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Generalized Tetanus in A Patient with Infected Sutured Wound: A Case Report

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ABSTRACT

Introduction: Tetanus is a disease caused by *Clostridium tetani*, which produces an exotoxin. Tetanus can rapidly progress into life-threatening muscle spasms accompanied by respiratory insufficiency with or without autonomic dysfunction. **Case:** A 43-year-old male patient was referred from the public health center to Tora Belo Hospital with mouth stiffness and difficulty swallowing food. He also had stiffness and pain in the neck, abdomen, and lower back. Seven days prior, the patient received lacerations on his right forearm caused by a machete. The patient's wound had been stitched up without an anti-tetanus injection at the public health center. The symptoms worsened on the second day of admission, and the patient died from respiratory failure. **Conclusion:** It is very important to enhance public awareness that tetanus is a preventable disease, with proper vaccination and sanitization potentially lowering mortality and morbidity.

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INTRODUCTION

Tetanus is still a significant health issue, especially in developing countries. Lack of public knowledge about the risk of tetanus infection causes a low level of concern with contaminated objects, so the wound can potentially cause tetanus.[1]

Tetanus is a life-threatening disease but can be prevented by vaccination. Tetanus is defined as an acute infectious bacterial disease caused by *Clostridium tetani*, a gram-positive anaerobic bacillus naturally found in soil, dust, and human and animal feces that produces an exotoxin. Under favorable conditions, these bacteria can produce tetanospasmin toxin and cause violent spastic paralysis by blocking the release of Gamma-Aminobutyric Acid (GABA), which presents as an increased contraction of skeletal muscle that produces stiffness and spasm. In addition, these bacteria can also produce tetanolysin.[2,3]

According to the Centers for Disease Control and Prevention (CDC), 70 to 35 new cases of tetanus are reported each year. Most of these cases are in people over 60 years old, implying that the protective effect of the primary vaccination has reduced.[4]

In 2015, the United States reported 29 cases of tetanus with a 13.2% mortality rate.[5] Tetanus mortality was recorded at more than 50%, with the estimated number of deaths ranging between 800,000 and 1,000,000 per year in developing countries. There were 156 cases of tetanus with a mortality rate of 35.2% at the neurology department of Hasan Sadikin Hospital, Bandung, in 1999–2000.[1]

The diagnosis of tetanus is based on clinical findings from the patient's history and physical examination. Tetanus is classified into localized tetanus, generalized tetanus, and cephalic tetanus.[6] Generalized tetanus often begins with trismus that progresses to nuchal rigidity, abdominal rigidity, and tetanic spasm of the extremities.[7]

Poor access to immunization programs is reported to be one of the causes of the high prevalence of tetanus. Tetanus immunity doesn't last forever, so if a person gets a wound that could get tetanus, a booster injection is needed.[8]

This case report presents the tetanus case of a male patient who was hospitalized in the Intensive Care Unit (ICU) with an infected sutured wound on the front of the right forearm and died from respiratory failure.

CASE

A 43-year-old man with stiffness in the mouth and difficulty swallowing food was referred from the public health center to the emergency room (ER) of Tora Belo Hospital, Sigi Regency. Other symptoms include pain from the wound on the right forearm, tension, and stiffness in the neck, which makes movement difficult. In addition, there was discomfort and a burning sensation throughout the body, especially in the stomach and lower back. He was suffering from difficulty standing, so he could only lie down. Other symptoms, such as convulsions, shortness of breath, and cough, were denied.

The patient had a history of lacerations on the right forearm caused by a machete seven days ago. The public health center stitched up the wound without administering an anti-tetanus injection; just mefenamic acid and amoxicillin were prescribed. The wound wasn't regularly cleaned. The patient has no history of tetanus vaccination, hypertension, diabetes mellitus, or head and neck trauma. There was also no history of punctured nails or thorns, and no contact with animals, such as being bitten, scratched, or licked on the wound. The patient worked as a farmer and wore footwear while working.

Physical examination using the Glasgow coma scale was E4V5M6. The blood pressure was 96/53 mmHg, the pulse rate was 99x/minute regular, the respiration rate was 22x/minute symmetrical and regular, and the temperature was 36.6 ^{o}C. The oxygen saturation on the right hand of finger 1 was 98%, finger 2 was 99%, finger 3 was 96%, finger 4 was 99%, and finger 5 was 99%. Visual Analog Scale (VAS) 8/10. The cardiopulmonary examination, conjunctiva, lymph nodes, and right and left ears were normal. We found trismus and positive neck stiffness. It was difficult to evaluate the cranial nerves, but there wasn't an impression of nerve paresis. The patient also had abdominal pain and rigidity. There was pus, swelling, redness, and pain around the wound, with 11 stitches on the front of the right forearm, indicating an infection (Figure 1 and 2). Blood tests showed leukocytosis (15.200/mm3), neutrophilia (82.2%), and lymphopenia (9%). The electrolytes, blood sugar level, and renal and liver functions were normal. The COVID-19 rapid antigen test was negative. The ECG examination was normal. Chest and arm x-rays were also unremarkable.

The patient was counseled about the diagnosis of tetanus with secondary wound infection. Treatment began promptly with open wound care and the intravenous infusion (IV) of antibiotics: ceftriaxone (1000 mg) and metronidazole (500 mg). The patient was given an intramuscular (IM) injection of anti-tetanus serum (1.500 IU) and an intravenous (IV) infusion of diazepam 100 mg in Ringer's lactate 500 cc. The patient displayed dysphagia that required nasogastric intubation, and then the patient was moved to the Intensive Care Unit (ICU) for observation in an isolation room with minimal light

and sound stimulation. For wound exploration, the surgical team was consulted, and the wound was left exposed for daily cleaning. The symptoms worsened on day 2 of ICU admission. The patient became unconscious and developed tonic-clonic seizures, so midazolam IV was added to the regimen. He developed generalized spasticity, labile blood pressure, and a rapid heart rate. His oxygen saturation dropped, so he was placed on oxygen, but unfortunately, he died from respiratory failure.

DISCUSSION

Tetanus can generally be diagnosed with a history and physical examination without laboratory confirmation. In 80% of all cases, generalized tetanus is the most prevalent kind. The incubation period for tetanus is 3 to 21 days, and the shorter the incubation period, the higher the risk of death. Tetanus has a clinical diagnosis characterized by the clinical triad of rigidity, muscle spasm, and, in severe cases, autonomic dysfunction.[9] A muscle spasm is usually the first clinical sign to appear. Painful spasms may also involve the muscles of the neck, trunk, and extremities. If left untreated, spasms of the facial and pharyngeal muscles would then progress to dysphagia and grimacing, or *risus sardonicus*. Generalized muscle spasms with severe pain, drooling, uncontrolled urination and defecation, and back arching spasms (opisthotonus) may lead to respiratory distress.[1] Most cases of tetanus were reported in patients with unclear or incomplete immunization status.[9]

Transmission of *Clostridium tetani* bacteria into the body occurs after contamination of the wound, especially through the deep penetrating wound, where bacterial growth is facilitated under anaerobic conditions or a lack of oxygen. Bacteria can also enter through the cut end of the umbilicus in neonates, postpartum infection or abortion, skin ulcers, abscesses, gangrene, burns, dental infections, unsterile injection procedures, and even minor trauma can cause tetanus in up to 30%.[10]

Spore-forming *Clostridium tetani* produces tetanolysin and tetanospasmin, which can spread through blood vessels and lymphatic channels. Tetanolysin will destroy the surrounding tissue and lyse red blood cells. Tetanospasmin will bind to synaptobrevin/vesicle-associated membrane protein (VAMP), which is associated with the release of neurotransmitters from nerve endings through the fusion of synaptic vesicles with the nerve plasma membrane. Tetanus toxin can spread retrogradely in the lower motor neuron (LMN) axons that eventually reach the spinal cord or brainstem. Furthermore, the toxin will cross the synapse and be taken up by the nerve endings of GABA inhibitors (Gamma-Aminobutyric Acid) or glycinergic nerves that control LMN activity. Tetanospasmin prevents the release of the inhibitory neurotransmitters glycine and GABA, resulting in sympathetic overactivity.[8,11]

A wound was discovered on the patient's right forearm, which was suspected of being the source of bacteria entry. We also found trismus, meningismus in the neck, and opisthotonus. The spatula test had high sensitivity and specificity. In 94% of tetanus patients, positive results were obtained. In this case, the result of the spatula test was positive.[8]

Generalized tetanus is often accompanied by autonomic symptoms such as increased blood pressure, temperature, excessive sweating, and tachycardia, which can lead to cardiac arrest. This is associated with increased levels of catecholamines. The appearance of autonomic symptoms may indicate that the toxin has reached the brainstem.[1,8,12] In this case, the patient, had unstable vitals followed by autonomic symptoms on the second day of ICU admission.

The laboratory test is rarely used for diagnosing tetanus. However, some reference labs would help rule out the differential diagnosis of tetanus. Isolation of *Clostridium tetani* from the wound doesn't have enough sensitivity and specificity; only 30% are positive. Serologic testing for antitetanus antibodies is usually done to look for inadequate vaccination, which gives a low or negative level. Unfortunately, tetanus can occur even in the presence of protective levels of antibodies.[8,13] The results of leukocytosis, neutrophilia, and lymphopenia were found in this patient. Cultures and serological examinations were not performed because the patient had spontaneous seizures and limited access to tools and materials.

Tetanus patients with clinical manifestations are treated by neutralizing toxins that aren't bound to tetanus immunoglobulin, removing the source of tetanospasmin by wound debridement, and giving supportive care to minimize discomfort and excessive stimulation.[8,12] Tetanus immunoglobulin can be used as a treatment for toxin neutralization and should be given immediately after a diagnosis to neutralize toxins that have not yet bound and have not reached the central nervous system. Antitoxin with human tetanus immunoglobulin (HTIG) can be administered IM at a dose of 3000–6000 IU, divided into three equal doses, and injected at three different sites.

According to recent CDC recommendations, researchers have yet to establish an optimal dose, but giving a single 500 IU dose appears to be as effective as the previous dose and more comfortable for patients. Contraindications to the administration of HTIG include a history of hypersensitivity to previous immunoglobulin or human immunoglobulin components, severe thrombocytopenia, or other

coagulation conditions that may contraindicate intramuscular administration. Anti-tetanus serum (ATS) can be given at a dose of 100,000–200,000 IU or at a dose of 500–1,000 IU/KgBB if HTIG is unavailable.[1,8,14,15]

National guidance on tetanus vaccination and post-exposure prophylaxis classify the following types of wounds as tetanus-prone:

1. Wounds or burns that need surgical intervention that have been delayed for more than six hours,
2. Wounds or burns that show a significant degree of devitalized tissue or a puncture-type injury, including animal bites or contact with soil,
3. Wounds containing foreign bodies,
4. Compound fractures, and
5. Wounds or burns in patients who have systemic sepsis.

CDC recommends using the tetanus vaccine in patients with clean wounds, minor wounds, unknown vaccination data, or less than three vaccinations.

In addition to the tetanus vaccine, tetanus immunoglobulin should be given for minor injuries with dirty wounds. Additional tetanus immunoglobulin, aggressive wound care, and antibiotics should be given on major injuries such as avulsions, stab wounds, burns, and contaminated wounds due to soil contamination, dust, and saliva. In patients with a complete vaccination history, vaccines for clean and dirty wounds are unnecessary. The dose of tetanus toxoid (TT) vaccine is 0.5 mL intramuscularly (IM) and on a different side of the antitoxin administration.[5,8,16,17] The patient should be given tetanus immunoglobulin and anti-tetanus because he had dirty wounds and no history of previous tetanus vaccination. The patient was only given 1,500 IU of anti-tetanus serum IM because of the limited availability of materials.

It is important to practice basic first aid and wound care. Early recognition of the signs and symptoms of tetanus and the timely seeking of medical care are essential. Healthcare workers, including nurses and pharmacists, must emphasize the importance of immunization. Protection against tetanus by vaccines is essential because there is no natural immunity against tetanus. According to the World Health Organization (WHO), TIG is essential in the treatment and prophylaxis of tetanus cases and should be available in all countries.[18,19]

Wounds suspected of being the source of infection should be thoroughly cleaned and debrided to reduce the bacterial load and prevent the further release of toxins. Antibiotics need to be given to eradicate the bacteria. Benzylpenicillin was previously used at a dose of 0.6–1.2 grams divided four times a day, but its use has been abandoned due to penicillin's ability to act as a competitive inhibitor of GABA(A) receptors, potentially increasing muscle stiffness. Metronidazole has become the drug of choice in several health services because it has a good safety profile and shows a better reduction in mortality when compared to benzylpenicillin. Metronidazole is given intravenously (IV) with an initial dose of 15 mg/kg BW followed by a dose of 30 mg/kg BW/day every 6 hours or can also be given at a dose of 500 mg three times a day. The administration duration is recommended to range from 7 to 14 days. Metronidazole also effectively reduces the number of vegetative forms of *C. tetani*.[1,12] In this case, the patient was given metronidazole at an appropriate dose of 3 x 500 mg (IV). The patient's wound, which had previously been sutured, was opened and cleaned again for further debridement by a general surgeon after optimizing the general condition.

Supportive therapy is another option for treatment. Benzodiazepines can be used to control muscle stiffness and spasms. Diazepam is effective in treating spasms and hypertonicity without depressing cortical centers. Diazepam can be administered intravenously, rectally, or orally. The dose is 0.1–0.3 mg/kg, which can be repeated every 1–4 hours. Diazepam can also be given as a continuous infusion at a dose of 3–10 mg/kg over 24 hours. However, the presence of a long metabolic time can lead to the accumulation of the drug.

The use of midazolam can also be considered in varying doses. In addition to being available in intravenous form, midazolam is also known to have a shorter half-life. Side effects of benzodiazepines include respiratory depression and lactic acidosis, so close monitoring is required. Airway management is a priority, and this is because muscle spasms, laryngeal spasms, aspiration, or the use of large doses of sedative drugs can cause respiratory tract disorders. The patient should be properly positioned and suctioned periodically if there is excessive secretion to help prevent respiratory complications such as aspiration pneumonia. In patients with severe symptoms of tetanus, consideration should be given to tracheostomy or mechanical ventilation, especially in patients receiving high doses of sedation to control seizures or muscle spasms. Sudden laryngeal spasms, diaphragmatic muscle paralysis, and inadequate respiratory muscle contractions often occur when ventilator access is unavailable, resulting in respiratory failure. Beta-blockers, for example, propranolol and labetalol, have been used to control hypertension and tachycardia. However, propranolol has been linked to sudden cardiac arrest as one of the causes of death.

All tetanus patients, especially those with severe symptoms, should be treated in a special treatment room away from other patients and in the Intensive

Care Unit (ICU) so that they can be monitored continually . Loud noises or bright lights can trigger paroxysmal spasms, so the patient should be treated in a dark, quiet room. Early enteral feeding is recommended in patients with tetanus. This is due to the symptoms of difficulty swallowing and an increase in the body's metabolic rate caused by excessive muscular and autonomic activity, so it is important to provide nutritional support that can be achieved through enteral or total parenteral nutrition until the patient is fully recovered.

Clinical signs get better when there are no longer spontaneous spasms, stiffness in the body, respiratory problems, impaired consciousness, or coma.[1,11,12,20] In this case, the patient was given 100 mg of diazepam in 500 cc of Ringer's lactate. He had dysphagia that required nasogastric intubation. The patient was transferred to the ICU isolation room with minimal external stimulation. The patient's condition worsened, and he received midazolam (3 cc/hour) via a syringe pump on the second day of admission. It is important to control breathing by placing a tracheostomy or using mechanical ventilation, but this cannot be done due to limited facilities and infrastructure.

It is important to determine the degree of disease in a patient with tetanus to assess the prognosis and guide how aggressive the therapy can be. Prognostic assessment is also one of the most important components for determining mortality risk. There are several systems of tetanus scoring, one of which is the Ablett scoring system (Table 1), which is proposed and the most widely used. In addition, the Phillips score (Table 2) and the Dakar score (Table 3) were also used, which included criteria for the incubation period and the onset period, as well as neurological and cardiac manifestations. The Phillips score also consists of the patient's immunization status. Phillips scores <9 for mild severity, 9–18 for moderate severity, and >18 for severe severity. The Dakar scores 0–1 for mild severity with 10% of the mortality rate, 2–3 for moderate severity with 10–20% of the mortality rate, 4 for severity with 20–40% of the mortality rate, and 5–6 for very severe with >50% of the mortality rate.

The Phillips score has high sensitivity (89%), but low specificity (20%). The Dakar score has good specificity (98%), but is less sensitive (13%). The outcome of tetanus patients is highly dependent on the severity of the symptoms of the disease and the available treatment facilities. The mortality rate is 13% to 25% in better treatment facilities. However, in some studies, patients rarely survive. Some patients may develop persistent electroencephalographic (EEG) abnormalities and impaired balance, speech, and memory. Psychological support should also not be forgotten.[1,11,17]

Based on Ablett's classification, the patient in this case belongs to category 2 (moderate). The Phillips score found an incubation period of about 7 days with a score of 3, the location of infection on the forearm with a score of 2, no protection status with a score of 10, and injury with a score of 4. The total Phillips score was 19, with severe severity. The Dakar score found an incubation period of 7 days with a score of 0, the onset period with a score of 1, the site of wound entry with a score of 1, spasms with a score of 1, fever with a score of 0, and tachycardia with a score of 0. The Dakar score was 3 with a mortality rate 10–20%.

CONCLUSION

Indonesia still has a high mortality rate from tetanus cases. This case illustrated the importance of early recognition of tetanus and adequate immunization as the most effective interventions against tetanus. It is crucial to raise public awareness that tetanus is preventable and that its mortality and morbidity could be lowered with proper vaccination and sanitization.

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Author contributions
NT contributed to the conceptualization, resources, writing, review, and editing. MMDRR contributed to the resources and review.

Conflict of Interest
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TABLES AND FIGURES

Table 1. Ablett classification of tetanus[1]

Grade	Severity	Symptoms
1	Mild	Mild trismus, general spasticity, no respiratory compromise, no spasm, no dysphagia
2	Moderate	Moderate trismus, rigidity, short spasm, mild dysphagia, moderate respiratory involvement, respiratory rate >30 breaths/min
3	Severe	Severe trismus, generalized rigidity, prolonged spasms, severe dysphagia, apneic spells, pulse >120 beats/min, respiratory rate >40 breaths/min
4	Very severe	Grade 3 with autonomic dysfunction

Table 2. Phillips score[1]

Factor	Score
Incubation time	
<48 hours	5
2-5 days	4
5-10 days	3
10-14 days	2
>14 days	1
Site of infection	
Internal organ and umbilical	5
Head, neck, and body wall	4
Peripheral proximal	3
Peripheral distal	2
unknown	1
State of protection	
None	10
Possibly some or maternal immunization on neonatal patients	8
Protected >10 years ago	4
Protected <10 years ago	2
Complete protection	0
Complicating factors	
Injury or life threatening illness	10
Severe injury or illness not immediately life threatening	8
Injury or non-life threatening illness	4
Minor injury or illness	2
ASA grade 1	0

Table 3. Dakar score[1]

Prognostic factor	Dakar score	
	Score 1	Score 0
Incubation period	< 7 days	≥ 7 days or unknown
Period of onset	< 2 days	≥ 2 days
Entery site	Umbilicus, burn, uterine, open fracture, surgical wound, intramuscular injection	All others plus unknown
Spasms	Present	Absent
Fever	> 38.4 ºC	< 38.4ºC
Tachycardia	Adult > 120 beats/min Neonate > 150 beats/min	Adult < 120 beats/min Neonate < 150 beats/min

Figure 1. Post hecting wound at the public health center

Figure 2. *Aff Hecting at the ER*