Tetanus is a life threatening infection that is rarely encountered in clinical practice. Knowledge of the condition is necessary to ensure optimal management. A 30-year-old male presented with classic signs and symptoms of the disease, including trismus, risus sardonicus, paroxysmal muscle spasms and autonomic instability. The pathophysiology and modern management of this condition are reviewed.

Case report

A 30-year-old labourer who had recently emigrated from Pakistan, presented to a local clinic with a 6-hour history of “back spasms.” The patient was managed with intravenous fluids, “vitamins” and parenterally administered diclofenac. His condition deteriorated over the following 6 hours, with increasing muscle spasms. He was then referred to our emergency department (ED).

In the ED, the patient was alert but unable to talk, secondary to trismus. Initial vital signs were: blood pressure 130/170 mm Hg, pulse 115 beats/min, respirations 22 breaths/min, oxygen saturation 97% on room air, and temperature 37.2 °C. The patient displayed frequent, dramatic paroxysmal spasms of his facial, trunk and extremity mus-
The extensor back spasms, at times, almost caused him to launch over the stretcher rails. Risus sardonicus was also noted (Fig. 1). On further examination, a deep open wound, which the patient had suffered 3 days earlier, was identified over the plantar aspect of the left great toe (Fig. 2). A provisional diagnosis of tetanus was made.

Initial care involved 10 mg of diazepam given intravenously (IV). This resulted in immediate muscle relaxation. However, the effect was short lived, and the patient required repeated doses every 30 minutes. Tetanus immune globulin (5000 IU [20 mL]) was given intramuscularly in divided doses. Tetanus toxoid was also given at a separate site. He received penicillin G (1 million units) and metronidazole (500 mg IV). A further 3 million units of penicillin G were given 3 hours into the ED course.

Because of the risk of airway compromise, a decision was made to intubate. An unsuccessful attempt at nasotracheal intubation was made in the ED. This procedure precipitated a profound sympathetic response with rapid sustained increases in blood pressure and pulse rate. A definitive airway was later achieved with rapid-sequence intubation using fentanyl and atracurium. Initial laboratory testing revealed a leukocyte count of $13.2 \times 10^9/L$ with 93% neutrophils and an elevated serum creatine phosphokinase of 2175 U/L. The remaining laboratory values, including serum calcium, were normal. Surgical consultation was obtained, and the left toe was explored and debrided under a digital block in the ED. He was subsequently admitted to the intensive care unit (ICU).

The patient had a long, complicated hospital course, spending more than 9 weeks in the ICU. He required neuromuscular blockade with a continuous vecuronium drip for the first 15 days. Sedation, with a midazolam infusion (30 mg/h) was used. Because he experienced significant autonomic instability (i.e., sudden increases in blood pressure with sensory stimulation) a morphine (20 mg/h) and magnesium sulfate (3 g/h) drip were added. The serum creatine phosphokinases peaked at 4589 U/L on day 2 and then slowly fell over the next month. Three days after admission, it was recognized that a deep focus of infection may be persisting in his wound, liberating more toxin. The wound extended into the interphalangeal joint, and a decision was made to amputate the great toe. The tissue culture grew Clostridium tetani. A tracheostomy was done on day 12. Heavy sedation continued to be required during his 68-day stay in ICU in order to control muscle spasms and increased tonicuity. He was finally weaned off all his medications and was transferred to the general ward, where he underwent extensive rehabilitation.

### Discussion

Tetanus is an infectious disease that results from wound contamination with the gram-positive, anaerobic bacilli C. tetani. The organism and its spores are ubiquitous in nature, being found in soil and in the feces of animals and humans. Low oxygen tensions in injured tissue favour the germination of C. tetani into its toxin-producing vegetative form. Clostridial toxins are generally regarded as among the most poisonous substances known. Tetanospsmin is the neurotoxin responsible for the clinical manifestations of the disease. It is released by the germinating organism and spreads hematogenously to peripheral nerves. The toxin then travels retrogradely along the nerve fibers to deposit in the central nervous system, where it blocks the release of γ-aminobutyric acid (GABA) from inhibitory neurons. This
loss of inhibitory control on motor neurons leads to the muscle spasms, characteristic of the disease. Toxin binding appears to be irreversible, with recovery depending on the sprouting of new axonal terminals, which can take several weeks. In severe forms of tetanus, the autonomic nervous system may also be affected, resulting in sympathetic hyperactivity. This is characterized by labile hypertension, tachycardia, hyperthermia and excessive bronchial secretions.

Generalized tetanus is the most common form of the disease and carries the highest mortality. Other forms include localized, cephalic and neonatal tetanus. Incubation periods for the generalized form range from a few hours to greater than one month. Shorter incubation periods correlate to more severe disease.

The diagnosis of tetanus is based solely upon clinical evidence. Trismus or lockjaw is the initial presentation in 75% of cases. Facial muscle spasm may cause the classic sneering grin of risus sardonicus. Motor findings progress to involve the neck, trunk and extremities, eventually leading to abdominal rigidity and opisthotonus. The muscle spasms may be sustained or paroxysmal and can be precipitated by minimal sensory stimuli. This is an important consideration when caring for the patient.

The US Centers for Disease Control documented 122 cases of tetanus in the United States from 1995 to 1997. An antecedent acute injury was identified in 77% of cases. Injury to the extremities proved to be the source in over 80% of cases. Puncture wounds were responsible for one-half of all acute injuries leading to tetanus. The 23% of cases not related to acute injury were associated with underlying medical conditions, including chronic wounds, intra-venous drug use and malignant tissue necrosis.

Included in the differential diagnosis of tetanus are oral or facial infections causing trismus, dystonic reactions induced by such drugs as phenothiazines and metoclopramide, hypocalcemia, meningitis, encephalitis and rabies. Strychnine poisoning may be difficult to distinguish from tetanus. Both tetanospasmin and strychnine block the release of inhibitory motor neurotransmitters in the central nervous system and have a similar clinical presentation.

As always, the initial priority of management is airway control and maintenance of ventilation. In moderate and severe cases, the risk of laryngeal spasm and ventilatory compromise is high. Propylhexyl intubation should be employed. Rapid-sequence intubation with midazolam and succinylcholine is safe and effective in achieving an early definitive airway. Blind nasotracheal intubation should be avoided due to the excessive sensory stimulation.

Passive immunization with human tetanus immune globulin (HTIG) helps to neutralize free tetanospasmin. It should be given after airway control and before wound debridement. In an evaluation of 545 cases by Blake and colleagues, it was demonstrated that an HTIG dose of 500 IU was equally as effective as the standard dose of 5000 IU. It should be emphasized that the exact effective dose of HTIG has yet to be established. Acceptable doses range from 500 to 10,000 IU. Toxin released during a tetanus infection is insufficient to provide immunity. Consequently, active immunization must be initiated at the time of presentation, either with a booster or a primary immunization series of 3 doses of tetanus toxoid.

A third principal in management is the eradication of the source of toxin production. The offending wound must be thoroughly debrided, with removal of all foreign bodies and devitalized tissue. The efficacy of antibiotics is unclear. Penicillin G has traditionally been considered the initial drug of choice; however, because of its potential to act as a GABA antagonist, its use has fallen into disfavour. Metronidazole, 500 mg IV every 6 hours, is now recommended as the first-line antibiotic.

Supportive care includes sedation, neuromuscular blockade and management of autonomic instability. As GABA agonists, benzodiazepines are effective in countering much of the toxic effects of tetanospasmin. A continuous midazolam drip (5–15 mg/h) is preferred, and is the standard agent for extended management. Tetanic spasms refractory to benzodiazepines require non-depolarizing muscle blocking agents. Either vecuronium or pancuronium may be used in these circumstances. Although it is often difficult in a busy ED, every effort should be made to limit excessive external stimuli. Autonomic instability is common in severe tetanus. Sympathetic overactivity can be managed with a labetalol infusion at 0.25–1 mg/min. Magnesium sulfate or morphine sulfate infusion may be used as an alternative. No single drug or combination of drugs has consistently been shown to be successful in controlling cardiovascular disturbances.

A study by Trujillo and coworkers reported that the impact of ICU care resulted in a decrease in mortality from 44% to 15%. Recovery may be prolonged, as evident in the case we presented.

Our patient presented with classic symptoms and signs of generalized tetanus, with an obvious focus of infection. The initial choice of nasotracheal intubation was clearly inappropriate and resulted in excessive sensory stimulation, precipitating sympathetic overactivity. Primary rapid-sequence intubation would have been the preferred method of airway control. Confusion also existed on the proper initial choice of antibiotics. The penicillin G that was administered could have had a potentially deleterious effect. A more aggressive approach on initial wound management may have prevent-
ed further release of tetanospasmin during his early course in hospital. This likely would have resulted in a shorter hospital stay. All these areas of concern help to outline the need for awareness of this condition in order to avoid these common pitfalls in management.

Conclusions

Tetanus is rarely encountered in developed countries. Knowledge of the condition is essential to ensure the timely diagnosis and optimal management of this life-threatening infection.

References


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