CASE REPORT

A 9-year-old boy with severe diphtherial infection and cardiac complications

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SUMMARY

The incidence of diphtheria has decreased since the introduction of an effective vaccine. However, in countries with low vaccination rates it has now become a re-emerging disease. Complications from diphtheria commonly include upper airway obstruction and cardiac complications. We present a 9-year-old boy who was diagnosed with diphtheria. He presented with fever, tonsillar plaques, respiratory failure and an incomplete vaccination history. He was endotracheal intubated and received diphtheria antitoxin and penicillin on the first day of hospitalisation. He developed progressive arrhythmias and fulminant myocarditis despite early identification and treatment with equine antitoxin and antibiotics. After a temporary transvenous pacemaker insertion due to third-degree atrioventricular block and hypotension for 1 week, he developed myocardial perforation from the pacemaker tip resulting in pericardial effusion. The treatment included emergency pericardiocentesis and pacemaker removal. His electrocardiogram showed a junctional rhythm with occasional premature ventricular complexes. He then developed ventricular tachycardia and cardiac arrest and finally died.

BACKGROUND

Diphtheria is a vaccine-preventable, but potentially fatal disease. The burden of disease lies mainly in developing countries.¹ Severe cases of diphtheria commonly present with a bull neck, cyanosis, dyspnoea and hoarseness. Death typically results from toxin-mediated tissue destruction and necrosis causing myocarditis and respiratory failure.^{2–4}

Paediatric diphtheria with significant symptoms is associated with myocarditis in 10–16.5% of cases and typically presents within 2 weeks of the initial infection.^{4–8} A study in severe diphtheria reported that all patients showed evidence of myocardial involvement.⁶ Diphtheritic myocarditis is associated with a mortality rate of 14–75% and severe conduction abnormalities including complete heart block, which is often fatal.^{3 5–11} Even after the recovery period, patients can have persistent or progressive conduction defects.^{12–14} A 10-year retrospective review in Bangkok identified 38 paediatric patients with diphtheria and cardiac complications. Common cardiac complications included myocarditis, cardiac dysrhythmia, heart block and non-specific ECG changes. The overall case fatality rate was 5.8% and there were significant associations between death and the presence of a bull neck, laryngeal patch, upper airway obstruction and cardiac complications.¹⁵

CASE PRESENTATION

A 9-year-old boy was referred to the Chiang Mai University Hospital (CMUH) with a low-grade fever, cough and sore throat for 5 days. On the first day of illness he had been taken to a rural clinic and diagnosed with pharyngitis. The patient was prescribed an unknown oral antibiotic and acetaminophen. By the third day of illness his fever had gradually declined and the sore throat had resolved. However, he subsequently became worse and experienced neck swelling, dyspnoea and dysphagia. He also had a harsh breathing sound. On the fifth day of illness his parents took him to a local hospital. His vital signs showed a blood pressure of 110/90 mm Hg, heart rate of 153 bpm, temperature of 37.5°C, respiratory rate of 22 breaths/min and room air oxygen saturation of 75%. His tonsils were inflamed and had white patches, and he had inspiratory stridor and poor air entry but no adventitious sounds. He was subsequently endotracheally intubated at the local hospital and had copious amounts of white as well as bloody secretions suctioned from the tube. A nasogastric tube was placed and revealed 20 mL of fresh blood and a substantial amount of coffee ground emesis. He was given a bolus dose of normal saline (20 mL/kg) and 2 g of ceftriaxone before referral to our hospital. The laboratory results from the local hospital were significant for a leucocytosis of 30 300 cells/mm³ and a high creatinine level of 1.7 mg/dL.

On initial evaluation at our hospital, the patient was afebrile (37.5°C), had tachycardia (130 bpm), a normal respiratory rate (20 breaths/min) and normal blood pressure (106/74 mm Hg). His weight was 22 kg (10th centile) and his height was 130 cm (50th centile). He was fully alert. He was also able to follow commands, move all his extremities equally well and open his eyes spontaneously. His pupils were equal, round and reactive to light with normal accommodation. The examination revealed bilateral neck tissue swelling that was soft, tender and without fluctuation or rash (figure 1). His tonsils were enlarged, bleeding and had white patches on them. His lungs were bilaterally clear to auscultation.

The patient was born at a rural hospital in Thailand via normal vaginal delivery and his birth weight was 2700 g. He had received Bacille Calmette-Guérin and hepatitis B vaccinations at birth, but not any other additional vaccinations. He had no known previous medical problems. In the patient's house there were a total of nine people including his mother, grandparents, aunt and cousins. The patient had no history of close contact with other sick patients.

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Figure 1 Photographs of the patient on admission to Chiang Mai University Hospital on the fifth day of illness showing bilateral neck tissue swelling.

INVESTIGATIONS

The complete blood count was notable for haemoglobin (11.4 g/dL), haematocrit (31.4%), a white cell count of 22 600 cells/mm³ (neutrophils 74%, lymphocytes 12% and monocytes 11%) and platelet count of 80 000/mm³. The patient's blood urea nitrogen (40 mg/dL) and creatinine (1.0 mg/dL) were elevated at admission. Liver function tests and erythrocyte sedimentation rate were within normal limits. Urinalysis showed 5–10 red blood cells per high-power field, 10–20 white cells count per high-power field, 2+ albumin and trace glucose.

The troponin T level was 74 ng/mL (normal <14) and creatine kinase-MB level was 7.6 ng/mL (normal 0.63–5.1). Pro-brain natriuretic peptide was 1236 ng/L (normal <355 ng/L for age 8–13 years). A throat swab Gram stain showed Gram-positive bacilli (figure 2). A throat swab culture showed *Corynebacterium diphtheriae*. The Elek test for detection of toxigenic *Corynebacterium* strain was positive.

A chest radiograph showed bilateral neck swelling and patchy right lower lobe infiltration. The ECG on the first day of admission

Figure 2 Throat swab Gram stain showing Gram-positive bacilli.

was unremarkable showing a normal sinus rhythm at 90 bpm without significant ST segment changes, a left ventricular ejection fraction of 55% (within normal range), cardiac output of 2 L/min, cardiac index of 2.5 L/min/m², mild tricuspid regurgitation, no chamber enlargement and no pericardial effusion.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses included pharyngeal diphtheria with myocarditis, infectious mononucleosis, retropharyngeal abscess, acute epiglottitis, severe pneumonia and exudative tonsillitis.

TREATMENT

On the first day of hospitalisation the patient was started on diphtheria antitoxin (120 000 units intravenously, after hypersensitivity testing), penicillin G (200 000 U/kg/day intravenously every 6 h), cefotaxime (150 mg/kg/day intravenously every 6 h) and milronone. Intravenous methylprednisolone (2 mg/kg/day) was also given to treat the patient's severe myocarditis.

OUTCOME AND FOLLOW-UP

On the third day of hospitalisation the patient became bradycardic (80 bpm) but was asymptomatic and had normal blood pressure. ECG showed an ectopic atrial rhythm (inverted P wave in lead II) and incomplete right bundle branch block (figure 3A). The patient was subsequently given immunoglobulin (IVIG 1 g/kg/day) to treat the severe myocarditis.

Later he developed a third-degree atrioventricular (AV) block with a rate of 40–70 bpm (figure 3B) and hypotension (90/50 mm Hg). A temporary transvenous pacemaker was inserted via the right internal jugular vein with echocardiographic guidance, and the tip of the pacemaker was placed properly on the right ventricular apex. The pacemaker rate was set to 80 bpm and the patient had no additional hypotensive episode (figure 3C). Chest radiography after pacemaker insertion confirmed that the pacing catheter was in proper position.

On the 10th day of hospitalisation the follow-up ECG showed that the tip of the pacemaker had penetrated the myocardium (figure 4) and the patient had a moderate amount of pericardial effusion. Percutaneous intrapericardial catheter drainage was performed and thereafter the pacing catheter was removed. Approximately 200 mL of bloody pericardial fluid was drained. The patient remained bradycardic (60 bpm) and hypotensive (93/67 mm Hg). ECG showed a junctional rhythm with occasional premature ventricular complexes (figure 3D). Repeated ECG 2 h later showed no increase of the pericardial effusion. The patient remained in a junctional rhythm (40–60 bpm) but had no further dysarrhythmias and hypotension.

On the 13th day of hospitalisation, the ECG showed a new onset of complete left bundle branch block, which indicated ongoing conduction system damage from diphtheria toxin. Later, the patient developed ventricular tachycardia (200 bpm) and received inotropic drugs (dobutamine and amiodarone). However, he still had hypotension and underwent synchronised cardioversion (1 J/kg). The heart rates were converted to a junctional rhythm (80 bpm) for a short period; the patient then had repeated ventricular tachycardia and underwent a second synchronised cardioversion (2 J/kg). After that his heart rates were converted to a normal sinus rhythm and an ECG showed a minimal pericardial effusion with an ejection fraction of 45%.

On the 16th day of hospitalisation, the patient's cardiac function was getting worse and the ECG showed an ejection fraction of 8%. He then received a maximum dose of milrinone and dobutamine. He subsequently had an asystolic cardiac arrest and

Figure 3 ECG showing: (A) ectopic atrial rhythm (inverted P wave in lead II) and incomplete right bundle branch block; (B) third-degree atrioventricular (AV) block (AV dissociation); (C) left bundle branch block (after temporary transvenous pacemaker insertion); (D) junctional rhythm and rare premature ventricular complexes (after temporary transvenous pacemaker removal).

Figure 4 ECG showing the pacemaker tip (white arrow) in the patient's right ventricle.

died. The major cause of death was suspected to be progressive fulminant myocarditis.

The patient's household contacts were investigated and chemoprophylaxis with erythromycin for 10 days was performed by a local public health centre. There were no diphtherial carriers and no outbreak in the community resulted from this patient.

DISCUSSION

This is a case of a 9-year-old boy who presented with subacute fever, soft tissue neck swelling, tonsillar plaques, respiratory failure and history of incomplete vaccination. The patient developed fulminant myocarditis with progressive arrhythmias.

After immunisation against diphtheria was introduced in the Expanded Programme on Immunisation in 1977, diphtheria has gradually decreased in Thailand. According to the Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health of Thailand, the incidence of diphtheria in Thailand was 2–13 cases per year from 2002 to 2009¹⁶ with an overall case fatality rate of 15.87%. The most common complication of childhood diphtheria in Thailand is upper airway obstruction as reported in 42.3% of cases.¹⁵

The primary aim of emergency tracheostomy is the management of upper airway obstruction. In our patient, the intubation process may have introduced diphtheria to his lower respiratory tract. Therefore, we recommend that physicians avoid endotracheal intubation in such patients to prevent the spreading of bacteria.

Cardiac involvement is the second most common complication of childhood diphtheria. Myocarditis was reported in 10% of diphtheria cases in a case series from Thailand and in 16.5% in a retrospective case series from India.^{10–15} Common cardiac complications were myocarditis, cardiac dysrhythmia, heart block and non-specific electrocardiographic changes of, mostly, the ST segment or T-wave. A study in Vietnam reported that 93% of patients had prolonged QT intervals, usually present on the first recording.⁶ In a retrospective observational study from Thailand there were significant associations between death and the presence of a bull neck, laryngeal patch, airway obstruction and cardiac complications,¹⁵ as in our case.

Common ECG changes in diphtheria are prolongation of the PR interval, T-wave abnormality, intraventricular conduction delay and AV conduction block.¹⁷ Acute fulminant myocarditis with progressive arrhythmia is the major cause of death. The left bundle branch block, as occurred also in our case, was associated with a mortality rate of 50–58%.^{10–17} There was a significant association between the rate of ventricular ectopy present at the time of admission to the hospital and mortality. A 24 h Holter ECG was also useful in predicting the development of symptomatic diphtheritic cardiomyopathy after hospital admission. Initially, this patient presented with first-degree AV block with normal left ventricular ejection fraction; thereafter, sinoatrial node dysfunction and complete AV block; and finally a left bundle branch block and decreased left ventricular ejection fraction. The electromechanical dysfunction was most likely caused by the myocardial injury, which was confirmed through the presence of elevated cardiac enzymes.

Studies on the role of temporary transvenous pacemakers in diphtheritic myocarditis have shown varied results. Case series of diphtheritic myocarditis with temporary transvenous pacemaker placement report case fatality rates that range from 56% to 100%.¹¹ Insertion of a pacemaker in children and adolescents who are severely ill with diphtheria is a difficult and potentially life-threatening procedure. Pacemaker insertion can cause complications including infection, thrombus formation and

myocardial perforation, which occurred in our patient. Clues for diagnosis of myocardial perforation include a new pericardial effusion and increasing of the pacing threshold. In this case, late onset of cardiac perforation could not be prevented. Estimates of myocardial perforation after transvenous pacemaker insertion range from 0.5% to 3%.^{18–20} In a previous study, the rapid development of conduction disturbances (before day 10 of the illness), the presence of a bleeding diathesis and the development of acute renal failure before insertion of the pacemaker were poor prognostic indicators.²¹

In general, the therapy for myocarditis during the acute phase in children includes supportive care to maintain haemodynamic stability and adequate systemic perfusion. In fulminant cases mechanical support of the circulation with extracorporeal membrane oxygenation or a ventricular assist device followed by cardiac transplantation may be necessary.

Children with diphtheritic myocarditis are challenging to manage. Often, several organ systems are affected by the infection and toxin. Disease prevention through vaccination and early identification/treatment are the major keys in reducing the morbidity and mortality of this particular disease.

Learning points

- ▶ Paediatricians should routinely check vaccination histories and schedules of all children under their care, especially newly migrated children.
- ▶ Physicians should avoid endotracheal intubation in diphtheria with upper airway obstruction because it could introduce bacteria to the lower respiratory tract causing severe complications and mortality.
- ▶ Diphtherial cases with cardiac complications treated with transvenous pacemakers should be followed-up intermittently for complications such as pericardial effusion and cardiac perforation.

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Contributors Sina wrote the proposal, collected data, wrote the manuscript and read the final draft. CHW and KM wrote and edited the manuscript and read the final draft. PO wrote the proposal, the manuscript, supervised the overall work and read the final draft of the manuscript.

Competing interests None.

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