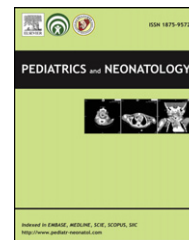




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CASE REPORT

Autonomic Dysfunction Because of Severe Tetanus in an Unvaccinated Child

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autonomic dysfunction;
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Tetanus is rare in a country with a national vaccination program. When it does occur, the associated autonomic dysfunction is a challenge for physicians. We report here a case of an unvaccinated 5-year-old boy who suffered from tetanus complicated by autonomic dysfunction, which was successfully controlled by the infusion of magnesium sulfate. This is the first case that demonstrated the therapeutic effect of magnesium sulfate in a child with tetanus. This case highlights the importance of implementing a vaccination program.

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1. Introduction

Tetanus is caused by tetanospasmin, a neurotoxin released by *Clostridium tetani*.¹ It is rare in a country with a national vaccination program, such as Taiwan, where tetanus mainly affects the elderly.² Its presentation is a clinical triad of

rigidity, muscle spasms, and if severe, autonomic dysfunction, which manifests as tachycardia and hypertension; bradycardia, hypotension, and cardiac arrest may occur. Frequently, *C. tetani* cannot be recovered from wounds of those with tetanus. The diagnosis of tetanus is based entirely on clinical findings. Tetanospasmin plays the leading role in the pathogenesis of tetanus. It binds to peripheral motor neuron terminals and is transported to the cell body in the brainstem and spinal cord by retrograde transport. It inhibits the release of the inhibitory neurotransmitters gamma-aminobutyric acid (GABA) from vesicles. The clinical symptoms and signs develop thereafter. Principles of management include neutralizing unbounded

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toxin, removal of the infectious source, control of rigidity and spasms, control of autonomic dysfunction, and supportive intensive care treatment.¹

Because of minimal controlled studies, there is no standard treatment for autonomic dysfunction caused by tetanus.¹ The mortality rate is greater than 50% in countries without intensive care units and 10% in developed countries, mostly attributed to autonomic dysfunction.^{1,3} Here is a case of tetanus complicated by autonomic dysfunction and controlled by magnesium sulfate infusion.

2. Case Report

A 5-year-old boy presented with a 2-day history of progressive generalized spasms. He was in good health until 7 days before admission, when he acquired an abrasion over his left ankle after falling down from a bicycle. He was brought to the local clinic where the wound was cleaned. He was prescribed oral antibiotics but no tetanus toxoid or tetanus immune globulin. Fever, lockjaw, dysphagia, intermittent convulsion-like painful muscular spasms, and progressive generalized rigidity developed 2 days before admission. There was no head injury or other medication usage history. He was brought to our emergency department and then admitted to the Pediatric Intensive Care Unit.

On physical examination, the patient was alert and cooperative. Body temperature was 36.8°C. Pulse was 132 per minute in regular beat. Respiratory rate was 39 per minute. Opisthotonus (Figure 1), trismus, and hyperreflexia were noted. An abrasion with necrotic tissue and pus over his left ankle was found. There was no other remarkable finding. Hemogram showed a white blood cell count of 11,710/uL. The patient's serum sodium, potassium, and calcium levels were within normal range. Lumbar puncture was performed, and cerebrospinal fluid (CSF) was collected later. His CSF was clear and sterile. Cranial computed tomography was arranged, and it revealed no lesion.



Figure 1 Generalized spasticity and opisthotonus in the case patient.

Tracing back the patient's vaccination history, he had missed all diphtheria, tetanus, and pertussis immunization. He was diagnosed with generalized tetanus based on clinical history and typical clinical manifestations, although without *C. tetani* culture from his wounds.

Tetanus immunoglobulin and penicillin G were given immediately whereas diphtheria, tetanus, and acellular pertussis vaccine was given thereafter. However, the patient's condition quickly deteriorated, and any stimulus caused a period of generalized cramping. Diazepam 2.5 mg and meperidine 13 mg were added. The patient was intubated for an anticipated respiratory distress. Nonetheless, severe generalized spasms and rigidity persisted.

On the second hospital day, rocuronium bromide 80 mg twice daily was added. Diazepam was replaced by midazolam 78 mg q 12 hours. The frequency of spasm decreased gradually, but cardiovascular instability developed and presented as severe hypertension and tachycardia, with relative hypotension and bradycardia. Ten percent magnesium sulfate 2.5 cc q 6 hours (Mg: 0.81 mEq/mL) infusion was given on Day 6, and the storm calmed down on Day 8. Magnesium sulfate was discontinued on Day 24. The patient's heart rate and medications for autonomic instability are shown in Figure 2.

The patient's condition improved gradually. On Day 38, he was extubated. He was transferred to the general ward for further rehabilitation on Day 40 and was subsequently discharged on Day 53.

3. Discussion

According to the Ablett classification of tetanus severity, a patient with severe trismus, generalized spasticity, prolonged spasms, severe dysphagia, apneic spells, and autonomic dysfunction presenting as severe hypertension and tachycardia with relative hypotension and bradycardia, is classified as suffering from very severe tetanus.¹ The case presented here had all of the clinical features described earlier. The differential diagnosis included conditions also producing trismus, such as alveolar abscess; strychnine poisoning; dystonic drug reactions (e.g., phenothiazines and metoclopramide); and hypocalcemic tetany. In addition, meningitis/encephalitis, rabies, and an acute intra-abdominal process might be considered. Markedly increased tone in central muscles (face, neck, chest, back, and abdomen), with superimposed generalized spasms and relative sparing of the hands and feet, strongly suggested tetanus.

As modern intensive care prevents death from acute respiratory failure, autonomic dysfunction has become the most life-threatening complication of very severe tetanus, which remains a challenge for most physicians. There is no standard treatment for severe tetanus with autonomic dysfunction, and most publications are as case reports or small series. Analgesics, sedatives, anticonvulsants, and muscle relaxants are initially used, but autonomic dysfunction is often refractory to medications. Other agents with potential curative effects include labetalol, clonidine, verapamil, morphine, meperidine, and magnesium sulfate.^{1,4-8}

In the current case, diazepam, midazolam, meperidine, and rocuronium bromide were used initially but in vain. The

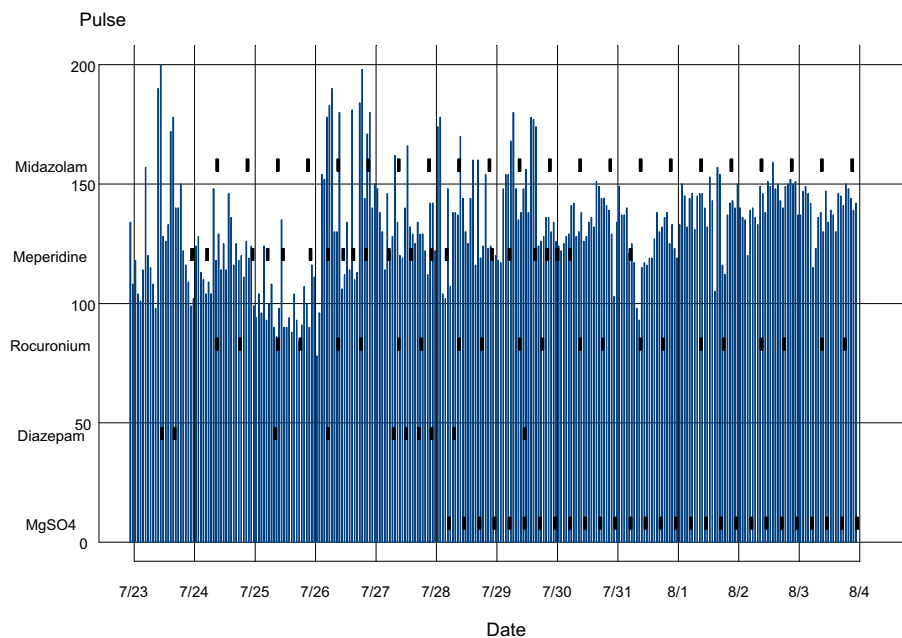


Figure 2 The patient's heart rate and the medication used to control autonomic instability. Multiple drugs were used but in vain. Fluctuations of heart rate decreased 2 days after magnesium sulfate infusion.

patient's autonomic storm calmed down only 2 days after magnesium sulfate infusion. "Magnesium sulfate reduces the requirement for other drug to control cardiovascular instability in patients with tetanus" was the conclusion in a previous randomized trial.⁹ However, only people older than 15 years were included in the trial. In this case report, the child with tetanus responded to magnesium sulfate dramatically well. To our knowledge, this is the first case report that demonstrated the effect of magnesium sulfate in a child with severe tetanus.

Tetanus is rare in Taiwan. Since primary immunization for tetanus was launched in 1954, the number of cases markedly decreased (1004 in 1956 vs. 17 in 1986).² In the period 2001–2007, 104 tetanus cases were reported in Taiwan, 100 (96.2%) of which were in adults.¹⁰ Patients with generalized tetanus present with trismus in 75% of cases. Other presenting complaints include stiffness, neck rigidity, dysphagia, restlessness, and reflex spasms. Neonatal tetanus presents with an inability to suck 3–10 days after birth. Presenting symptoms include irritability, excessive crying, grimaces, intense rigidity, and opisthotonus. In 73% of patients with tetanus in the United States, it occurred after an acute injury, including puncture wounds (50%), lacerations (33%), and abrasions (9%). Risk factors for neonatal tetanus are as follows: unvaccinated mother, home delivery, and unhygienic cutting of the umbilical cord increase susceptibility to tetanus.

Recovery in tetanus occurs through regeneration of synapses within the spinal cord and, thereby, the restoration of muscle relaxation. The most important factor that influences outcome is the quality of supportive care. Mortality is highest in the very young and the very old. Sequelae of hypoxic brain injury, especially in infants, include cerebral palsy, diminished mental abilities, and behavioral difficulties.

Tetanus in children is extremely rare, which may be the reason why physicians may ignore their potential risk in children with injury. This case should remind physicians to ensure that children with injury are fully immunized. This case also reveals that there is still room for improvement regarding the implementation of a vaccination program.

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