A report of two pediatric tetanus cases

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SUMMARY: Aydın-Teke T, Bayhan Gİ, Afşarlar ÇE, Öz FN, Akansel AR, Tanır G. A report of two pediatric tetanus cases. Turk J Pediatr 2011; 53: 437-440.

Tetanus is still a difficult-to-treat disease with high morbidity and mortality. Although it most commonly occurs in non-immunized children, it can also be seen in partially immunized or immunized children[11]. We report herein two pediatric cases of generalized tetanus. Case 1 presented with signs of acute abdomen, while Case 2 presented with the typical clinical findings of tetanus. In this report, we highlight the importance of obtaining a history of the vaccination status of pediatric patients as an essential part of the evaluation. Furthermore, the differential diagnosis of non-immunized children with abdominal rigidity should include generalized tetanus.

Key words: tetanus, muscle spasms, acute abdomen, antitoxin, vaccine.

Tetanus is a vaccine-preventable disease and is more common in developing countries. The incidence of tetanus varies throughout the world. In the United States, the average annual incidence rate during 1998-2000 was 0.16 cases per million population[1]. Italy has the highest reported number of tetanus cases among European countries, with an estimated incidence of 0.2/100,000 in the 1990s[2]. Tetanus is a Class A notifiable disease, and the incidence of tetanus is 0.02 per 100,000 population in Turkey[3]. According to the Ministry of Health of Turkey, 11 cases were reported in 2000, 16 cases in 2002, 10 cases in 2006, 14 cases in 2007, and 14 cases in 2008.

Case Reports

Case 1

A previously healthy six-year-old male was admitted to our hospital with anorexia and abdominal pain. On physical examination at admission, he had abdominal tenderness and defense with palpation. His physical examination was otherwise unremarkable. Blood analysis was significant only for an elevated white blood cell count to 36,800/ml (80% neutrophil, 10% lymphocyte, 8% monocyte, 2% basophil) and C-reactive protein (CRP) to 99.8 mg/L (reference value: 0-8 mg/L). Serum urea, electrolytes, calcium, and magnesium were in normal ranges. Abdominal ultrasonography demonstrated only 17x6 mm mesenteric lymphadenopathy. Because of the suspicion of perforated appendicitis, exploratory laparotomy was performed. Approximately 10 hours after laparotomy, muscle spasms triggered by stimuli and trismus were observed. Thus, the child's history was retaken and revealed a minor foot injury involving a nail one week before admission. The wound area was cleaned and one dose tetanus toxoid vaccine was given; no tetanus antitoxin or tetanus immunoglobulin had been given in another emergency department. On the re-examination, a small healing wound on his left foot was detected. In a few hours, risus sardonicus and opisthotonus developed. The diagnosis of generalized tetanus was made on the basis of clinical manifestations in combination with a history of missed childhood vaccinations and the recent history of injury with incomplete prophylaxis. He was monitored in a silent, dark room with limited disturbance. Treatment was initiated immediately with the administration of tetanus antitoxin (75,000 IU: 25,000 IU tetanus antitoxin was administered intravenously (iv), and the remaining 50,000 IU was administered in 4 equally divided doses

intramuscularly (im) to all extremities after testing for sensitivity and desensitization) and metronidazole (30 mg/kg/day iv). Sedation and relaxation consisted of diazepam (0.1 mg/kg/dose iv). Despite treatment, his condition continued to deteriorate over a few hours. He was intubated, and mechanical ventilation and fentanyl (1 μg/kg/h iv) and midazolam (1 μg/kg/min) infusion were started, but the frequency and severity of muscle spasms and trismus significantly worsened. The dosage of diazepam was increased and phenobarbital was added to the regimen. His condition progressively worsened with tachycardia and hypertension. Electrocardiogram showed ST segment changes. Propranolol (2 mg/kg/day by nasogastric tube) and magnesium sulfate (25 mg/kg/dose iv) were started. Creatine kinase (CK)-MB, troponin-I levels and bedside echocardiography were normal. CK, potassium and phosphorus levels were elevated. After the findings of rhabdomyolysis and severe acidosis ensued, he experienced cardiac arrest with no response to cardiopulmonary resuscitation maneuvers.

Case 2

A 15-year-old male presented to our hospital with a one-week history of jaw pain and difficulty in opening his mouth and chewing. For the last two days, he could barely walk and was experiencing back pain. There was a history of injury to his right heel while collecting rubbish. No prophylaxis for tetanus had been administered after the injury. His childhood immunization schedule was completed initially with three vaccinations in the first year of life and a first tetanus booster. Due to the family's poor socioeconomic condition, he could not attend school and was thus not vaccinated in primary school. On the physical examination, he had generalized muscular rigidity, trismus, risus sardonicus facies, rigid abdomen, and nuchal rigidity. He could sit and walk with difficulty. The trismus of the patient was moderate, such that he could speak and swallow. There was abdominal rigidity without tenderness. He did not have opisthotonic posture. There was a healing wound measuring 2x2cm on the right heel. The rest of the examination was unremarkable. Blood analysis, CRP, and serum urea, electrolytes, calcium, and magnesium were in normal ranges. On the basis of the history of a dirty wound without tetanus prophylaxis and presence of tetanus clinical findings in the incompletely vaccinated patient, the diagnosis of generalized tetanus was established. He was treated with tetanus antitoxin, intravenous antibiotics and diazepam. Tetanus immune globulin (TIG) was not available; therefore, tetanus antitoxin at a dose of 75,000 IU was given as mentioned above. Metronidazole (30 mg/kg/day iv) was started. Sedation and relaxation consisted of diazepam 0.2 mg/kg/dose per 6 hours. On the 8th day of hospitalization, his muscle spasms began to decline. On the 12th day from onset of the illness, muscle spasms completely resolved. He was discharged from the hospital 15 days after admission.

Discussion

Tetanus is caused by *Clostridium tetani*, a gram-positive, spore-forming, anaerobe bacillus. It produces its clinical effects via a powerful exotoxin (tetanospasmin) that disrupts neurotransmitter release in inhibitory neurons, leading to peripheral muscle rigidity and spasms. It is not transmitted person to person. Most cases of tetanus occur in unvaccinated individuals and in adults.

Prevention of tetanus is through vaccination, which is highly safe and efficacious. Tetanus toxoid was first produced in 1924 and tetanus toxoid immunizations were used extensively in the armed services during World War II[4]. Routine childhood vaccination began in Turkey in 1989. In our country, the complete immunization schedules end with the 6th dose of the vaccine in the 8th grade of primary school. Afterwards, men are vaccinated during their military service and women during pregnancy against neonatal tetanus. Tetanus prevention measures after injury consist of inducing active immunity to tetanus toxin and of passively providing antitoxic antibody. Active immunization should be instituted in all partially immunized and non-immunized persons and those recovering from tetanus. Infection does not confer immunity. Our first patient was unvaccinated and received no antitoxin prophylaxis after a dirty wound injury. The second patient had a history of dirty injury and a healing wound. No prophylaxis for tetanus had been administered after the

injury. His childhood immunization schedule was completed with three vaccinations in the first year of life and a first tetanus booster in the 18th month, but he was not vaccinated in primary school.

Four clinical forms of tetanus are recognized: generalized, neonatal, localized, and cephalic tetanus. The most common form is generalized tetanus. Usually, the first symptom in generalized tetanus is difficulty in opening the jaw - trismus or lockjaw. Subsequently, the spasm spreads to other body parts and the patient develops dysphagia, rigidity and pain in the neck, abdomen and back. Facial muscle contraction is known as risus sardonicus. Generalized muscle spasms occur spontaneously or due to minor stimuli such as noise, touch or nursing procedures, which cause opisthotonus. We described herein two cases of generalized tetanus. Case 1 presented with perforated appendicitis initially. His history of injury was learned when his parent was queried again after the clinical findings of tetanus developed. In the literature, a few cases of tetanus mimicking acute abdomen were reported[5-7]. Tetanus infection may cause abdominal rigidity as in acute abdomen because of the involvement of muscles. Other than tetanus, some extra-abdominal conditions including zona zoster infection, rib fracture and some heavy metal and metoclopramide intoxications may cause rigidity of abdominal muscles. After surgery, the patient developed typical clinical findings including trismus, risus sardonicus, opisthotonus, and severe muscle spasms, and the diagnosis of generalized tetanus was established. Despite treatment, his condition continued to deteriorate in a few hours and autonomic dysfunction developed. He had persistent severe hypertension and tachycardia. In view of the autonomic dysfunction involving the cardiovascular system and complete presence of severe trismus, generalized spasticity, reflex prolonged spasms, respiratory rate >40 per minute, apneic spells, severe dysphagia, and heart rate >120 per minute, this patient was described as "very severe" or a Grade IV case according to Ablett classification[8]. The severity of disease, age of the patient, clinical form of tetanus, short incubation period, and presence of autonomic dysfunction determined the outcome. Severe tetanus and autonomic dysfunction in this case seem to be the important predictors of fatality. The surgical intervention might be responsible for the progression of his clinical condition. Case 2 was admitted to our hospital with a history of puncture wound contaminated with dirt without tetanus prophylaxis and typical clinical findings of tetanus. It was easy to diagnose tetanus in this patient compared to Case 1. We described this case as 'mild' according to Ablett classification[8]. He had moderate trismus, generalized spasticity, little dysphagia, no respiratory involvement, and no spasms. We thought that the preexisting antibodies related to the previous four-dose tetanus toxoid may have moderated his course of illness.

The organism is difficult to isolate, and there are no laboratory findings characteristic of tetanus. Laboratory tests are useful only to exclude other diseases. Diagnosis is based on a high index of suspicion, pertinent history and clinical manifestations. Vaccination status should also be evaluated. Our first case presented with acute abdomen, and diagnosis of tetanus was difficult in this case because of the unknown history of injury and atypical presentation. Although rigidity of abdominal muscles is known as a classical finding of generalized tetanus, due to the absence of other clinical findings of tetanus, presence of significant leukocytosis and elevated serum CRP level, perforated appendicitis could not be excluded in the present case. We believe that such cases may be confused with acute abdomen in children. The differential diagnosis for tetanus includes parapharyngeal, retropharyngeal or dental abscesses, meningitis, acute encephalitis involving the brainstem, subarachnoid hemorrhage, epilepsy, hypocalcemic tetany, hysterical conversion reaction, drug-induced movement disorders, stiff man syndrome, drug withdrawal, rabies, and strychnine poisoning.

Eradication of *C. tetani*, neutralization of the toxin, muscle relaxation, advanced supportive care, and maintenance of adequate airway and nutrition are appropriate treatments in generalized tetanus. Specific therapy should include antimicrobial therapy for *C. tetani*. Metronidazole seems to be an effective antibiotic choice. Human tetanus immune globulin (TIG, single dose, 3000-6000 units im recommended) should be administered immediately. TIG

neutralizes circulating tetanospasmin that has not entered the nervous system. It was recommended that tetanus antitoxin should be given elsewhere only if TIG is not available[9]. TIG is not available in Turkey so equine tetanus antitoxin was used in our cases. The child with tetanus should be sedated, and protected from all unnecessary sounds and touch. All patients with generalized tetanus need muscle relaxants. The quality of supportive care determines the outcome. Respiratory failure was the commonest cause of death previously. With the development of intensive care and control of respiration by artificial ventilation, other causes like cardiac arrhythmia, hyperpyrexia, paralytic ileus, septic shock, nosocomial infections, and renal failure are now responsible for death. Autonomic dysfunction described by Ablett[8] was severe hypertension and tachycardia alternating with relative hypotension and bradycardia, either of which may be persistent. Beta-blocking agents appear to be the agents of choice to treat hypertension. It remains the major clinical challenge, since hypotension, arrhythmia and cardiac arrest are important predictors of fatality. Our first case was complicated by autonomic dysfunction and the resulting cardiovascular instability was difficult to control, eventually being fatal. We could not perform an autopsy in this case, but Pomara et al. [10] recently described autopsy findings of a 65-year-old male who died from tetanus. They found tetanic necrosis of the heart in that case.

In conclusion, tetanus remains a difficult-to-treat disease with substantial morbidity and mortality. Although it most commonly occurs in non-immunized children, it can also be seen in partially immunized or immunized children[11]. Classical symptoms may be absent at presentation, such that high index of suspicion and pertinent history may guide the management. History of the vaccination status of pediatric patients should be an essential part of the evaluation. The differential diagnosis of non-immunized children with abdominal rigidity should include generalized tetanus.

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