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# 1. Introduction

Tetanus is a rare but potentially fatal disease, caused by Clostridium Tetani. This microorganism is very common in the environment and may be transmitted through open wounds.<sup>1</sup> Immunization and proper wound care are the best ways of prevention of tetanus.<sup>2</sup>

Mortality caused by tetanus can vary between 10 and 80% in nonimmunized individuals, especially in both extremes of age.<sup>2</sup> Full immunity against the disease may not be achieved in all hosts even if the primary vaccination is completed.<sup>1</sup> Having said that studies confirm the non-immunized individuals who have got infected with tetanus have a more severe disease compared to immunized population and they have a higher rate of mortality.<sup>1,3</sup>

Tetanus represents a great risk for unregistered refugees, populations who implement anti-vaccination, and people who live in areas which are not covered by a vaccination program. In this case series, we aim to highlight the increasing frequency of tetanus by discussing two fatal cases seen in unvaccinated, unregistered refugees whose numbers are recently growing.

### 2. Case presentation 1

An 18-year-old male presented to emergency department with abdominal pain. He was a difficult historian due to the language barrier. He had no past medical history and did not use any medications. He had severe abdominal pain but could not disclose the characteristics of his symptoms. In physical examination, his Glasgow Coma Scale (GCS) score was 15, body temperature was 37.5 C°, otherwise his vital signs were within normal range. Abdomen was very tender with guarding. An abdominal X-ray was performed to rule out perforation, but it revealed no abnormalities apart from increased bowel gas. Due to the severity of his abdominal pain, an abdominal computed tomography (CT) with contrast was performed to rule out ileus and other possible causes of acute abdomen but showed no abnormalities. Laboratory tests including white blood cell count, C-reactive protein and serum lactate levels were unremarkable. A more detailed physical examination revealed opistotonus, trismus and risus sardonicus (Fig. 1) and puncture wounds on the sole of the feet (Fig. 2). A more detailed history was obtained later, by a language interpreter. Patient was an unregistered refugee from Afghanistan and was working in construction sites unofficially. He confirmed being injured a couple of times with rusty nails but did not seek any medical attention. He wasn't sure about his history of tetanus vaccination, so the patient was accepted as unvaccinated. Metronidazole  $4 \times 500$ mg intravenous (IV), 0.5 ml of diphtheria-tetanus toxoid vaccination intramuscular (IM), human tetanus immunglobulin 3000 IU IM and benzodiazepin 3mg IV were administered with a provisional diagnosis of tetanus. During his stay in the department, his muscle spasms got worse. Creatine kinase (CK) level was 22.666 U/L. Patient was intubated to control the spasms and prevent further organ damage. Unfortunately, he died on day 15 of his intensive care unit (ICU) admission.

# 3. Case presentation 2

A 26-year-old male patient was brought to emergency department with 7 days history of worsening fever, muscle spasms and rigors. His relatives disclosed that he was an unregistered refugee from Afghanistan. He had no past medical conditions, did not use any medications. He had no allergies, denied any alcohol or drug use. On arrival, his GCS score was 15 with a temperature of 38.5 C° and otherwise normal vital signs. He was being observed in the department with a provisional diagnosis of an upper respiratory infection when he developed muscle spasms and tremors which is thought to be trismus and opistotonus. His laboratory results showed a CK level of 21.027 U/L with mildly elevated alanine aminotransferase, aspartate aminotransferase, lactate and lactate dehydrogenase levels. A more focused history for a possible tetanus infection revealed that the patient had a puncture wound caused by a rusty nail 45 days ago but did not present to hospital since he had no insurance. His past medical history revealed that he had not received any dose of tetanus vaccine. 0.5 ml of diphtheria-tetanus toxoid vaccination IM, 3000 IU of human tetanus immunglobulin IM, metranidazol  $4\times500\text{mg}$  IV started for a possible

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Fig. 1. Case 1, risus sardonicus



Fig. 2. Case 2, nail marks.

diagnosis of late incubation tetanus. He died in the ICU after 30 days.

## 4. Discussion

# 4.1. Epidemiology

Being more common in tropical climates, in 2013 tetanus caused 58,900 deaths worldwide. $^4$ 

The total number of reported tetanus cases in Turkey in 1983 was 162 according to World Health Organization (WHO) data. This number decreased to 58 in 2003 due to the successful immunization strategy. Only 15 cases were reported in 2013 whereas the number of cases was slightly increased to 25 in 2017.<sup>5</sup> We believe this increasing trend in recent years is mainly caused by immigration from Turkey's neighboring countries which have ongoing low-intensity conflicts. The immunization status of this population is very difficult to be followed.

Painful contractions and stiffness especially around the neck, causing jaw-locking called trismus and the hyperextension of the body called opistotonus are the common findings of tetanus. More serious symptoms of this condition are respiratory distress, coma and death.<sup>1</sup>

The most effective ways to prevent this disease are proper wound cleaning and effective immunization. Studies have shown that tetanus is less severe in vaccinated patients than in non-vaccinated individuals, even if it has lost its effectiveness. Causes of tetanus cases occurring in vaccinated patients have been shown to be expired vaccines, ineffective vaccination and the inappropriate storage conditions of the vaccine.<sup>1</sup>

Even though the current edition of the Canadian Immunization Guideline has already indicated that the reminder doses of the tetanus vaccine should be repeated in 10-year intervals, it is also pointed out that the optimal timing of the doses should be reviewed with new evidence.<sup>6</sup> Both Turkish Ministry of Health and Turkish Medical Association also suggest reminder doses to be repeated in 10-years intervals.<sup>7,8</sup>

In a cross-sectional study conducted in Italy in 2011 and 2013, the antitoxin serum levels of 23% of the 5275 construction workers were shown not to be protective. In this study, the reasons for the lack of vaccination were related to advanced age, low education level and being an immigrant.<sup>9</sup>

A large number of publications claim that foreign populations are the most important populations at risk of tetanus due to inadequate immunization. A prospective study in a refugee clinic in Australia between 2000 and 2002 showed that, only 5% of 136 East African pediatric patients had a documented vaccination, and only 15% had protecting levels of serum tetanus antitoxin10. In a retrospective study conducted in the American immunization database between 2008 and 2013, it was emphasized that a variety of different cultural subgroups with a non-American background had incomplete immunization, and the risk of the disease was significantly higher especially in cultures that refused vaccination.<sup>11</sup>

In this article, two illegal construction workers from Afghanistan were diagnosed with generalized tetanus, and the patients needed ICU admission with ventilator support. These cases underline the fact that the lack of immunization in different refugee populations may be a significant risk for the increased incidences of preventable diseases.

#### 4.2. Diagnosis

Diagnosis of tetanus is compelling because, currently, there are no specific tests to confirm the diagnosis of tetanus. Furthermore, if the patient is a refugee, parameters such as language barriers to communication, unknown or suspicious past medical history about tetanus vaccination, delayed application due to lack of health insurances and fear of deportation among the illegal immigrants make diagnosis even more difficult. If the medical history about tetanus vaccination is suspicious, it is sensible accepting the patients as unvaccinated because majority of the immigrants from undeveloped countries have improper vaccination procedures.<sup>9–11</sup> Diagnosis is mainly clinical.<sup>12</sup> According to the WHO definition, following a history of injury, at least one of the following symptoms is necessary for the diagnosis of adult tetanus; 1) trismus, 2) risus sardonicus 3) increased painful contractions with stimuli.<sup>13</sup>

In the presented cases, central nervous system infection was not considered because the inflammatory markers were within normal limits and patients' levels of consciousness were not impaired. After other possible causes were excluded, tetanus was considered since patients were from a more vulnerable population, and examination findings such as opistotonus, risus sardonicus and trismus confirmed the diagnosis.

# 4.3. Treatment

Immunotherapy, antibiotherapy, control of muscle spasms, stiffness and autonomic dysfunction, isolation from the external stimuli and airway control are the main treatment steps in tetanus patients.<sup>12,13</sup>

When tetanus is diagnosed, the patient should be given human derived tetanus immunoglobulin IM or IV, and vaccinated IM from another site.<sup>13</sup> Traditionally, 3000–6000 IU of human derived tetanus immunoglobulin is recommended.<sup>14</sup> However, in both the WHO and the American Centers for Disease Control and Prevention Center (CDC) recommendations, a dose of 500 IU of human induced tetanus immunoglobulin was found to be as effective as higher doses and caused less side effects.<sup>13,15</sup>

Metronidazole IV 4 × 500 mg is the first choice of antibiotics. Benzodiazepines should be used as a first choice for muscle spasms and stiffness whereas magnesium sulphate is recommended for autonomic dysfunction.<sup>13</sup> Patients should be kept in a room isolated from external stimuli such as light and sound, and wounds should be debrided, and proper wound care should be performed.<sup>12</sup> Close monitoring is required in all patients.<sup>12–14</sup> Endotracheal intubation may be considered in patients with respiratory depression or intensifying muscle contractions.<sup>13</sup> Vecuronium is the first choice for neuromuscular blockade.<sup>14</sup> Most patients will need physical therapy after contractions are completely resolved. Prior to discharge, a dose of tetanus vaccine should be given, and the patient should be followed up in four weeks for a repeat assessment and another dose of the vaccine.<sup>12</sup>

### 5. Conclusion

Preventable infectious diseases such as tetanus are more common in vulnerable populations including communities against vaccination, illegal immigrants, refugees who are not vaccinated. These conditions should be considered in the differential diagnosis since their incidences in these patient groups are higher compared to general population.

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### Author contribution statement

Gökhan AKSEL and Mehmet Muzaffer İSLAM and Serkan Emre EROĞLU conceived and designed the study; Bilge Kağan SEKTİOĞLU performed the patient management and collection of the data Can ÖZEN, Mehmet Muzaffer İSLAM and Gökhan AKSEL wrote the paper.

### Conflict of interest statement

The authors declare no conflict of interest.

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