

Tetanus in the Elderly: The Management of Intensive Care and Prolonged Hospitalization

Hiroki Isono^{1,2}, Taiju Miyagami³, Kohta Katayama², Momoko Isono²,
Ryuichi Hasegawa⁴, Harumi Gomi⁵ and Hiroyuki Kobayashi²

Abstract

Tetanus is a potentially fatal infection. Approximately 100 cases are reported in Japan each year; however, little is known about its clinical course and outcomes in the current era of treatment. We herein report three cases of tetanus in elderly patients who survived after mechanical ventilation and intensive care. These patients, together with six other similar cases, had a median weaning period of 31 days and median length of stay of 77 days. In elderly patients, severe systemic forms of tetanus require prolonged mechanical ventilation and hospitalization. To improve prevention, tetanus vaccination should be promoted more aggressively among those who are susceptible to the disease.

Key words: tetanus, prolonged mechanical ventilation, vaccination, intensive care

(Intern Med 55: 3399-3402, 2016)

(DOI: 10.2169/internalmedicine.55.7131)

Introduction

Tetanus is an infection caused by *Clostridium tetani*, a bacterium that is found in the soil and which enters the body through skin wounds. After an incubation period of 7-10 days, the disease starts with focal symptoms, such as spasmodic laughter, trismus, and dysphagia, and progresses to systemic symptoms, including respiratory failure and opisthotonus. Severely affected patients may suffer the paralysis of the respiratory muscles and autonomic disturbances that ultimately lead to death (1).

Tetanus is more common in elderly patients than in younger individuals. In Japan, the tetanus vaccine has been available since 1953; the diphtheria-tetanus-pertussis (DTP) vaccine was introduced for children in 1968 as a routine vaccination that is required by vaccination law (2). At present, approximately 100 cases of tetanus occur each year; 94% of the patients are ≥40 years of age and 18% of the patients are ≥80 years of age (2). A previous study showed that the mortality rate had decreased from 43% to 15% after

the introduction of the intensive care unit (ICU) (3). In fact, the annual mortality rate in the past 10 years has been as low as 8% in Japan (4).

However, little is known about the prognosis of elderly patients who survive severe tetanus. It is therefore important to form an appropriate discharge plan for tetanus patients who are treated in acute care hospitals. We therefore report three cases of tetanus in elderly patients who required mechanical ventilation and prolonged hospitalization.

Informed consent was obtained from each of the three patients for the publication of this case report and the use of the accompanying images. This report was reviewed and approved by the research ethics committee of the authors' institution.

Case Reports

Case 1

A previously healthy 85-year-old male farmer presented to our otolaryngology department with swallowing difficulty

¹Department of Primary Care and Medical Education, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Japan, ²Department of Medicine, Mito Kyodo General Hospital, University of Tsukuba, Japan, ³Department of General Medicine, Juntendo University School of Medicine, Japan, ⁴Department of Emergency and Critical Care Medicine, Mito Kyodo General Hospital, University of Tsukuba, Japan and ⁵Center for Global Health, Mito Kyodo General Hospital, University of Tsukuba, Japan

Received for publication January 18, 2016; Accepted for publication March 10, 2016

Correspondence to Dr. Hiroki Isono, hirokisono@gmail.com



Figure 1. The clinical findings on admission in Case 2. A: Trismus was observed. B: The abrasion on the patient's upper extremity is shown.



Figure 2. The clinical findings on admission in Case 3. A puncture wound from a tree branch with a small incision on the dorsal side of the left hand is shown. Redness and swelling are visible around the site of injury.

and trismus without generalized muscle rigidity. He had no history of injury. He had never been immunized for tetanus. His laboratory data were unremarkable. The possibility of deep neck infection was excluded by laryngeal endoscopy and contrast-enhanced computed tomography. Based on these findings, he was clinically diagnosed with tetanus. He initially declined hospitalization and returned home; however, he returned to our emergency department (ED) the next day due to the worsening of trismus. He was admitted to the ICU and required endotracheal intubation due to the possibility that he may develop opisthotonus and respiratory failure. After 4 days, he was extubated because he did not develop systemic symptoms. However, he was immediately reintubated on the same day as a result of expectoration difficulties and dysphagia.

Case 2

A previously healthy 81-year-old male farmer was transferred to our ED by ambulance due to a 3-day history of progressively worsening trismus and swallowing difficulty (Fig. 1A). The previous week, he had sustained an abrasion on his left arm while using pruning clippers (Fig. 1B). He

had never been immunized for tetanus. A physical examination revealed rigidity of the jaw and left upper extremity and muscle spasms of the left upper arm. He was clinically diagnosed with tetanus and was admitted to the ICU, where he required endotracheal intubation. The next day, his muscle spasms became aggravated due to opisthotonus after external stimuli.

Case 3

A previously healthy 91-year-old man was transferred to our ED by ambulance because of new-onset speech difficulties, which he first noticed upon getting up in the morning. He had never been vaccinated for tetanus. A physical examination revealed a puncture wound with redness and swelling on the dorsal side of the left hand, which had occurred 1 week previously while pruning a garden tree (Fig. 2). He was alert but could not speak. Trismus and rigidity of the neck and left arm were noted. He was clinically diagnosed with tetanus and was admitted to the ICU, where he required endotracheal intubation. Opisthotonus developed the next day.

Clinical course

On admission, all of the patients received human tetanus immune globulin (HTIG) and tetanus toxoid. Propofol or midazolam was administered for sedation to manage the patients' muscle spasms and fentanyl was administered for pain relief; muscle relaxants were not used. Case 3 had persistent muscle spasms for 36 days and received magnesium sulfate for 3 days. Wound debridement was performed for the two patients who had a clear source of infection (Fig. 1B and 2). All of the patients received antibiotics. Case 1 received penicillin G (4 million units, four times a day for 10 days); Case 2 received penicillin G (4 million units, four times a day for 7 days); and Case 3 received ampicillin/sulbactam (3 g, four times a day for 7 days).

In all cases, tracheostomy was performed within 2 weeks of admission. In addition, enteral nutrition and heparin pro-

Table. Clinical Characteristics of Severe Tetanus Cases in the Elderly in Japan.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Age (yr), sex	85, M	81, M	91, M	75, M	87, M	82, M	78, F	77, M	82, F
Latest vaccination	None	None	None	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Incubation period (d)	Unknown	4	5	7	4	13	Unknown	12	7
Source of infection	Unknown	Abrasion on the upper extremity	Puncture wound on hand	Cut on the thumb	Wound on the elbow	Right lower leg	Unknown	Cut on the forearm	Abrasion on the forearm
First symptom	Dysphagia	Trismus and difficulty in elevating the left upper extremity	Speech difficulties	Dysphagia	General feeling of malaise	Trismus	Dysphagia	Trismus	Pharyngeal discomfort
Interval between onset of the first symptom and admission (d)	4	3	1	4	4	6	3	2	Unknown
Symptom on admission	Trismus and dysphagia	Generalized tetanus	Generalized tetanus +	Generalized tetanus	Generalized tetanus +	Generalized tetanus +	Generalized tetanus +	Generalized tetanus +	Generalized tetanus
Autonomic dysfunction	None	None	+	None	+	+	+	+	None
Duration of mechanical ventilation (d)	60	18	Weaning not feasible	17	31	14	35	47	Unknown
Duration of intubation (d)	82	21	Weaning not feasible	45	unknown	14	35	Unknown	68
Complication in ICU	VAP, CRBSI, acalculous cholecystitis	VAP, DVT	VAP, CRBSI	Unknown	unknown	Unknown	Unknown	Unknown	Unknown
Duration of hospitalization (d)	101	38	151	76	77	35	60	90	85
Out come	Discharged	Transferred to a care facility and then discharged on day 59	Died in other hospital on day 204	Discharged	Discharged	Discharged	Discharged	Discharged	Discharged

Cases 1, 2, and 3 are described in the present study. Cases 4–9 are from previous reports.

ICU: intensive care unit, HTIG: human tetanus immune globulin, VAP: ventilator-associated pneumonia, CRBSI: catheter related bloodstream infection, DVT: deep vein thrombosis

phylaxis were administered as preventive measures against gastric ulcer and pressure sore formation, and physical therapy was provided. Because of their prolonged critical illness, the patients experienced complications, including ventilator-associated pneumonia (VAP), catheter-related bloodstream infection, and deep vein thrombosis.

Autonomic dysfunction was observed in Case 3, with fluctuating vital signs. Spasms were triggered, leading to the elevation of systolic blood pressure to >200 mmHg and a decrease in tidal volume. Noradrenaline was also administered to treat his abnormally low blood pressure. Weaning and liberation from mechanical ventilatory support were not feasible for this patient due to the weakness of his respiratory muscles.

The weaning periods in Cases 1 and 2 were 60 and 18 days, respectively; weaning was not achieved in Case 3. All three patients were eventually transferred out of the ICU. Despite the fact that these patients had no underlying diseases and were independent in their activities of daily living (ADL) before admission, prolonged hospitalization and rehabilitation were required to achieve a functional recovery. Case 1 remained in our hospital for 101 days. Case 2 was hospitalized for 38 days, then transferred to a care facility, from which he was discharged on day 59. Case 3 remained at our hospital for 151 days but died in another hospital on day 204. The ADLs of the other two patients improved after they were discharged.

Discussion

The clinical courses of these patients highlight two important points. First, patients with severe tetanus requiring mechanical ventilation need prolonged mechanical ventilation (PMV) and hospitalization. Second, sufficient vaccination is important for preventing tetanus in elderly individuals.

In the present study, Case 1 continued to suffer from dysphagia and VAP, while Cases 2 and 3 continued to suffer muscle spasms, which prolonged the period of bed rest and sedation. As a result, long-term rehabilitation was necessary due to the severe decline in the patients' general condition after discharge from the ICU. Two patients were transferred to another facility for further rehabilitation.

Six cases of elderly patients (≥75 years of age) with tetanus who required mechanical ventilation have been reported in Japan (Table) (5-9). The continuous variables were presented as median [interquartile range (IQR)]. When combined with the three cases of the present study, the median weaning period, time to extubation and length of hospitalization (in the acute care hospital) were 31 days (18-41 days), 40 days (25-62 days), and 77 days (60-90 days) respectively. One patient, who was not weaned from ventilatory support, was excluded from the analysis of the weaning period and the time until extubation.

A study in the United States reported two cases of tetanus

in patients of >90 years of age (10). Similarly to our cases, these patients required mechanical ventilation for more than 3 weeks and spent more than 2 months in different medical facilities. The cost of hospitalization was more than 200,000 USD for each patient (10).

Severe tetanus in older adults requires PMV for 1 month and hospitalization for 2 months. PMV is known to be associated with increased health care costs, morbidity, and mortality (11). It is important for intensivists to collaborate with general physicians, physical therapists, social workers, and the family to achieve functional recovery and to plan for a smooth discharge from the acute care hospital.

In Japan, the overall annual incidence of tetanus was 0.98 cases/million in 2008, which was approximately 10-fold of that in the United States (12, 13). Furthermore, the incidence in the Japanese individuals of ≥ 80 years of age was 3.6 cases/million (4). We therefore wish to highlight the importance of preventing tetanus and its associated morbidities by achieving sufficient vaccination coverage in older adults. The three patients in the present study had never been vaccinated against tetanus. A worldwide study demonstrated the effectiveness of the vaccine by a decrease in the annual incidence of tetanus from approximately 110,000 cases in 1980 to around 9,600 cases in 2010 (14). Nevertheless, most Japanese adults of ≥ 50 years of age have no history of vaccination, and their antibody levels remain at 30% (13).

We should engage in efforts to enlighten the population with regard to tetanus vaccination. In general, vaccination with tetanus toxoid is required three times. Routine vaccination with booster doses every 10 years is also recommended (15). We believed that tetanus toxoid and HTIG should have been administered immediately after the onset of injury to patients with a history of injury. Because tetanus can re-occur even among patients with a history of the disease, tetanus patients should be vaccinated after treatment and discharge.

In the present case report, one patient received a continuous intravenous infusion of magnesium sulfate to treat muscle spasms. A meta-analysis showed that magnesium sulfate did not reduce mortality and that its effects on the total duration of ICU stay or hospital stay were unclear (14). A randomized controlled study demonstrated that magnesium sulfate was effective in reducing the use of other drugs but that it did not reduce the need for mechanical ventilation (16). Further research is needed to determine the role of magnesium sulfate in the management of tetanus.

In conclusion, although elderly patients with severe tetanus can be transferred out of the ICU, they will probably require PMV and hospitalization for approximately 1 and 2 months, respectively, because of complications, including severe deconditioning. Tetanus vaccination should therefore be promoted more aggressively among populations that are susceptible to the disease: tetanus vaccination should be in-

cluded in the primary vaccination series of adults who have never been vaccinated and a booster should be administered every 10 years to those who have completed the primary series.

The authors state that they have no Conflict of Interest (COI).

References

1. Cook TM, Protheroe RT, Handel JM. Tetanus: a review of the literature. *Br J Anaesth* **87**: 477-487, 2001.
2. Infectious Disease Surveillance Center; 2009 [Internet]. [cited 2015 Nov. 29]. Available from: http://www.mhlw.go.jp/shingi/2010/05/dl/s0519-6j_08.pdf (in Japanese).
3. Tetanus cases by age, 1999-2008: Infectious Disease Surveillance Center 2009 [Internet]. [cited 2015 Nov. 29]. Available from: <http://idsc.nih.gov/jiasr/30/349/de3491.html>
4. Trujillo MH, Castillo A, Espana J, Manzo A, Zerpa R. Impact of intensive care management on the prognosis of tetanus. Analysis of 641 cases. *Chest* **92**: 63-65, 1987.
5. Yabuta K, Imashuku Y, Hashimura T, et al. A case of tetanus with dysphagia as initial symptom. *Journal of the Japanese Society of Intensive Care Medicine* **19**: 415-416, 2012 (in Japanese).
6. Obi K, Kagohashi M, Hatano T, et al. Four cases of tetanus: its diagnosis and management of complications. *Juntendo Medical Journal* **56**: 68-72, 2010 (in Japanese, Abstract in English).
7. Koga Y, Murakami M, Takamatsu Y, Kashiwagi T. Two cases of tetanus. *Journal of Japan Surgical Association* **70**: 2941-2944, 2009 (in Japanese, Abstract in English).
8. Narukawa M, Maruyama M, Yasuoka A, Funada H, Kobayashi M. Generalized tetanus with intractable autonomic cardiovascular instability in an aged woman. *The Journal of the Japanese Association for Infectious Disease* **79**: 556-560, 2005 (in Japanese, Abstract in English).
9. Ogino S, Sasaki N, Hasegawa Y, Osige N, Miyazawa T. Reversible bronchial stenosis in an aged patient with tetanus. *Nihon Naika Gakkai Zasshi (J Jpn Soc Int Med)* **97**: 138-140, 2008 (in Japanese).
10. Helbok R, Brenneis C, Beer R, et al. Intensive care management in very old adults: two cases with clostridium tetani infection. *J Am Geriatr Soc* **59**: 552-553, 2011.
11. Lone NI, Walsh TS. Prolonged mechanical ventilation in critically ill patients: epidemiology, outcomes and modelling the potential cost consequences of establishing a regional weaning unit. *Crit Care* **15**: R102, 2011.
12. Tetanus surveillance---United States, 2001-2008. *MMWR Morb Mortal Wkly Rep* **60**: 365-369, 2011.
13. Mizuno Y, Yamamoto A, Komiya T, Takeshita N, Takahashi M. Seroprevalence of tetanus toxoid antibody and booster vaccination efficacy in Japanese travelers. *J Infect Chemother* **20**: 35-37, 2014.
14. Rodrigo C, Samarakoon L, Fernando SD, Rajapakse S. A meta-analysis of magnesium for tetanus. *Anaesthesia* **67**: 1370-1374, 2012.
15. Kim DK, Bridges CB, Harriman KH. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older: United States, 2015*. *Ann Intern Med* **162**: 214-223, 2015.
16. Thwaites CL, Yen LM, Loan HT, et al. Magnesium sulphate for treatment of severe tetanus: a randomised controlled trial. *Lancet* **368**: 1436-1443, 2006.

The Internal Medicine is an Open Access article distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).