

# Diagnosis of Severe Tetanus Assisted by Next-Generation Sequencing Analysis of Etiology: A Case Report

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## Case report

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## **Abstract**

We shared our successful treatment experience of a severe tetanus patient in China. A 50 year old male patient was admitted to our hospital 10 days after the right arm injury due to pain and masticatory weakness. The pathogen of wound secretion was confirmed to be clostridium tetanus by next-generation sequencing (NGS).The patient's condition rapidly progressed to a severe state with autonomic instability. After debridement and comprehensive treatment in ICU, including deep analgesia and sedation with dexmedetomidine, ventilator support and anti-infection treatment, the patient finally recovered and discharged. This case suggested that early diagnosis and reasonable intervention of severe tetanus could reduce mortality.

## **Introduction**

Tetanus is a life-threatening and serious infectious disease with a high morbidity and mortality<sup>1</sup>. Clostridium tetani is a gram-positive bacillus producing tetanospasmin, the toxin leading to its disabling and fatal manifestations such as autonomic instability<sup>2</sup>.Generalized tetanus is the most classical form. However, tetanus may prove to be difficult diagnoses to arrive to, in view of its unusual presentation<sup>3</sup>. Looking into the journals and scientific literature, we can find very few publications related to diagnoses or long-term prognosis<sup>4,5</sup>.Hence, this case report becomes important to impart knowledge to treating doctors in Intensive Care Units to learn features of tetanus for early recognition and need for prompt diagnosis and treatment.

## **Case Report**

A 50-year-old male building worker presented with history of an injury to the right arm 10 days before presentation, followed by recent onset of difficulty in opening mouth .Debridement and suturing were performed in the local hospital and tetanus antitoxin immunotherapy was injected 10 days before. A 10 cm longitudinal incision was seen on the palmar side. He represented to our hospital, complaining of painful of the injury site and lockjaw.

After admission, the patient was transferred to SICU single ward immediately to reduce sound and light stimulation. Human tetanus immunoglobulins, 1000 IU IM, were given to the patient to neutralize the circulating toxins. For muscle spasm, diazepam infusion of 1 mg/kg/day was given .Penicillin and metronidazole were given as antibiotic coverage.He developed respiratory failure the following day, the severity of his illness required mechanical ventilation and subsequent tracheostomy. Further surgical debridement was then performed,along with administration of tetanus toxoid (TT)(Fig. 1). Clostridium tetanus was identified in wound secretions by next-generation sequencing(NGS) analysis of etiology(Fig. 2). The wounds were washed with hydrogen peroxide solution every day. Autonomic instability became apparent 7 days after transfer, with rapid and extreme fluctuations in heart rate and blood pressure. We gave him neuroblockers, analgesics and sedatives .His antibiotic regimen altered to intravenous metronidazole and ceftriaxone soon .Because of the use of large doses of sedative and

analgesic drugs, the patient's gastrointestinal peristalsis was weakened, and there was a lot of gastric juice every day. Therefore, we gave the patient pyloric feeding later to strengthen nutritional support.

Recognition of the tetanus pathophysiology ,comprehensive treatment in ICU and choice of sedative medications, including dexmedetomidine for its anti-sympathetic effect, led to successful discharge. The patient was discharged after 28 days in SICU and 15 days more in respiratory ward. Except for a little stiffness in the joints, the patient had clear mind, fluent speech and free movement of joints at the time of discharge.

After discharge, the family members complained that the patient had an involuntary shaking of left leg when sleeping at night, and then head MRI showed multiple ischemic lesions in his right frontal lobe and bilateral parietal lobes .Within 3 months after discharge, this kind of left leg involuntary shaking had always existed.

Assent for case presentation were obtained from his wife and daughter, and a study protocol was approved by the Hospital Ethics Committee.

## Discussion

The rarity of tetanus and the difficulty of cultivation of Clostridium tetani, which leads to early clinical diagnosis mainly relying on the experience of doctors. Recently,NGS has shown an advantage in etiological diagnosis.The NGS technology allows for the detection and identification of ('difficult-to-culture')microorganisms using a culture-independent strategy<sup>6</sup>,especially in the diagnosis of unexplained encephalitis<sup>7</sup>.We report a case of tetanus confirmed by NGS sequencing, suggesting that there are still many possibilities in the etiological diagnosis of tetanus.

In severe patients, heavy sedation, ventilation and neuromuscular blockade are the standards of treatment. Particularly in autonomic instability, the best choice therapy remains unclear<sup>8</sup>. Autonomic instability is often accompanied by typical clinical symptoms in the second week,such as hypertension, tachyarrhythmia or sweating, less frequently bradyarrhythmias, resistant hypotension and cardiac arrest<sup>2</sup>.Dexmedetomidine is a high selective α-2-receptor agonist. It has combined analgesic and anti-sympathetic effect, make it sensible to consider in this setting<sup>2</sup>.There have been several studies describing its successful use in severe tetanus use ,especially in generalised tetanus complicated by uncontrolled autonomic instability<sup>9</sup>. The longest duration was about 7 days<sup>9</sup>.Here we present a case of generalised tetanus complicated by autonomic crises managed with dexmedetomidine infusion about for 14 days.The half-life of dexmedetomidine was short and without respiratory system depression. Except for the allowable hypotension and bradycardia,we did not find the damage of liver and kidney function in the course of continuous use. In this case,the administration of dexmedetomidine reduced the use of sedative drugs to control muscle spasms and cardiovascular instability. There is no upper limit in dose or frequency of sedative agents.This case illustrates that very high doses of all sedatives were required for almost 3 weeks.

Fortunately, the patient finally recovered. We still don't know whether the limb shaking in sleep, the denaturation in the head MRI and tetanus toxin were related. We will follow up the patient's long-term prognosis. Finally, we should not detract from the importance of general ICU management in treating severe tetanus. Appropriate wound care and debridement, antibiotics and the administration of antitoxin are all essential<sup>10</sup>. Also, as tetanus infection does not lead to development of protective antibodies, immunisation with tetanus toxoid is mandatory, as it will reduce the chances of developing tetanus from subsequent wounds.

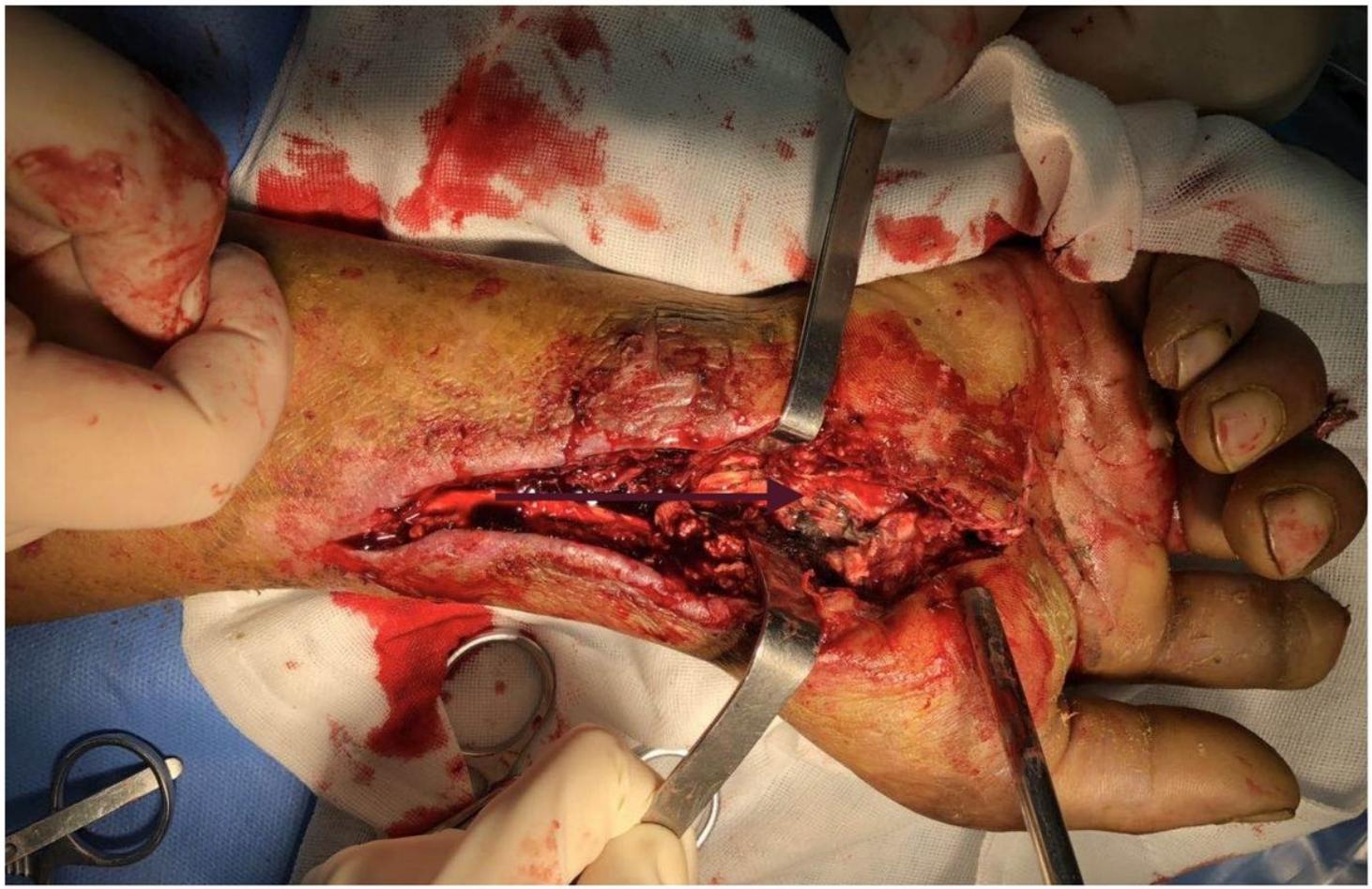
## Declarations Of Interest

None.

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## Figures



**Figure 1**

Intraoperative debridement picture( arrow shown building cement sands)

## 检测结果

原核微生物					
类型	中文名	拉丁名	置信度	特异序列数	
G+	破伤风梭菌	<i>Clostridium tetani</i>	高	326	
G+		<i>Paenibacillus thiaminolyticus</i>		74	
G+		<i>Terrisporobacter glycolicus</i>		58	

病毒					
类型	中文名	拉丁名	置信度	特异序列数	
样本未检出明确致病病毒					

真核微生物					
类型	中文名	拉丁名	置信度	特异序列数	
样本未检出明确致病真核微生物					

Figure 2

NGS report of wound secretions