





The Myriad Presentations of Tetanus: Where Do You Look for Clinical Clues in an Intubated Highly Sedated Patient?

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Tetanus, a potentially fatal yet treatable disease, presents a significant global health concern with an estimated 73,000 cases and 34,000 associated deaths reported annually worldwide.¹ Notably, mortality rates are significantly affected by delays in treatment or prophylaxis.² This case report presents a challenging case of generalized tetanus with both typical and atypical features. A thorough history review and careful examination allowed for early diagnosis and management, leading to favorable neurological outcome. This case emphasizes the importance, despite diagnostic advancements, of comprehensive clinical assessment and recognizing early classic presentations to help avoid unnecessary and costly investigations.

(50–70 Hz), involving bilateral shoulders, trunk, and hips. These episodes lasted 2 to 10 minutes with 1- to 2-minute intervals and were triggered by visual, auditory, and tactile stimulation (Video 1). The patient also exhibited spasms in arms, legs, and hands. There was no carpopedal spasm. Additionally, visual, auditory, and tactile stimulation induced symptoms including excessive sweating, high-grade fever (38.5°C), tachycardia (170 beats/min), and tachypnea (42 breaths/min), contrasting with baseline values of a heart rate of 70 beats/min and a respiratory rate of 14 breaths/min, respectively, at rest (Video 1). A large post-debridement wound measuring 20 × 15 cm² was evident on the left foot, showing no signs of purulent discharge.

Case report

A 51-year-old farming Thai woman with poorly controlled type 2 diabetes mellitus (HbA1C, 9.2%), frequently worked barefoot on her farm. She was admitted to another hospital with necrotizing fasciitis from a contaminated woodcut on her left foot. Intravenous ceftazidime (6 g/day) was initiated for treatment. Notably, tetanus toxoid was not administered at this stage and her last tetanus vaccination had occurred during childhood. On the day 8, she developed jerky movements, involving bilateral shoulders and trunk at the beginning, which rapidly became generalized over the following 5 days, leading to respiratory compromise. Phenytoin (450 mg/day) and levetiracetam (3000 mg/day) were administered under the presumptive diagnosis of seizures. Additionally, to control muscle spasm, continuous infusion of midazolam (5 mg/h) was initiated before transferring the patient to our hospital.

At admission to our hospital (day 15), the patient continued to experience frequent episodes of synchronous jerky movements



Video 1. Multiple episodes of intermittent jerky movements beginning at bilateral shoulders, abdomen, bilateral hips, and legs lasting from 2 to 10 minutes. These movements were aggravated by visual, auditory, and tactile stimulation. Excessive sweating, tachycardia, and tachypnea were also observed along with the movements. Video content can be viewed at <https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13935>

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Keywords: presentations of tetanus, generalized tetanus, clinical clues, sedated patient. Relevant disclosures and conflict of interest are listed at the end of this article.

Received 22 July 2023; revised 6 November 2023; accepted 11 November 2023.

Published online 9 December 2023 in Wiley Online Library ([wileyonlinelibrary.com](http://www.wileyonlinelibrary.com)). DOI: 10.1002/mdc3.13935



Video 2. The abnormal movements completely resolved. The patient was able to walk with assistance after 1 month of follow-up. Video content can be viewed at <https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13935>

At that moment, intubation, generalized hyperkinetic movements, and the patient's heavily sedated state may cause the examiner to overlook jaw trismus; however, additional information from a referral letter indicated the presence of jaw trismus before intubation.

Laboratory tests showed mild anemia (Hct, 31.8%), leucocytosis (white cell count 12,790/ μ L; neutrophils, 77.7%), and elevated creatinine phosphokinase (1766 μ g/L; normal range: 29–168 μ g/L). Cerebrospinal fluid (CSF) analysis, serum and CSF serology for autoimmune and paraneoplastic antibodies were negative, ruling out progressive encephalomyelitis with rigidity and myoclonus (PERM). Brain magnetic resonance imaging disclosed a small cavernoma in the left caudate nucleus without mass effect. Electroencephalogram showed no epileptiform discharges, ruling out the previously diagnosed status epilepticus. Electromyography and masseter inhibitory reflex tests were not performed because of unavailability and the unstable condition of the patient. In addition, the history of jaw trismus and the rapid development of severe autonomic storm indicated the possibility of tetanus (grade 4 by modified Ablett classification).³ Treatment included intramuscular human tetanus immunoglobulin (6000 IU), a 2-week regimen of intravenous metronidazole (3600 g/day) to reduce the toxin level, midazolam (480 g/day) to control muscle spasms, and magnesium sulfate to reduce autonomic dysfunction and replace the low levels of

magnesium sulfate (4 g/day for 4 days, serum magnesium concentrations from 0.45 to 1.4 mmol/L). This comprehensive approach led to a gradual improvement, with the patient achieving assisted walking at 1-month follow-up post discharge (Video 2).

Discussion

Tetanus remains a significant health issue, more prevalent in low-income countries. In 2019, Sub-Saharan Africa, Southeast Asia, and South Asia reported the highest fatality rates, ranging from 0.74 to 1.25 per 100,000.¹ People in these regions often lack access to tetanus vaccination, possess improper wound care knowledge, and engage in an agricultural lifestyle.⁴ The potent neurotoxin produced by *Clostridium tetani*, commonly found in soil and on rusty tools, poses a risk for wound contamination, causing tetanus.⁴ Our patient exhibited several risk factors predisposing her to tetanus, including a lapse of over 10 years since her last tetanus vaccination, an underlying diabetic condition impacting immune function, resulting in increased susceptibility to wounds and lower anti-tetanus antibody levels.⁵ Additionally, her occupational activities predispose frequent contact with soil, further elevating her risk to tetanus.^{2,6}

In recent times, the decreasing prevalence of tetanus has led to a reduced level of awareness and recognition of its clinical presentations among healthcare practitioners.^{1,7} This decline in cases has also made early diagnosis more challenging because of the diverse range of clinical manifestations associated with the disease.⁷ Although classic symptoms, such as jaw trismus and generalized muscle spasms are evident in over 80% of cases, atypical forms, such as cephalic tetanus, occur in only 1% to 3% of cases (Table 1).^{4,8–11} In our case, we encountered a rare presentation characterized by stimuli-sensitive jerky movements, strongly indicative of spinal myoclonus—an atypical manifestation of generalized tetanus. There has been only one previous report of stimuli-sensitive jerky movements associated with tetanus.¹¹ However, in that case, the onset of myoclonus was observed over a longer duration after the onset of the illness (11 weeks vs. 13 days in our case) and exhibited different distribution patterns, affecting the eyelids, neck, and arms rather than the trunk.¹¹

One of the investigative tools for confirming trismus is the masseter inhibitory reflex test, which typically reveals a loss of silent period on electromyography when the masseter is activated, resulting from central neuronal hyper-excitability. However, it was not performed here because of unavailability, the patient's unstable condition, and the potential for false negatives from high doses of sedation, magnesium sulfate, or timing of the test, which has been reported to occur after 9 weeks of disease onset.^{12,13} Differential diagnoses, including PERM, strychnine poisoning, and carpedal spasm, can be distinguished based on initial symptoms and progression patterns (Table 2).^{14–17} A comprehensive review of clinical findings emphasizes the continuous

TABLE 1 Typical, atypical manifestations, and the Ablett classifications based on severity of tetanus.

Typical manifestations ^{4,8}	Atypical manifestations ^{9–11}	Ablett classifications based on severity
<ul style="list-style-type: none"> • Jaw trismus (93%–98%) • Generalized rigidity and muscle stiffness (95%) • Dysphagia (83%) • Muscle spasms (46%–80%) • BT >38.4°C (76%) • Tachycardia >120 beats/min (34%) 	<ul style="list-style-type: none"> • Dyspnea (7%) • Cephalic tetanus (1%–3%) • Focal limb spasms (<1%) • Brainstem/spinal myoclonus (<1%) 	<p>Grade 1: mild</p> <ul style="list-style-type: none"> • Mild to moderate trismus • Generalized spasticity • No respiratory compromise • No spasms • Little or no dysphagia <p>Grade 2: moderate</p> <ul style="list-style-type: none"> • Moderate trismus • Marked rigidity • Mild to moderate but short spasms • Moderate respiratory compromise with an increased respiratory rate (>30 breaths/min) • Mild dysphagia <p>Grade 3: severe</p> <ul style="list-style-type: none"> • Severe trismus • Generalized spasticity • Reflex prolonged spasms • Increased respiratory rate (>40 breaths/min) • Apnoeic spells • Severe dysphagia • Tachycardia >120 beats/min <p>Grade 4: very severe</p> <ul style="list-style-type: none"> • Clinical features of grade 3 tetanus • Violent autonomic disturbances involving the cardiovascular system • Severe hypertension and tachycardia alternating with relative hypotension and bradycardia (either of which might be persistent)

importance of fundamental neurology assessments even in this era of advanced diagnostics, helping to avoid costly and unnecessary extensive tests such as lumbar punctures and extensive

autoimmune antibody panels, and lowering the risk of severe autonomic complications, including ventricular tachycardia-induced cardiac arrest.

TABLE 2 Differential diagnoses of tetanus and characteristics.

Diseases	Origin	Progression	Duration
PERM ¹⁴	Limb pain or rigidity advancing to the trunk	Brainstem or spinal myoclonus	<1–96 months with 44% of presentations described as subacute
Strychnine poisoning ¹⁵	Acute excitability, followed by vomiting and muscle spasms	Opisthotonic posture	1–2 h
Carpopedal spasms ^{16,17}	Painful flexion of metacarpophalangeal joints with extension of the interphalangeal joints of the fingers and thumb, triggered by voluntary movement	Increased in severity of flexion of metacarpophalangeal joints with extension of the interphalangeal joints of the fingers and thumb	1–2 days

Abbreviation: PERM, progressive encephalomyelitis with rigidity and myoclonus.

Our treatment followed standard protocols, using anti-toxin and metronidazole as primary therapies.^{4,18} Additionally, we administered high doses of midazolam for severe muscle spasms.¹⁹ A 4-day magnesium infusion was also provided because of its short-term effectiveness in reducing muscle spasms and autonomic instability.¹⁹ Our case showed gradual improvements within 1 month, in contrast to a similar case with matching presentations and incubation period that took 3 months to improve.¹¹ Early treatment with human tetanus immunoglobulin, high dosages of anti-toxin and antibiotics, and management of autonomic dysfunction in our case may have promoted early recovery.

In summary, this case of generalized tetanus with combined typical and atypical manifestations highlights the importance of considering diverse tetanic presentations in patients with incomplete or absent booster immunization, particularly when tetanus-prone wounds are involved to facilitate early diagnosis and prompt initiation of appropriate management. When clinical examination is not conclusive and diagnosis remains uncertain, detailed review of clinical history may provide important clinical clues, enabling early treatment and favorable neurological outcomes.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

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P.W.: 3B

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Disclosures

Ethical Compliance Statement: The authors confirm that the ethics board clearance was not required for this work. The subject has provided written consent to the video. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Funding Sources and Conflicts of Interest: No specific funding was received for this work, and the authors declare that there are no conflicts of interest relevant to this work.

Financial Disclosures for the Previous 12 Months: R.B. received a salary from Chulalongkorn University and a stipend from the Royal Society of Thailand. He has also received consultancy and/or honoraria/lecture fees from Abbott, Boehringer-Ingelheim, Britannia, Ipsen, Novartis, Teva-Lundbeck, Takeda, and Otsuka pharmaceuticals. He has received research funding from the Thailand Science and Research Innovation Bureau, Thailand Research Fund, Crown Property

Bureau, Chulalongkorn University, and the National Science and Technology Development Agency. He holds patents for a laser-guided walking stick, a portable tremor device, a nocturnal monitoring device, and an electronic Parkinson's disease symptom diary as well as copyrights on Parkinson's mascot, dopamine lyrics, and teaching video clips for common nocturnal and gastrointestinal symptoms experienced by Parkinson's disease patients. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. ■

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