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Atrioventricular Block in a Toxic Child: Do Not Forget Diphtheria

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Abstract. We describe a 4.5-year-old girl who presented with severe febrile throat infection and who, after a few days, developed ventricular tachycardia followed by atrioventricular block. Although a pacemaker was inserted, she died of cardiogenic shock. Throat cultures were positive for *Corynebacterium diphtheriae.*

Key words: Diphtheria — Immunization — Atrioventricular block — Pacemaker

Diphtheria is extremely rare in developed countries: in the United States, fewer than five cases annually have been reported in recent years [1]. In Israel, only one other case, also fatal, was reported between 1976 and 1996 [6]. However, diphtheria remains endemic in many countries with inadequately immunized populations. Up to two-thirds of patients show some evidence of myocarditis and 10% to 25% develop clinical cardiac dysfunction. The risk for cardiac dysfunction is directly correlated to the extent and severity of local disease in the patient [11].

Case Report

A 4.5-year-old girl was admitted to the emergency room at Hadassah Hospital in Jerusalem following a week of fever and sore throat. During the 5 days preceding admission, there had been low-grade fever, purulent nasal discharge, and bilateral neck swelling with refusal to drink. She had been examined by many physicians, but despite repeated recommendations for hospitalization the parents preferred to treat her with home remedies, with no improvement. On the day of admission, her general condition had deteriorated and she was brought to the emergency room.

The child was born at home with the assistance of a midwife following an uneventful pregnancy. Because her parents did not notify the Department of Interior of her birth, she was unknown to health providers in Jerusalem and therefore there was no community outreach. There was no known history of family illnesses and she had no known allergies or illnesses; this was her first hospital admission. No immunizations against any vaccine-preventable diseases had been administered because of family beliefs against conventional medicine.

On examination, the girl appeared ill, pale, and thin with mild dehydration and minimal neck stiffness. She was not dyspneic and had normal saturation at room air. Skin examination revealed a petechial–purpuric rash. She suffered from malodorous purulent throat mucus and bright gray necrotic masses were seen around the tonsils. Heart, lungs, and abdomen were normal, as were the neurological findings. Preliminary laboratory results revealed normal blood pH, pO_2, pCO_2, and HCO_3; hemoglobin, 12.7 g/dl; leukocytosis with 25,000/mm^3 white blood cells. Differential count showed 75% granulocytes and thrombocytopenia with 16,000/mm^3 platelets. Blood electrolytes were normal; creatinine phosphokinase 94 U, and myocardial band isoenzyme fraction 0%. Electrocardiogram showed normal sinus rhythm (100 beats per minute). Chest x-ray showed normal cardiac silhouette.

A clinical diagnosis of diphtheria was made. She was treated with erythromycin, penicillin, gentamicin, and platelets. Diphtheria antitoxin was not available and could not be obtained within the following 48 hours. The admission echocardiogram was normal, but on the second day she developed sudden severe bradycardia (20 beats per minute) and shock. Resuscitation was performed and improvement followed, but rhythm disturbances continued. Ventricular tachycardia was treated with lidocaine and an electrocardiogram showed complete atrioventricular (AV) block. A temporary pacemaker was inserted with clinical improvement and restoration of normal blood pressure, but during the next 6 hours the ventricular function gradually deteriorated despite increasing doses of vasopressors. After a long period of cardiac resuscitation (50 minutes), the child died with the clinical and echocardiographic picture of cardiogenic shock.

The family refused autopsy. Biopsy of a necrotic lesion showed fibrinopurulent discharge mixed with necrotized squamous cells. Throat and nose cultures, obtained at admission, were reported as positive for *Corynebacterium diphtheria* after her death.

Discussion

The diphtheria bacillus was first isolated 115 years ago by Friedrich Loeffler [10]. *Corynebacterium diptheriae* is the pathogen responsible for the development of pharyngeal diphtheria. After invasion by a bacteriophage, the organism produces an exotoxin causing local tissue necrosis and, when absorbed into the bloodstream, sys-

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temic complications including cardiac, neurological, hepatic, and renal damage. Cardiac damage, which occurs in 10% to 25% of patients, involves the myocardium and the conduction system. Histological changes in the heart include edema, congestion, infiltration by mononuclear cells, and fatty changes within muscle fibers and the conduction system [9]. Electrical disturbances are common and include bradyarrhthmia, tachyarrythmia, AV block, and bundle branch blocks. In a recent study of 46 children with diphtheric myocarditis, all 7 patients with third-degree AV block died despite pacemaker implantation [12]. It was suggested that AV block is probably a sign of extensive carditis and that, in this situation, pacing cannot restore cardiac function. Myocarditis death is up to 60%, with most deaths occurring within the first 3 or 4 days.

Behring and Kitasato discovered the antitoxin to diphtheria more than 100 years ago [5]. The disease was endemic in most countries until the introduction of mass immunization programs in the 1940s and 1950s. At the beginning of the century, diphtheria was the leading infectious killer of children [8]; it has become rare in countries with efficient immunization programs: in the United States, fewer than five cases have been reported annually in recent years [1]. Despite reductions in disease incidence and availability of antitoxin treatment [4], diphtheria remains endemic in many developing countries, with noncutaneous diphtheria fatality rates between 5% and 10% in most countries. In the former USSR, overall reported cases of diphtheria increased from 839 in 1989 to approximately 48,000 in 1994 [2]. The reasons for this outbreak are not fully understood, but contributing factors probably include lapses in vaccination coverage and spread of toxigenic strains of *C. diphtheriae,* facilitated by crowding and population movements associated with the disintegration of the Soviet Union [2]. Another outbreak is reported to have occurred in 1994 in Thailand [3]. In Israel, diphtheria is extremely rare: the only other reported case in the past 20 years occurred in 1988 in a never-vaccinated 6-year-old boy who died of the disease [6].

This case is a good example of a disease in which, due to its rarity in many countries, diagnosis and treatment are often delayed. Although diphtheria was suspected by the referring physician, there was debate regarding this diagnosis, even among the infectious diseases specialists. The staff was not fully aware of the potential for rapid deterioration despite administration of adequate antibiotic treatment. Moreover, intensive efforts to find the antitoxin in Israel were unsuccessful, so it could not be administered prior to the child's death.

One must question whether the current control measures are adequate. In Israel, immunization with diphtheria toxoid has been routinely recommended and administered since 1951. The current protocol consists of five doses, one each at 2, 4, 6, and 12 months of age, and a booster dose in the third grade (8 or 9 years). Coverage levels in Israel exceed 90%. However, this child came from an ultra-Orthodox Jewish neighborhood in which immunization coverage is only 60%. In such a population, there is a high probability of sporadic cases and potential for an epidemic.

Localized outbreaks can occur even among populations with high immunization rates. The reappearance of diphtheria in Scandinavia [7], with an immunization rate of 95% to 99%, should spark a red alert in all regions of the world, regardless of immunization efficiency. Medical staff should be oriented to and informed about the possibility of diphtheria and antitoxin preparations made readily available within hours. Although diphtheria antitoxin neutralizes circulating toxin, it has no effect on toxin that is bound to the tissue, so the antitoxin must be administered as soon as possible. Such steps could prove instrumental in preventing further fatalities from this rare, yet dangerous, disease.

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