An experience in treating generalized tetanus: A case report

Jen-Tse Chen¹,², Pin-Wen Liao¹,³, Mei-Ching Lee¹,³

ABSTRACT

Tetanus is a rare but lethal disease in developed countries. We report a case involving a 68-year-old man who presented to our hospital with trismus, opithotonus with neck pain, and episodic apnea. He had an open wound in his right index finger that had not received appropriate treatment. Tetanus immunoglobulin G was administered. Endotracheal intubation and subsequent tracheotomy with a ventilator were performed with total sedation with midazolam and diazepam. To relieve the persistent muscle spasm, magnesium sulfate and baclofen were added. He completely recovered after 40 days of hospitalization. Although tetanus-related mortality is rare in Taiwan, prompt diagnosis and empirical treatment are necessary.

Keywords: tetanus, trismus, opithotonus, magnesium sulfate

BACKGROUND

Tetanus is a rare and life-threatening nervous system disorder characterized by localized or generalized muscle spasms. The cause of the disease is tetanospasmin, a toxin produced by the anaerobic, spore-forming rod Clostridium tetani, which enters the central nervous system through retrograde axonal transport and causes characteristic muscle spasms and tonic contractions. Tetanus usually follows an injury such as a puncture wound, abrasion, or laceration. The generalized form is the most common and can cause mortality by inducing autonomic instability, respiratory arrest, and cardiac arrest. Considering the severity of the disease and the complexity of managing patients with tetanus, we described our experience in treating generalized tetanus.

CASE REPORT

The patient was a 68-year-old man with hypertension and chronic hepatitis B. He developed difficulty in swallowing and a sensation of tight-
ness in the neck five days before presenting to us. He was admitted to the ward under an initial impression of stroke in the emergency service. On the first admission day, he complained of difficulty in opening his mouth. The tightness and painful sensation worsened and radiated to the back. The patient then experienced three episodes of transient apnea with severe spasms of the whole body, especially after an agitated mood. We also noted hyperextension in his head, neck (Fig. 1), and back (opithotonus). He regained his consciousness soon and showed spontaneous breathing. Because of the trismus, opithotonus, and episodic generalized muscle spasm with apnea, tetanus was considered. We also noticed a gangrenous necrotic wound on his right index finger (Fig. 2). His complete blood count was within the normal limit on the first admission day, but the white cell count increased to 13990/µL 3 days later. Electrocardiography showed sinus tachycardia. According to his family, he sustained the traumatic wound when he built some furniture by himself with rusty tools at home one week ago. He did not care for the wound or receive any appropriate management. After admission to the ward, he was transferred to the intensive care unit (ICU). To neutralize the unbound toxin and stop toxin production, adequate wound debridement was performed with local injection of tetanus immunoglobulin (IG) 250 U around the wound. Tetanus IG 2750 U was administered by intramuscular injection. The wound and blood cultures were negative. The patient also received metronidazole for 10 days after consulting infection specialist. He underwent endotracheal intubation with ventilator support and subsequently underwent tracheostomy for better tracheal suctioning and pulmonary toilet. Midazolam was give first and diazepam was

Figure 1. The appearance of the face and neck of this patient. The facial appearance in the ward; trismus and contraction of the sternocleidomastoid with neck hyperextension, was observed in the upper body.

Figure 2. The open wound on the right index finger of this 68-year-old man showed gangrenous necrosis.

Figure 3. The open wound after debridement of this patient.
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given one day later for a longer effect to ensure a total sedative condition. Due to the persistent muscle spasm and continuous elevation of creatine phosphokinase (CPK) levels, we used intravenous baclofen when benzodiazepine was administered. Two days later magnesium sulfate (MgSO₄) was added. The muscle spasm reduced gradually 2 days after MgSO₄ administration. Creatine phosphokinase (CPK) level decreased from 5050 IU/L to normal limits under adequate hydration and good response to muscle relaxant. The reduction in CPK levels was more rapid after initiation of MgSO₄ administration. After supportive treatment in the ICU for 30 days, he was successfully weaned from the mechanical ventilator. Because of the long-term immobilization, he began to undergo rehabilitation and muscle training after ventilator weaning. He had fully recovered over 40 days of hospitalization.

DISCUSSION

The clinical features and the history of preceding trauma in this case allowed the diagnosis of tetanus. Trismus and dysphagia are the most common presenting symptoms. This case shows typical generalized tetanus after a traumatic wound injury. The patient recovered successfully without any sequelae after undergoing adequate wound debridement and good supportive management with tetanus IG.

Many tetanus cases are caused by minor traumas and gardening, but tetanus development may not be related to the trauma severity(1-4). Tetanus should be considered in cases with typical clinical presentation even there is no apparent entry point (5).

The diagnosis of tetanus is based on clinical presentation. The WHO definition of adult tetanus requires at least one of the following signs: trismus (inability to open the mouth) or risus sardonicus (sustained spasm of the facial muscles) or painful muscular contractions (6). According the previous report(7), trismus and dysphagia were the two most common initial presentations. Most patients subsequently developed generalized tetanus. There are no confirmatory laboratory tests although serum antitoxin titers can be helpful. However, due to the necessity for prompt treatment with immunoglobulin, waiting for the results of such assessments is not practical, because results may take up to several days. A reflex spasm of the masseters on touching the posterior pharyngeal wall is a positive test result. This test had a high specificity (100%) and sensitivity (94%) for diagnosing tetanus when it was performed on patients presenting with symptoms(7).

Antibiotics are administered to patients with tetanus to prevent the local proliferation of C. tetani at the wound site. The antibiotics that can be used include penicillin G, metronidazole and doxycycline. However, penicillin produces a non-competitive voltage dependent inhibition of GABA-A receptors obtunding post-synaptic inhibitory potentials. Penicillin in large doses might cause seizures and have proposed to potentiate the action of tetanospsamin theoretically(9). According to a study back to 1985 (10), metronidazole had a better mortality benefit compared to penicillin. Many experts also recommended metronidazole over penicillin (11,12).

To control the muscle spasm and rigidity, diazepam and midazolam are administered as a standard treatment and baclofen and even MgSO₄ are added for a better muscle relaxing and sedative effect. Sedation with benzodiazepines is
currently the mainstay of treatment for tetanus. As inhibitors of an endogenous inhibitor at the GABA_A receptor, benzodiazepines oppose the effects of tetanus toxin on the GABA_Aergic neurons. Diazepam is the most commonly used drug, although it has a long half-life. An alternative drug is intravenous midazolam, which has a shorter half-life. In this patient, midazolam was used initially and then shifted to diazepam to keep this patient completely sedated. Baclofen, a GABA_B agonist (8), and the directly acting muscle relaxant dantrolene (9), have been used, but their use is not widespread. MgSO_4 can be used alone or in combination with benzodiazepines to control spasms (10) and autonomic dysfunction (11,12). Magnesium is a physiological calcium antagonist and has both pre- and post-junctional neuromuscular blocking effects and reduces myofibrillar excitability (13). We added MgSO_4 to relieve the muscle spasm of this patient although he was deeply sedated. The spasm seemed to improve 2 days after the use of MgSO_4 and was correlated to the decrease in CPK levels. Although magnesium seems to be effective in treating muscle spasm, more controlled trials are needed to assess the effect of MgSO_4 (14).

The incidence of tetanus in developed countries reduced with the introduction of universal vaccination of children in 1940. In 2015, there were still more than fifty thousand deaths caused by tetanus worldwide. About one third deaths occurred in neonatal and two thirds occurred in children and adults. However, the global mortality rate due to neonatal tetanus dropped by 90% and that due to non-neonatal tetanus dropped by 81% from 1990 to 2015 by the scale up of global immunization programs (20). Cases still occur in Taiwan, particularly in elderly people owing to their reduced immune protection. Since the efficient implementation of tetanus vaccination, the average number of tetanus cases reported each year is about 10 in Taiwan. The incidence was approximately 0.03-0.1/100,000 population in recent 5 years in Taiwan (21). A higher incidence was observed in the older people. Cases older than 40 years old was 82% in the reported patients (7). According to the surveillance data collected by the Taiwan CDC, the number of tetanus death has been merely 5 for the past decade. One death from tetanus occurred in the years 2005, 2006, 2011, 2012 and 2013. The tetanus cases occurred mainly among elder people which was different from the cases occurred in the third world. This incidence difference could be contributed to the well-organized public health and vaccination policy in Taiwan. In Taiwan, the routine childhood vaccination schedule recommends a dose of DTaP-Hib-IPV vaccine to children 2, 4, 6 and 18 months of age and a dose of Tetanus-Diphtheria (Td) vaccine to children prior to elementary school entry (15). Because of an antibody titer retention of only about 10 years, the positivity rate of the anti-tetanus antibody titer markedly decreases after 40 years of age in Japan (16), Brazil (25) and Singapore (26). Therefore, older children and adults should receive a booster dose every ten years after completion of the initial childhood series to prevent the sporadic tetanus infection in the elder people.

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全身性破傷風：病例報告

陳仁澤 1,2，廖品雯 1,3，李美靜 1,3

中文摘要

破傷風之病原為破傷風梭狀芽胞桿菌，通常是由沾有細菌的物品造成皮膚損傷而進入體內。破傷風梭狀桿菌會產生破傷風痙攣毒素造成中樞神經和自主神經受損，干擾肌肉正常收縮的能力，使肌肉異常痙攣。常見之症狀為頜部、腹部僵硬及肌肉痙攣，典型破傷風痙攣現象為「角弓反張」及牙關緊閉，伴隨強烈的肌肉收縮疼痛。由於台灣公共衛生之普及與疫苗注射之完善，每年破傷風感染之病例數均為個位數，死亡個案更為稀少。我們報告一位 68 歲男性因一周前右食指傷口形成壞死，因吞嚥困難、背部肌肉疼痛住院。其後因持續間歇性呼吸停止接受氣管內插管，其後氣管切開術合併呼吸器使用以維持心肺功能。診斷為破傷風後，使用鎮靜劑及硫酸鎂以緩解其肌肉痙攣，同時施行傷口清創合併抗生素注射和破傷風免疫球蛋白及支持性療法，個案於住院 40 天之後完全復原出院。因破傷風病例稀少容易被忽略，因此迅速正確的診斷才能給予病人完備的治療。

關鍵字：破傷風；牙關緊閉；角弓反張；硫酸鎂

1國泰綜合醫院神經內科
2國立陽明大學醫學院醫學系神經科
3輔仁大學醫學院醫學系
收稿日期：2017年11月27日
接受日期：2018年03月8日
通訊作者：陳仁澤 電子信箱：drpsycho123@gmail.com