

A case report of severe tetanus infection in a rural ICU setting: Role of intravenous magnesium

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ABSTRACT:

Tetanus is a life-threatening condition often complicated by repetitive spasms, dysautonomia, and neuromuscular respiratory failure, contributing to high mortality in its severe form. Benzodiazepines and neuromuscular blockers used to treat muscle spasms pose a high risk of respiratory failure requiring mechanical ventilation, which increases hospital stay and morbidity and is inaccessible for many. Magnesium sulfate, a cheap and widely available medication in all urban and rural health centers used for the treatment of eclampsia, can be used to control muscle spasms and dysautonomia. In our case report, the use of magnesium sulfate was found to be effective in reducing muscular spasms along with other supportive medications, leading to better control of dysautonomia, withdrawal from mechanical ventilation, and shorter ICU stays.

Keyword: Tetanus, Trismus, Magnesium, Ventilator, Vaccine

INTRODUCTION:

Tetanus is a serious life-threatening disease caused by exotoxin produced by *Clostridium tetani*, an anaerobic, gram-positive, spore-forming bacillus that is found in soil and animal excrement [1]. Tetanus is often a diagnosis of exclusion with clinical features of hypertonia and muscle spasm in the absence of a more likely diagnosis [2]. Infection occurs when bacterial spores enter the body through a wound or trauma to the skin and then germinate under anaerobic conditions. The bacteria produce an exotoxin, tetanospasmin, which binds at the neuromuscular junction and results in painful muscle contractions [2].

Tetanus can be classified into three different clinical forms: generalized, localized, and cephalic [3]. The most common presentation is generalized tetanus; the patient presents with trismus or spasms of the masseter muscle. This progresses to painful, generalized spasms of muscles of the neck, abdomen, and extremities and potential abdominal rigidity [3]. There can be autonomic instability, which can lead to cardiac arrest and death. Localized tetanus occurs with spasms in a certain muscle group, typically near the wound [3]. Cephalic tetanus is associated with wounds to the head or face and it is the

rarest form. It presents differently from the other forms, with cranial nerve palsies resulting in flaccid paralysis rather than spasms. Both localized and cephalic tetanus can progress to the generalized form [3]. Once recognized as tetanus, prompt treatment is recommended with, tetanus toxoid, tetanus immunoglobulin, aggressive wound care, and antibiotics with anaerobic cover. Medications for the treatment of muscle spasms should be used, with benzodiazepines being the preferred agent [3].

Unvaccinated individuals, the elderly, diabetics, and illicit-injection drug users are the populations at an increased risk for tetanus infection. Vaccination, timely wound treatment, injection of tetanus antitoxin after injury, maintaining strong neonatal tetanus surveillance, hygienic delivery practices and umbilical cord care, and vaccination for pregnant women and women of reproductive age can prevent tetanus [4,5].

CASE REPORT:

A 19-year-old male, Asian, a shepherd by occupation was brought to the emergency department with a 2-day history of generalized weakness, body aches, and headache. He was accompanied by his friends. He

presented with a fever of 38.8 degrees Celsius, involuntary jerky limb movements, and generalized spasticity. He had a jittery smile and was having frequent spasms. There was no significant past medical history.

He was awake and obeying simple commands. His vitals were stable except for the fever. He was assessed by a neurologist, and although the neurological examination was limited by his condition, there was diffuse hypertonia and hyperreflexia and bilateral ankle clonus; an initial working clinical diagnosis of tetanus infection was made.

There was recent body injury or cut wounds, however, mild foot abrasions were noted as he sometime walks outside barefooted.

The vaccination history could not be verified as the patient doesn't remember his immunization history.

Initial blood investigations and computerized tomography scans of the brain were unremarkable, and treatment for generalized tetanus infection was started after discussion with the infectious disease physician.

The patient developed respiratory distress with progressive lower limb weakness (paraparesis). An emergency intubation was performed and commenced on mechanical ventilation with sedation. The patient was shifted to the medical ICU.

Human immunoglobulin (IVIG) 20 gm was infused over 18 hours for 3 days due to the unavailability of tetanus immunoglobulin. On the same night, the patient developed two episodes of generalized tonic-clonic convulsions while on mechanical ventilation and sedation. His sedation was increased with midazolam and fentanyl infusions and started on iv. levetiracetam 750 mg iv bd. He also required muscle relaxant, iv. cis-atracurium continuous infusion. He was also given metronidazole 500 mg iv qid and Ceftriaxone 2gm iv bd. Nasogastric feeding was started.

Covid-19 IgG antibodies were found to be high on admission suggestive of recent covid-19 infection. The repeat coronavirus disease-19 swab on day 4 turned out to negative. On day 5, the patient's respiratory symptoms deteriorated; a repeat chest X-ray showed a new pneumonic patch, therefore, the antibiotic escalated to iv. piperacillin and tazobactam and mechanical ventilation continued as per the ARDS guidelines. Initial blood culture collected on admission showed no growth, but respiratory culture came positive for *Acinetobacter baumannii* (heavy growth) susceptible to piperacillin and tazobactam.

On day 9, the patient was still having spasms and rigidity despite on minimal stimulus while positioning in bed, requiring deep sedation and muscle relaxation for longer periods. MRI brain ruled out encephalitis. A tracheostomy was discussed with the patient's relatives, but they refused for it. Follow-up respiratory culture on

day 20 grew carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* complex, both susceptible to ciprofloxacin. Ciprofloxacin 400 mg iv was added to the treatment plan. The patient was still having frequent muscle spasms, so we decided to start him on low-dose intravenous magnesium sulphate at 1gram infusion daily. To avoid overdose, the patellar reflex was monitored, and therapeutic drug monitoring was done to keep serum magnesium levels below 4 mmol/L.

After initiation of magnesium, the patient's condition gradually improved over the next few days and he was weaned from mechanical ventilation and sedation and was extubated successfully on day 29. He stayed a further 4 days in the ICU and shifted to the medical ward on day 34. He continued to receive physiotherapy and nutritional support and was discharged home on day 39th of his admission.

DISCUSSION:

Tetanus is a clinical diagnosis defined by hypertonia with painful muscle contractions or spasms. Generalized tetanus is a disease characterized by a progression from trismus to stiffness of neck muscles with difficulty swallowing. The differential diagnosis for those presenting with trismus and muscle spasm as seen in tetanus includes dystonia, strychnine poisoning, dental infection, seizure, or hypocalcemic tetany [6]. Tetanus patients may also present initially with non-specific symptoms, like weakness, dysphagia, facial pain, and trismus. Laboratory tests and imaging may help in ruling out other diagnoses but do not assist in the confirmation of tetanus. As the diagnosis of tetanus is purely clinical and patients commonly present with non-specific symptoms, the diagnosis on initial presentation may be difficult. However, all the patients with tetanus should be admitted for monitoring [7].

So many case reports have described patients who presented with tetanus-like symptoms but were initially diagnosed and treated for otitis media or sinusitis [8, 9]. A vaccination history and a history of recent wounds are necessary for risk stratification.

In the developing world, there is rising interest in the management of tetanus due to the limited data regarding alternate therapies over conventional management. The use of magnesium in tetanus is gaining popularity, while trials regarding its efficacy are showing variable results. Magnesium plays a vital role in neuromuscular transmission and muscular excitability. Magnesium sulphate reduces striated muscle contractions and blocks peripheral neuromuscular transmission by reducing acetylcholine release at the myoneural junction. Additionally, magnesium inhibits Ca^{2+} influx through dihydropyridine-sensitive, voltage-dependent channels. It functions as a physiological antagonist of calcium at

the cellular level, causing vasodilatation, presynaptic neuromuscular blockade, and prevention of catecholamine release [10]. It also has anticonvulsant properties [11]. A safe serum therapeutic range of 2 to 4 mmol/l has been established for patients with eclampsia [12]. Autonomic dysfunction was significantly associated with higher urinary adrenaline excretion, which magnesium seemed to protect against (noradrenaline excretion did not show a similar correlation with clinical autonomic dysfunction). Autonomic dysfunction in tetanus is known to be associated with a higher rate of catecholamine release, especially that of adrenaline [13]. It is possible that magnesium exerts some of its beneficial effects by blocking adrenaline release.

In our case, the iv magnesium sulphate was given as a single daily dose instead of infusion as reported in some cases. This regime was highly effective in reducing the frequency of spasms and the need for heavy sedation. This resulted in early weaning from the ventilation proceeding to extubation and discharge from ICU to the medical ward.

Menelaos Karanikolas and others [14] claimed that in comparison with previous trials, their case series contributed meaningful additional information, including iv magnesium therapy used on patients already requiring mechanical ventilation while remaining effective for up to 26 days; it was significantly longer than in previous reports. They reported that the overall outcome was good in all their patients. However, the optimal dose and maximum safe duration of intravenous magnesium therapy were all unknown and required further research. Magnesium sulfate remains a relatively inexpensive treatment option to control muscle spasms and autonomic dysfunction in tetanus [15].

CONCLUSION:

Tetanus is a rare but life-threatening infection. In our case, along with benzodiazepine, magnesium sulfate was effective in reducing refractory muscular spasms, reduced need for mechanical ventilation, early extubation, and a shorter hospital stay. Although magnesium treatment alone does not reduce the need for mechanical ventilation in adults with severe tetanus, its use reduces the requirement for other muscle relaxants and improves cardiovascular instability. Magnesium is safe, inexpensive, and suitable for use in the developing world. Benefits could be greater in settings with little or no intensive care support. Magnesium is thus an important therapeutic advance in treating this major cause of morbidity and mortality in the developing world. Further work is needed to define its role in the less severely ill and in settings with limited facilities.

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Statement of Ethics:

The Hatta Hospital Ethics Committee approved this case report, and the patient provided informed consent for this publication.

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Author Contributions:

1. Dr. Anand Bhaskarrao Kotgire - Corresponding and Main author
2. Dr. Hisham Kewan – Literature review
- 3- Dr. Shayan Ahmed – Preparing the manuscript
4. Dr. Mahmud Elshahat – Preparing the manuscript
5. Dr. Mohamed Omar – Data collection
6. Dr. Hussain Kandeel – Data collection
7. Dr. Urooj Syed - Head of ICU and supervisor

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