

Tetanus in an intensive care unit of a Turkish hospital: Patient analysis of a 6-year period

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Aim: To retrospectively evaluate the clinical features of patients admitted to the medical intensive care unit (ICU) of our hospital between January 2001 and May 2007 due to tetanus.

Materials and methods: Patient vaccination history, incubation period, nosocomial infections, noninfectious conditions, mortality, and length of stay in the ICU and hospital were documented.

Results: Fifteen tetanus patients were admitted during the 6-year period. Mean age of the patients (9 male, 6 female) was 60 ± 13 years. Median length of stay was 42 days (range: 30-77 days) for survivors and 7 days (range: 1-59 days) for non-survivors. Mortality was consequent to severe tetanus in 5 patients, sepsis in 2 patients, and myocardial infarction in 1 patient. One patient died due to complications of acute renal failure, and another died due to acute pancreatitis and renal failure. The mortality rate was 66%. Seven patients had nosocomial infections (16 episodes). Ventilator-associated pneumonia was the most common infection, followed by primary bacteremia and urinary tract infection.

Conclusion: Although it is preventable with vaccination, tetanus remains a problem, especially for the elderly population. Despite intensive support, the mortality rate in our tetanus patients was high.

Key words: Tetanus, intensive care unit, nosocomial infection, mortality

Bir Türk hastanesi yoğun bakım ünitesi'nde tetanoz: 6 yıllık hasta analizi

Amaç: Bu çalışmada, Ocak 2001 ve Mayıs 2007 arasında hastanemiz dahiliye yoğun bakım ünitesinde (YBÜ) tetanoz tanısı ile izlenen hastaların klinik seyri retrospektif olarak değerlendirilmiştir.

Yöntem ve gereç: Hastaların aşılanma öyküsü, inkübasyon süreleri, nozokomiyal infeksiyonları, infeksiyon dışı durumları, mortalite ve hastane ve YBÜ'nde yatış süreleri kaydedilmiştir.

Bulgular: Onbeş tetanoz hastası bu dönem içinde izlenmiştir. Ortalama yaş 60 ± 13 yıl olarak kaydedilmiştir. Bu hastaların dokuzu erkektir. Ortanca yatış süresi yaşayanlarda 42 (30-77) gün ve kaybedilenlerde 7 (1-59) gün olarak saptanmıştır. Ölümünün beşi ağır tetanoz tablosu, ikisi sepsis ve biri miyokard enfarktüsü nedeniyle olmuştur. Bir hasta akut böbrek yetmezliğine sekonder gelişen komplikasyon nedeni ile, bir diğeri ise akut pankreatit ve akut böbrek yetmezliği nedeniyle kaybedilmiştir. Mortalite oranı % 66'dır. Yedi hastada nozokomiyal infeksiyon gelişmiştir (16 atak). Ventilator ilişkili pnömoni en sık görülen infeksiyon olup, bunu primer bakteremi ve üriner sistem infeksiyonu izlemiştir.

Sonuç: Aşı ile önlenilebilir olmasına karşın tetanoz, özellikle de yaşlı popülasyonda önemini korumaya devam etmektedir. Mortalite yoğun desteğe karşın hala yüksektir.

Anahtar sözcükler: Tetanoz, yoğun bakım ünitesi, nozokomiyal infeksiyon, mortalite

Received: 12.02.2009 – Accepted: 28.08.2009

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Introduction

Tetanus is an important infectious disease with a high mortality rate due to the toxins' action. It can be prevented with appropriate vaccination programs. Almost all tetanus patients are hospitalized in intensive care units (ICUs) due to the risks of mortality and morbidity, and are exposed to invasive interventions and possible nosocomial infections. The incubation period of the disease varies from 1 to 50 days (mean: 3-13 days) and it has been reported that the proximity of the wound to the central nervous system does not affect this period. Fever is unexpected during the course of tetanus, except in cases with complications, such as pneumonia and wound infection, and during the terminal stage of the disease. Typically, seizures with tonic, painful muscle spasms occur in tetanus and patients may suffer from seizures, even with the slightest stimulus. Death is mostly due to asphyxia; however, secondary infections may also contribute to mortality. The mortality rate varies between 5% and 35%; in neonates this rate may rise to about 60%.

Patients with tetanus should be vaccinated, as tetanus does not confer immunity. If a patient is not vaccinated or does not know his/her immunization status, vaccination should be performed, together with the administration of tetanus-immune globulin (TIG: 250-500 U). The aim of the present study was to determine the prevalence of tetanus in patients that were followed up in our hospital, the prognostic determinants of the disease, interventions undertaken during their follow-up in the ICU, acquired nosocomial infections, noninfectious complications, and the mortality rate (1,2,6).

Materials and methods

Patient population and analysis

The study included 15 tetanus patients that were follow-up in our hospital's ICU between January 2001 and May 2007. The patients were retrospectively evaluated with regard to vaccination, incubation period, total and ICU hospitalization duration, acquired nosocomial infections, noninfectious conditions, and the mortality rate. Data were obtained from registered files and from nurses' clinical observations. The causes of mortality were stated in

the written documents obtained during patient follow-up as well as in the death records.

Microbiologic methods

Microorganism isolation in the collected culture samples was conducted in the central laboratory of our hospital's microbiology department using the VITEK 2 automated identification system.

Statistical Analysis

The findings were registered in previously prepared forms and were statistically analyzed using SPSS v.11.5.

Results

Mean age of the 15 patients (9 male, 6 female) was 60 ± 13 years. None had been vaccinated in the previous 10 years. Seven patients had a history of posttraumatic vaccination, while 1 had a history of tetanus immunoglobulin administration. Mean incubation period was 6.5 days (range: 1-15 days). There was a history of head trauma in 2 patients, foot trauma in 7 patients, and hand trauma in 5 patients, whereas no focus could be identified in 1 patient. During treatment 6 patients (40%) had fever and the median baseline of creatine phosphokinase (CPK) was 1358 mg dL^{-1} (range: $315\text{-}5195 \text{ mg dL}^{-1}$). Nine patients presented to the emergency department with complaints of generalized contractions. The patients' characteristics are shown in Table 1.

Patient 4 had diabetes and patient 11 had hypertension. Urethral and central venous catheterization was performed in all patients. Tracheostomy was performed in 12 patients and, apart from 1 death at admission, all patients required mechanical ventilation. Median duration in the ICU was 8 days (range: 1-70 days), whereas the median hospitalization period was 13 days (range: 1-77 days). The median hospitalization period among the patients that died was 7 days (range: 1-59 days), versus 42 days (range: 42-77 days) among the survivors. At least 1 infectious attack occurred in each patient that survived. Five patients died due to a clinical entity of advanced-stage tetanus: 2 due to sepsis, 1 due to myocardial infarction, 1 due to acute kidney failure, and 1 due to complications of pancreatitis and acute kidney failure. The mortality rate was 66% (10 of the

Table 1. Characteristics of the study patients.

| Patient no. | Age | Gender | Vaccination history | Trauma region | Incubation Period (days) | Fever ¹ | CPK (mg dL ⁻¹) | Condition during visit* | Nosocomial infection | Result |
|-------------|-----|--------|---------------------|---------------|--------------------------|--------------------|----------------------------|-------------------------|----------------------|------------------------|
| 1 | 72 | Male | Absent | Foot | 4 | Present | 482 | C | Present | Recovered |
| 2 | 42 | Female | Absent | Hand | 7 | Present | 625 | C | Present | Exitus |
| 3 | 47 | Female | Absent | Foot | 7 | Absent | 965 | B | Present | Sequellae ² |
| 4 | 55 | Female | Absent | Foot | 4 | Absent | 5500 | B | Absent | Exitus |
| 5 | 65 | Male | Absent | ? | 1 | Absent | 4720 | D | Absent | Exitus |
| 6 | 50 | Female | Absent | Foot | 5 | Absent | 525 | D | Absent | Exitus |
| 7 | 75 | Male | Absent | Head | 15 | Present | 783 | D | Present | Recovered |
| 8 | 86 | Female | Absent | Hand | 15 | Absent | 1358 | D | Absent | Exitus |
| 9 | 73 | Male | Absent | Hand | 3 | Present | 13906 | A | Absent | Exitus |
| 10 | 39 | Male | Absent | Hand | 5 | Present | 5000 | D | Absent | Exitus |
| 11 | 57 | Male | Absent | Hand | 15 | Absent | 3823 | D | Present | Recovered |
| 12 | 51 | Female | Absent | Foot | 3 | Present | 5866 | D | Present | Recovered |
| 13 | 59 | Male | Absent | Foot | 7 | Absent | 35195 | A | Present | Exitus |
| 14 | 72 | Male | Absent | El | 5 | Absent | 725 | D | Absent | Exitus |
| 15 | 60 | Male | Absent | Foot | 2 | Absent | 315 | D | Absent | Exitus |

*A: Lock-jaw only; B: lock-jaw + stiff neck; C: lock-jaw + stiff neck and abdomen; D: generalized contractions.

¹Presence of fever during application.

²Hypoxic encephalopathy.

15 patients died). It was reported that deaths due to infectious causes occurred during later stages, whereas deaths due to advanced stage tetanus occurred most frequently during the first days of hospitalization. The duration of hospitalization according to cause of death is shown in Table 2.

In all, 16 nosocomial infection attacks were recorded in 7 patients; the most frequent type was ventilator-associated pneumonia, followed by primary bloodstream infection and urinary infection. Documented nosocomial infections and the corresponding microorganisms are shown in Table 3.

Discussion and conclusion

Tetanus was first described 3000 years ago in Egypt. The World Health Organization (WHO) reported 18,833 cases of tetanus in 2000, adding that the figure could actually be higher (11). This is due to the existence of many high-risk countries that do not report any cases to the WHO. Tetanus-related deaths are mostly reported from Africa (80%) and Southeast Asia (4). The survival rate from neonatal tetanus is 9%. Incidence of the disease has declined over the last 20 years due to primary vaccination programs. In many countries children born after the vaccination

Table 2. Causes of death and hospitalization duration.

| Patient no. | Cause of death | Duration of hospitalization (days) |
|-------------|-------------------------------------|------------------------------------|
| 2 | Sepsis | 42 |
| 4 | Advanced stage of tetanus | 4 |
| 5 | Advanced stage of tetanus | 4 |
| 6 | Myocardial infarction | 5 |
| 8 | Advanced stage of tetanus | 13 |
| 9 | Pancreatitis + acute kidney failure | 4 |
| 10 | Advanced stage of tetanus | 1 |
| 13 | Sepsis | 59 |
| 14 | Acute renal failure | 10 |
| 15 | Advanced stage of tetanus | 9 |

Table 3. Types of nosocomial infection and the corresponding microorganisms.

| Nosocomial infections | Agents | n | Total |
|---------------------------------|------------------------|---|-------|
| Ventilator-associated pneumonia | <i>A. baumannii</i> | 3 | 7 |
| | <i>P. aeruginosa</i> | 2 | |
| | Clinical diagnosis | 2 | |
| Primary bloodstream infection | <i>P. aeruginosa</i> | 2 | 4 |
| | <i>E. coli</i> | 1 | |
| | <i>S. aureus</i> | 1 | |
| Urinary infection | <i>Candida</i> species | 2 | 4 |
| | <i>P. aeruginosa</i> | 1 | |
| | <i>K. pneumonia</i> | 1 | |
| Soft tissue infection | <i>S. aureus</i> | 1 | 1 |
| Total | - | - | 16 |

program are at risk and need additional vaccination. Elderly individuals also represent a risk group, even in countries such as Turkey, which has an organized primary immunization program. The reason for this, apart from incomplete primary vaccinations, is that the level of protective antibodies decreases over time (9). A total of 53 adult tetanus patients were followed-up in our hospital between 1994 and 2000, whereas during the past 6 years, only 15 patients were followed up, which demonstrates a progressively dramatic decrease in the incidence of tetanus (7). It is important to note that our hospital remains a reference in the care of such patients. Nevertheless, the mortality rate was very high and was generally caused by nosocomial infections after a prolonged hospital stay.

Advanced age is regarded as an important risk factor for adult tetanus cases in Turkey. Almost all of our patients were older than 50 years of age, and none reported a vaccination history prior to the trauma. The general factors for high mortality are short incubation period, severe fever, advanced clinical entity, and poor prognosis at presentation. These patients are also exposed to infections in the ICU due to its specific requirements—mechanical ventilation, tracheostomy, and catheterization—and prolonged hospital stay. These conditions increase morbidity, prolong the duration of hospitalization, and increase mortality. Apart from nosocomial infections, tetanus patients are also prone to bedsores, tracheal obstruction, and gastrointestinal hemorrhage (1,11). Mortality rates have been reported to be very high in patients in the advanced stages of the disease and with acquired nosocomial infections (5). Early intubation and mechanical ventilation markedly reduce the mortality rate. It is also known that prevention of long-term complications, such as nosocomial pneumonia and deep venous thrombosis, has a positive effect on the prognosis (4). Another important finding of the present study was that the death of 2 patients in the late stage (42nd and 59th day) was due to sepsis. It has been reported that infection and other complications in patients with a severe course of tetanus prolong the duration of hospitalization (8). As such, it can be suggested that mortality during the early stage of the disease is due to the primary disease, whereas mortality during the late stage is due to complications.

Endotracheal intubation may be performed during the early stage; however, tracheostomy is reported to be a better option due to slow recovery and the long-term need for mechanical ventilation. Tracheostomy prevents spasms of the upper respiratory tract, as well as respiratory complications such as hypoventilation and asphyxia. This procedure requires the targeted areas to be frequently cleaned to maintain sterility. With long-term ventilatory support, the clinical course of tetanus may last 4-6 weeks. On the other hand, minor spasms and increased tonicity may last for months (4). Ventilator-associated pneumonia was the most frequently encountered nosocomial infection in the present study. As mechanical ventilation was performed in all patients, except 1 that died within the first 24 h of hospitalization, the prevalence of ventilator-associated pneumonia increased. Nosocomial pneumonia is the second most common cause of hospital-acquired infection and its mortality rate is estimated to be 30%. Its risk factors are trauma, respiratory system or cardiac disease, prolonged mechanical ventilation, re-intubation, tracheotomy, aspiration of gastric contents, and paralytic drug use (1). Most of these factors are seen in tetanus. It has been reported that nosocomial pneumonia is more frequent in patients with tetanus than in those with meningitis or other neurologic diseases; however, mortality associated with nosocomial pneumonia was lower than with other neurologic diseases (3).

Gram-negative microorganisms form the majority of agents responsible for nosocomial infections. These results correlate with our ICU surveillance data. The most frequently isolated agents of nosocomial infection were *Pseudomonas aeruginosa* and *Acinetobacter baumannii*; however, more detailed information regarding these agents' frequency and distribution could not be obtained due to the limited number of patients and infectious attacks.

Mortality in tetanus varies with patient age. In the United States mortality in adults younger than 30 years may be as low as zero; however, in those aged over 60 years, who account for 75% of tetanus deaths, mortality is above 50%. In Portugal between 1986 and 1990 mortality varied between 32% and 59% among all age groups (12-14). In the present study being elderly and admitting with progressive disease are

thought to be the reasons for poor prognosis and 66% mortality.

The incidence of tetanus has greatly declined, as compared to previous years, and the presence of even one case of this preventable disease is regarded as clinically important. This severe infectious entity,

which is closely followed up in the ICU, is susceptible to nosocomial infections. Patients and physicians are challenged equally with additional obstacles to survival. Despite advances in medical treatment, the poor prognosis of this disease highlights the need for national preventive health policies.

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