the patient.

Laboratory results showed procalcitonin of 185 ng/mL and WCC of 1.1 x 10^9/L which subsequently increased to 1.7 x 10^9/L (4% neutrophils, 39% monocytes, 52% lymphocytes, 3% band cells and 2% metamyelocytes). Although diphtheria was initially deemed unlikely as the child had received all age-appropriate vaccinations, the findings on laryngoscopy of a thick white adherent membrane that bled and revealed marked underlying inflammation on attempts to dislodge it raised concerns about possible diphtheria in this case. Histologically, the membrane showed areas of necrosis consistent with, but not diagnostic for, diphtheria. Additional swabs were submitted and cultured on selective media for *C. diphtheriae*. The case was notified to provincial and city health authorities as a suspected diphtheria, and specific patient management and appropriate public health response were initiated. The patient was isolated, and standard plus droplet precautions were instituted.

The initial management of the infant focussed on respiratory support and antibiotic treatment, and the process to procure diphtheria antitoxin (DAT) was initiated. Four days after initial presentation, 50 000 units of equine DAT was obtained and administered intravenously without adverse events. On day 6 of hospitalisation the child was successfully extubated, and eventually discharged home with no apparent sequelae of the illness. *C. diphtheriae* was not isolated from any specimens taken during hospitalisation; possible explanations include receipt of antibiotics prior to sampling, delay in transport of specimens to laboratory, and alternate diagnoses.

Pharyngeal swabs were taken on all household contacts, who also received erythromycin chemoprophylaxis and were monitored for symptoms. The infant's mother complained of a sore throat 3-4 days after her child was admitted; she was moved from the shared overnight accommodation and isolated, swabs were taken, and she was treated with appropriate antibiotics following which her symptoms improved rapidly. *Streptococcus pyogenes* was isolated from the mother's pharyngeal swab. Diphtheria vaccine was given to all household contacts as well as to ICU staff who had been in contact with the child.
Through the EPI programme, diphtheria immunisation is offered at 6, 10 and 14 weeks with boosters at 18 months as well as 6 and 12 years of age. The infant had in fact been fully immunised against diphtheria and did not require a booster, since antibody tests taken on admission showed protective titres of antibodies to diphtheria toxin.

The last laboratory confirmed case of diphtheria in South Africa was in February 2010 (reported in the February 2010 Communiqué). Although diphtheria is an uncommon disease in South Africa, there is concern that this potentially lethal disease may resurge, as it has in other regions of the world over the past decade - most notably Eastern Europe, Southeast Asia, South America and the Indian subcontinent. It is important that clinicians are aware of the range of clinical presentations and appropriate investigations in order to detect cases timeously and limit mortality. A presumptive diagnosis of diphtheria may be based on a number of clinical clues, including: mildly painful tonsillitis/pharyngitis associated with an exudate/membrane; adenopathy and cervical swelling; hoarseness and stridor; palatal paralysis; serosanguinous nasal discharge with associated mucosal membrane, and low-grade fever. Absorption of diphtheria toxin from the site of infection can cause systemic complications, including cardiac toxicity (myocarditis, acute congestive failure), neurotoxicity (paralysis of soft palate, cranial neuropathies and peripheral neuritis) and renal toxicity (renal failure). Confirmation of the diagnosis relies on the isolation *C. diphtheriae* from appropriate specimens; specimens should be taken from the nose and throat, and from beneath the membrane, if present. Multiple site sampling should always be considered

in a suspected case as this may increase the organism recovery rate. The specimens must be sent to the laboratory immediately since rapid inoculation of special culture media is extremely important for organism recovery; if the transportation is likely to be delayed, the specimens must be submitted in a suitable transport medium (e.g. Amie's). The laboratory must be contacted beforehand to ensure that the selective media is available and that the specimen is processed immediately on arrival. Following isolation of *C. diphtheriae,* the isolate/s are subjected to testing for toxigenicity since non-toxigenic *C. diphtheriae* may be isolated but do not cause clinical diphtheria.

The mainstay of treatment of a case of suspected diphtheria is prompt administration of DAT; this should be given without waiting for laboratory confirmation of a diagnosis. DAT only neutralises toxin before its entry into cells so it is critical that DAT be administered as a matter of urgency. The recommended dosage and route of administration depend on the extent and duration of disease. Antibiotics should also be given to suspected diphtheria cases, in order to eradicate carriage of the organism, limit transmission, and stop further production of diphtheria toxin. The current recommendations for antibiotic therapy of diphtheria include erythromycin or penicillin. Management of contacts should include screening for possible respiratory diphtheria, obtaining nasopharyngeal cultures for *C. diphtheriae,* administering chemoprophylaxis, and assessing diphtheria vaccination status.

Unfortunately, there are currently few manufacturers of DAT globally and supplies are limited to few facilities/institutions worldwide. South Africa does not stock any supplies of DAT, and it needs to be sourced from overseas suppliers on a case-by-case basis through an emergency MCC Section 21 application. DAT was sourced for this patient with the assistance of the Centers for Disease Control and Prevention (Atlanta, USA) and supplied by the Ministry of Health in Israel through an emergency MCC Section 21 application. The generous support and assistance of the many persons involved locally and internationally in this process and the rapid response to the call for DAT are gratefully acknowledged.

Source: Clinicians at Red Cross Children's Hospital; Groote Schuur NHLS laboratory; Western Cape Department of Health; Department of Public Health Surveillance and Response, NICD-NHLS