



Tetanus of the elderly

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The medical records of 20 tetanus patients who were treated at a university teaching hospital in Taiwan during the period from October 1991 to July 1999 were retrospectively analyzed. There were 18 adults (six males and 12 females) with unknown previous immunization status and ages ranging from 34 to 87 years old (mean 63 years). Two patients were children, aged 3 and 5 years old, respectively; both of them had incomplete tetanus immunization. Of the 17 patients reporting previous acute injury, 10 had tetanus-prone wounds. Four of six patients who sought medical help for wound management received tetanus toxoid, but none received tetanus immunoglobulins. The most common symptoms were trismus, dysphagia, and muscular rigidity. Specific treatment consisted of active and passive immunization, wound management, parenteral antibiotics, and benzodiazepines, muscle relaxants or neuromuscular blockades for control of spasms and sedation. All adults were admitted to the intensive care unit and an artificial airway was established. Fourteen of them required ventilator support during the illness. Prophylactic tracheostomy was performed within 24 h after arrival in 12 (92%) of 13 patients. Two patients died with an overall mortality rate of 10%. Sequelae were rare in the patients who survived. Because of inclusion of the diphtheria-pertussis-tetanus (DPT) vaccine in the national Children's Vaccine Program and improvement in obstetrical practices and neonatal care in Taiwan, tetanus mainly occurs in people older than 65 years instead of neonates or children. Waning immunity to tetanus in the elderly and poor wound management practices by primary care physicians were contributory factors.

Key words: Adult, tetanus, tracheostomy

Tetanus is a disease caused by *Clostridium tetani*, an anaerobic gram-positive rod that produces spores and exotoxins. After spore inoculation via a wound, germination with the release of tetanospasmin occurs, which binds to the presynaptic membrane and blocks the release of the inhibitory neurotransmitters, resulting in characteristic muscle spasm and rigidity [1,2]. No portal of entry is found in 7 to 30% [3-5] of patients. Clinical manifestations typically begin with trismus or lockjaw, followed by dysphagia, stiffness or pain in the neck, shoulder, back muscle and proximal limbs. Some patients develop generalized spasms which may reduce ventilation or cause apnea. Without management, these patients will die of respiratory complications, such as hypoxia resulting from prolonged muscle spasms, asphyxia due to unrelieved laryngeal spasm, and respiratory tract infections. With the advent of induced paralysis, ventilator support and intensive care medicine, the mortality rate due to tetanus has markedly declined. Complications related to prolonged ventilator

support, autonomic dysfunctions, or complications unrelated to tetanus *per se* still lead to substantial morbidity and mortality [6].

Tetanus is a preventable disease and always affects nonimmunized or partially immunized hosts or persons with waning immunity. It occurs predominantly in neonates and young children in countries without comprehensive immunization programs but predominantly in people older than 65 years in developed countries. In Taiwan, diphtheria-pertussis-tetanus (DPT) vaccination was initiated in 1954 and the annual number of cases of tetanus has decreased dramatically [7]. However, there have been more than 300 cases of tetanus during the past two decades and tetanus remains an important clinical or public health problem.

The objective of this study was to determine the clinical presentation and outcome of tetanus cases in southern Taiwan from October 1991 through July 1999. The clinical impact of early tracheostomy on adult patients with tetanus was also investigated.

Materials and Methods

ICD-9 code was used to search for cases of patients

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with tetanus admitted to National Cheng Kung University Hospital from October 1991 to July 1999. The records of patients with reportable diseases maintained by the Nosocomial Infection Control Committee were also reviewed to identify these cases.

The patients' medical charts were reviewed and clinical information was collected, including demographic data, clinical manifestations, portal of entry, previous immunization history, premorbid medical history, clinical management and outcome. Cases which were incorrectly diagnosed throughout the entire hospitalization, or did not have records available for the entire clinical course were excluded. The rating scale described by Bleck was used for scoring the disease severity in each case [1]. The rating system includes six items: incubation period less than 7 days; period of onset less than 48 h; high-risk portal of entry; generalized tetanus; core temperature above 40 °C; tachycardia (heart rate > 120/min in adults, > 150/min in neonates). Each item is scored one point. Score of 0 to 1 is rated as mild in severity, 2 to 3 moderate, 4 severe, and 5 to 6 very severe. Cephalic tetanus is scored as severe or very severe. Neonatal tetanus is scored as very severe [1]. The incubation period of tetanus was defined as the time from spore inoculation after acute injury to the first symptom and the period of onset indicated the latency from that first symptom to the first reflex spasm. A high risk portal of entry was defined as a portal of entry which was associated with a reduced chance of recovery, and included entry associated with burns, umbilical stumps, surgical procedures, compound fractures, septic abortions, intramuscular injections, or narcotic abuse. The presenting wounds were categorized as tetanus-prone or not based on the medical record. Tetanus-prone wounds were defined as those which were: 1. more than 6 h old; 2. stellate in shape or avulsions; 3. more than 1 cm in depth; 4. caused by missile, crush, burn, or frostbite; 5. presenting with signs and symptoms of infection; or 6. containing devitalized tissue or concomitants (dirt, feces, soil, saliva, etc). The indications for establishment of artificial airway were also categorized as: for relief of respiratory distress or for preventative purposes. The latter means that an artificial airway was established in a patient with no respiratory distress because subsequent airway compromise was anticipated. Respiratory distress was defined as the presence of one or more of the following conditions: 1. signs of upper airway obstruction, such as stridor; 2. excessive work to breath: tachypnea (respiratory rate > 30 /min), use of accessory muscles, or subcostal muscle retraction; 3. signs of apnea spell; 4. signs of hypoxemia, such as central cyanosis or a

PaO₂ less than 60 mmHg on room air; or 5. arterial blood gas pH less than 7.35 and PaCO₂ more than 50 mmHg.

Results

Demographic data

Tetanus was diagnosed in 20 patients who were admitted to the National Cheng Kung University Hospital from October 1991 through July 1999. There were 18 adults (mean age: 63 years; seven males, 11 females). One of the adult patients was less than 40 years old, eight were between 40 and 64, and nine were 65 or older (Fig. 1). Two patients were children, aged 3 and 5 years, respectively.

Previous vaccination history

None of the adult patients had documentation of previous vaccination or could recall any booster of tetanus vaccine in the past decade. The two children had not completed the four injections of the DPT vaccination schedule before the illness.

Portal of entry and primary management of wound

Tetanus developed after an identified acute injury in 17 (85%) of the 20 patients. In three patients, the portal of entry could not be determined by history-taking or physical examination on admission. The incubation period ranged from 2 to 60 days and was less than 1 week in seven cases. The most commonly reported types of injuries were lacerations (eight patients) and puncture wounds (seven patients). The injury site was located in the lower extremity in 10 patients; the upper extremity in four; the head or trunk in one; and esophagus in one. Ten of the 17 wounds were described as tetanus-prone. Five patients did not pay any attention to the wounds.

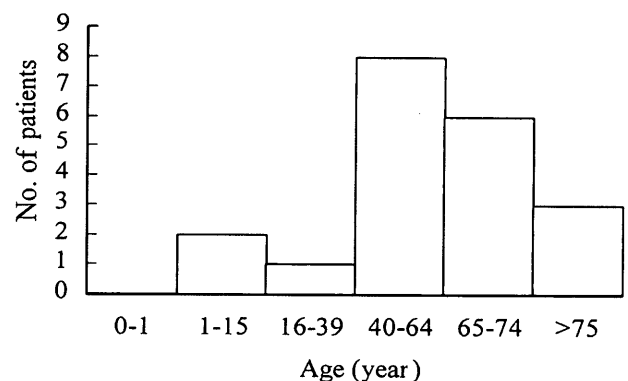


Fig. 1. Age distribution of 20 tetanus patients treated in a university teachin hospital.

Six patients cared for the wounds by themselves. Of the six patients who sought medical help after acute injury, four received tetanus toxoid immunization. None of the patients received tetanus immunoglobulins. When these patients were admitted to our hospital, the wounds had healed in seven patients and were complicated with necrotic lesion, pus or cellulitis in eight patients (five of which needed debridement and one of which needed a skin graft during hospitalization). Microbiological cultures of pus or discharge from the wound were obtained in six patients. All of the cultures revealed mixed flora, but *C. tetani* was not found. Initial surveillance blood culture was performed in all patients, but no isolate was identified.

Clinical manifestations and severity of illness

The clinical manifestations of the 20 cases were characteristic of generalized tetanus. The clinical courses of four patients were classified as mild in severity, nine moderate, four severe, and two very severe according to the Bleck rating scale.

Fever was noted initially in only two (10%) of the patients, and was associated with a wound complicated with cellulitis on the lower limb in one patient and with aspiration pneumonia in the other. Consciousness was clear on arrival in all but one patient. Besides trismus and dysphagia, which were present in 100% of patients, other symptoms included stiff neck (85%), rigidity of trunk or limbs (90%), muscle spasm (80%), risus sardonicus (30%), opisthotonos (50%), autonomic dysfunction (60%), sore throat (10%), nausea/vomiting (10%), and protrusion of the tongue (5%). Increased deep tendon reflex was detected in eight (57%) of 14 patients.

Thirteen patients were admitted directly to our emergency room, and the diagnosis of the remaining patients was made in other hospitals (five patients) or by the general physicians (two patients) before referral

to our hospital.

Management, complications, and clinical outcome

All patients were given an intramuscular injection of human tetanus immunoglobulin 250 to 5000 units after the diagnosis of tetanus. Tetanus toxoid was given simultaneously in 16 adults and DPT vaccines were given to the two children. Aqueous penicillin G was given parenterally to 19 patients and metronidazole to one patient. Diazepam with or without other benzodiazepines and various muscle relaxants were used in all patients. Nine patients developed severe rigidity and spasms requiring the use of neuromuscular blockade with sedation. Autonomic dysfunction resulting in cardiovascular instability developed in two patients. One was treated with morphine and the other one magnesium sulfate infusion.

All 18 adults were admitted to the intensive care unit. Artificial airways (orotracheal intubation or tracheostomy) were established during the illness for all adult patients either for preventative purposes or for relief of respiratory distress (Table 1). For preventative purposes, tracheostomy was performed within 24 h after arrival in our hospital in 12 (92%) of 13 patients and within 48 h in one. Orotracheal intubation was initially performed in three patients, followed by tracheostomy thereafter when a prolonged intubation was anticipated. Eleven episodes of complications related to tracheostomy developed, including subcutaneous emphysema, pneumomediastinum, dislodgement of the tracheal tube, stoma infection, tracheoesophageal fistula, and tracheal stenosis. Fourteen patients needed ventilator support and the duration of the use of a ventilator ranged from 2 to 38 days. The duration of stay in intensive care unit of the 18 adults ranged from 5 to 55 days. The two children with mild and moderate disease severity received medical care in the pediatric ward. The clinical

Table 1. Indications for establishment of artificial airway in 18 adult patients

	Prevention of complication (N = 14)	Relief of respiratory distress (N = 4)
Type of artificial airway		
Tracheostomy	13	2
Orotracheal intubation	1 ^a	2
Complications		
Subcutaneous emphysema	4	1
Pneumomediastinum	1	0
Stoma infection	2	0
Tracheoesophageal fistula	1	0
Tracheal stenosis	1	0

^aThe patient received preventive intubation at a local hospital before referral to our hospital.

course was uneventful for both of these patients. The overall mean length of hospitalization in all of the 20 patients was 35.8 days (ranged from 7-83 days).

One or more than one episodes of fever occurred during hospitalization in 15 (75%) patients. Infection (pneumonia in 11 patients, blood stream infection in six, urinary tract infection in three, wound infection in one and pansinusitis in one) was the most common cause of fever. Other complications during the clinical course included rhabdomyolysis (10 patients), complications related to artificial airway or ventilator (12 episodes in nine patients), upper gastrointestinal tract bleeding resulting from stress ulcers or duodenal ulcers (seven patients), acute renal failure (three patients), decubitus ulcers (one patient), acute myocardial infarction (one patient), acute embolic occlusion of the right brachial artery (one patient), and drug eruption (one patient).

Eighteen of the 20 patients survived (patient-fatality rate: 10%). Two patients, rated as very severe, died. One of them died of nosocomial bacteremia with multiple organ failure on the thirty-fourth day of hospitalization and the other, a 77-year-old woman, who had a short incubation period (2 days), a short period of on-set (less than 48 h), an abrasion wound complicated with cellulitis on her right leg and full-blown autonomic dysfunction on arrival, died on the seventh day of hospitalization because of severe metabolic acidosis, bradycardia and shock. Sequelae in surviving patients were rare, including contracture of limbs in three patients, urethral injury in one, mild tracheal stricture and left vocal cord palsy in one, and hypoxic encephalopathy in another.

Discussion

The diagnosis of tetanus is based on clinical findings and there is no specific test which can confirm it or to exclude it. The differential diagnosis for tetanus includes alveolar abscess, strychnine poisoning, dystonic reaction to dopamine blockade, meningitis/encephalitis, rabies, tetany and acute abdomen. Therapy should be initiated immediately once the clinical diagnosis is suspected. Cultures of the wounds frequently fail to reveal *C. tetani* even when anaerobic cultures are carefully performed. The organism can be isolated from wounds of the patients without tetanus [8]. Serum antitetanus antibody titers of concentration greater than 0.01 IU/mL are usually protective [9]. However, cases have been reported in patients with antibody levels higher than the protective concentration [10,11].

In Taiwan, tetanus has been designated as a reportable communicable disease since 1955. It was

redesignated in June 1999 as one of the class III communicable diseases, which should be reported to the Center for Disease Control and Prevention of Taiwan within one week after identification. Primary immunization for tetanus as a part of the national Children's Vaccine Program was launched in 1954 and the number of cases of tetanus has markedly declined since then (1004 cases in 1956 versus 17 cases in 1986). With improvement in delivery practices and medical care, mortality rate for this disease has also decreased (91.4% in 1956 versus 35.3% mortality in 1986) [7]. The epidemiology of the disease in the United States and other developed countries has changed. It now mainly affects people older than 65 years [5,12]. Similarly in our series, 17 (85%) patients were older than 40 years of age and nine (45%) were older than 65 years. There was no case of neonatal tetanus. Similar observations were made in two earlier reports from Taiwan [13,14]. Waning immunity in the elderly is most likely responsible for the increased incidence. A preliminary surveillance of titers of serum antibody against tetanus toxin in 133 cases in the general population in Taiwan revealed adequate protective antibodies in children and young adults, but 13.2% of the people older than 60 years of age did not have protective antibody levels [15]. A population-based serologic survey of immunity to tetanus in the United States indicated the rate of immunity to tetanus declined with age and 72% of the people older than 70 years of age did not have adequate protective immunity [16]. The National Coalition for Adult Immunization in the United States recommends a three-dose schedule of tetanus/diphtheria toxoids (Td) for individuals who have not received an initial immunization series in childhood. Boosters are then given every 10 years. At present, all children in Taiwan receive DPT vaccine as primary immunization for tetanus at the age of 2, 4, 6, and 18 months based on the national Children's Vaccine Program under the support of the government. However, failure to receive the recommended booster injection with tetanus toxoid thereafter every 10 years is often seen in Taiwan as well as in other countries [17,18]. This is probably due to the lack of compliance and awareness of both patients and doctors [5]. In our report, absence of documentation of prior immunization status was found in the 18 adult patients, and 16 of them were born before 1954 when the vaccination program was started. This finding reveals the need to immunize the high proportion of elderly individuals without primary immunization.

Eight of 14 patients with a tetanus-prone wound in this series did not seek medical care for their injuries

and only three of six patients who received medical assistance were given tetanus toxoid, and none of them received tetanus immunoglobulins, as recommended by the Immunization Practices Advisory Committee (ACIP) guidelines for wound management and tetanus prevention [19]. This highlights two important messages. First, there is lack of awareness among the general public about the potential risk of tetanus after injury. Second, inadequate prophylactic measures are provided for wound care at primary medical facilities. More effort is needed to improve public awareness and medical compliance with prophylaxis recommendations is essential.

Important issues in the management of tetanus include control of the airway and ventilation, administration of tetanus immunoglobulin, active immunization with toxoid, antibiotics, wound care, control of spasms, and treatment of autonomic instability. Human tetanus immune globulin (HTIG) is the antitoxin preparation of choice. It neutralizes the circulating tetanospasmin and unbound toxin in the wound, thereby shortening the course of the disease and reducing severity. As it has no effect on intraneural toxin, HTIG should be given as soon as possible. The commonly recommended dose is 3,000 units to 10,000 units intramuscularly though a dose of 500 units intramuscular injection has been shown to be as effective as larger doses [20]. Active immunization is also required for each patient to prevent recurrent tetanus because the amount of toxin that produces disease is insufficient to produce immunity [1]. Intramuscular administration of adsorbed tetanus toxoid, as tetanus-diphtheria vaccine (Td, 0.5 mL) or DPT (0.5 mL) as appropriate for age, in a different limb from that in which HTIG is given, is recommended. Although the value of antimicrobial therapy in tetanus remains unproved, antibiotic therapy is still given to eradicate the causative organism, *C. tetani*. The use of penicillin (10 MU to 12 MU intravenously, given daily for 10 days) has been recommended, but some authors preferred metronidazole (500 mg every 6 h for 7 to 10 days) on the basis of the result of one nonrandomized trial with lesser progression of disease and better survival in the metronidazole group than in the penicillin group, and the absence of the negative effect of penicillin, a known gamma-aminobutyric acid (GABA) antagonist [1,21].

Sedatives and muscle relaxants are widely used for the control of spasms and rigidity. Diazepam, a benzodiazepine and GABA agonist, is the mostly frequently used drug in tetanus. Lorazepam and midazolam are other choices. The dose should be titrated

to reduce spasms without causing oversedation and hypoventilation. Chlorpromazine and barbiturates are alternative agents. Various muscle relaxants, including baclofen and dantrolene, are also being investigated for relieving spasticity and shortening the clinical course [22,23]. Induced paralysis by using neuromuscular blockade with sedation and ventilator support are reserved for cases with severe rigidity and spasms. Curare-like agents, such as vecuronium, pancuronium, or atracurium, are the drugs of choice. The patient must be given adequate sedation to reduce the perception and electroencephalography should be continuously monitored during paralysis [1]. Standard management of autonomic dysfunction in severe tetanus has not been proposed due to the limitations of data obtained from case reports and the lack of comparative trials [24]. Agents that have been reported to have potential effect on the management of autonomic instability include magnesium sulfate, morphine, propranolol, labetalol and clonidine [25-27].

Respiratory complications are common in cases of severe tetanus and contribute significantly to both the morbidity and mortality rates [28]. Advances in ventilatory support techniques and intensive care management have decreased the mortality rate of tetanus. Trujillo *et al* compared the prognosis of tetanus cases with intensive care management with those treated conservatively. They found that intensive care management with induced paralysis and ventilator support markedly decreased the mortality rate from 43.5% to 15% [29]. A case series reported from northern Taiwan showed the mortality rate was 48% from 1971 to 1980 and 28.6% from 1981 to 1990. Thus, despite the improved survival rate in more recent years, a high mortality rate continues to be a problem even with better supportive care and modern therapeutic equipment. Aspiration pneumonia with subsequent respiratory failure was the most common cause of death [14]. Similar mortality rates were found in another study from southern Taiwan during the period from 1986 to 1989 (mortality, 21.7%; major cause of death, pulmonary complications) [13]. In the present study, 16 (80%) patients were rated as having moderate or greater severity and progression of the disease (an increase in trismus, rigidity, muscular spasm or presence of opisthotonus) after the initiation of treatment was noted in 15 patients. An artificial airway (tracheostomy in 15 patients, orotracheal tube in three) was established in all 18 adult patients and was most often performed for preventative purposes (12 patients) within 24 h after admission. Although pneumonia occurred and complications related to tracheostomy were not

uncommon, all were treatable and managed without significant sequelae. There was only one patient who had developed the complication of hypoxic encephalopathy, which resulted from profound hypotension instead of airway compromise. Because endotracheal intubation may induce laryngospasms with subsequent difficulty in intubation, an early tracheostomy may be beneficial [30]. The findings of this study suggest that early tracheostomy with ventilator support prevented respiratory compromise caused by the disease or treatment measures (sedation or neuromuscular blockades) and reduced the subsequent complications (asphyxia, aspiration pneumonia or hypoxic encephalopathy). This preventive measure may have significantly contributed to the lower mortality rate (10%) in this series compared with previous reports [13,14].

In summary, tetanus is a preventable disease. Immunization programs have markedly lowered the incidence of tetanus, especially in neonates and young children. As a result, tetanus now occurs predominately in adults and people older than 65 years without previous immunization or with an unknown immunization history. Although progress in intensive care treatment has significantly improved survival, the mortality is still around 10% to 15% in most developed countries [5]. Recovery from the disease still necessitates a long hospital stay for resolving the associated complications and for rehabilitation. Vigorous efforts are needed to implement strategies to reduce the incidence, and morbidity and mortality rates of this vaccine-preventable disease. The role of early establishment of artificial airway in moderate to severe tetanus patients needs further study.

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