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Tetanus: A Case Report following an Upper Extremity Injury

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Abstract

Clostridium tetani is a spore-forming, toxin-producing, anaerobic, gram-positive bacillus which enters the CNS causing painful muscle contractions within the host. These painful spasms and stiffness typically manifest initially in the form of trismus, or lockjaw. According to the CDC, tetanus treatment includes the administration of Tetanus Immune Globulin (TIG), a tetanus toxoid booster, agents to control muscle spasms (benzodiazepines), and antibiotics (metronidazole). Current recommendations on TIG use provide an accepted dosing range of 500 - 6,000 units. The optimal dosing regimen of TIG has not been well established. We describe a case in which a 33-year-old Hispanic male presented with trismus due to suspected tetanus. A tetanus antibody immunoglobulin assay was performed and provided a normal result of > 7.00 IU/mL, which coincides with a historically protective value, ≥ 0.01 IU/mL. TDap vaccination was immediately administered along with 500 units of TIG. The patient's symptoms resolved progressively and the patient was discharged home eight days after hospitalization.

Keywords

Tetanus, Immune, Globulin, TIG, Antitoxin

Case Report

A 33-year old Hispanic male presented to the emergency department with complaints of severe bilateral jaw pain and stiffness in his temporomandibular joint. The patient reported onset of symptoms approximately five days prior to presentation, coinciding with cutting his hand on a piece of sheet metal, with pain and difficulty opening his mouth becoming progressively worse over the two preceding days with a "low grade fever" at home, but denied sore throat or toothache. Temperature at admission was normal, 36.6 Celsius, and blood pressure was elevated at 158/96. The patient had a normal white blood cell count, 5.9. The patient was unable to verify when his last tetanus shot was administered but stated that it had "definitely been more than ten years ago." At the time of presentation, the patient was able to speak comprehensibly. However, he could open his mouth very little and not to an extent to allow for internal examination. The initial examination revealed a supple neck, non-tender with a full range of motion and no adenopathy or meningismus. A puncture wound was apparent on the right palmar surface with no evidence of erythema or necrosis. The patient was placed on NPO restrictions by the attending physician due to jaw limitations. His past medical history included only Attention Deficit Hyperactivity Disorder with a past surgical history of appendectomy. A maxillofacial CT scan was conducted and revealed no acute pathology. No dental or periodontal abscesses were identified nor were any fractures or subluxations noted. Diazepam was initiated in the emergency department to control muscle spasms and continued on as needed basis during the admission.

Given the patient's recent history of injury and clinical symptoms at presentation, a differential diagnosis of tetanus with trismus was made. A tetanus antibody immunoglobulin assay was performed and provided a normal result of > 7.00 IU/mL, which coincides with a historically protective values ≥ 0.01 IU/mL [1]. Our reference laboratory utilizes a protective level of > 0.10, which has been suggested to have a higher correlation to protection [2-3]. Due to concerns relating to paralysis, difficulty swallowing, and respiratory depression, the patient was admitted to the Intensive Care Unit (ICU). The patient was initiated on antibiotic treatment with ampicillin 1 gm IV q6h and metronidazole 500 mg IV q8h. Initially, 5,000 units of Tetanus Immune Globulin (TIG) (BayTet) was ordered, however that was discontinued and 500 units of Tetanus Immune Globulin (BayTet) was administered IM once, as was the Diphtheria, Pertussis (Acellular), Tetanus Vaccine (Adacel) 0.5 mL IM once.

On admission day 2 the patient was still unable to open his mouth, only able to slightly bare his teeth. On admission day 3 the patient reported jaw pain and spasms radiating down the left side of his chest and back, which he rated as mild-to-moderate. By admission day 4, the patient was able to open his mouth slightly better than the previous day of his treatment. His neck was also suppler upon examination than the previous day. At this time the patient was placed on a full liquid diet. Admission day 5 saw the patient able to open his mouth much more, to nearly one to one-and-a-half inches, and able to stick his tongue out. Due to this improved jaw mobility his speech became much clearer. The patient was still experiencing occasional neck spasms and jaw pain. At this time, the patient was transitioned to a soft diet. After five days of treatment metronidazole 500 mg IV q8h was discontinued, with the patient receiving a total of thirteen doses. On day 6 of admission the patient was transitioned to a regular diet. The patient remained afebrile throughout the entire duration of their hospitalization. The ampicillin 1 gm IV q6h was continued until discharge with the patient receiving a total of 30 doses. Throughout the duration of the patients stay he was administered methocarbamol

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2,000 mg/500 mL NS IV q6h for spasms. During the first five days of the patient's hospitalization, an order for diazepam 10 mg/2 mL IV q6h prn was maintained for control of spasms. On admission day 6, the patient was commenced on oral diazepam 2 mg tablets q8h prn. However, after this transition the patient required no further diazepam for the duration of the hospitalization. The last two days of the patient's hospitalization were associated with no evidence of further trismus or drooling and he was subsequently discharged on day 8.

Discussion

Pathophysiology

Clostridium tetani is a toxin producing, anaerobic, gram-positive bacillus. It is a spore forming pathogen with spores found naturally in soil, animal feces, and manure [4].Typically, spores are introduced into the body via an injury that causes a break in skin structure such as a laceration, puncture, or burn. Once *C. tetani* spores are within the body, they convert to their vegetative forms and multiply within the tissues at the site of injury. The anaerobes begin producing toxins, tetanolysin and tetanospasmin [4]. The tetanus toxin targets vesicle-associated membrane protein (VAMP) which is involved in neurotransmitter release from nerve endings. Therefore, a symptom of flaccid paralysis can be present when the toxin binds and interferes with the release of acetylcholine at the neuromuscular junction [5]. The toxin can be transported in the axons and thereby reach areas such as the spinal cord or brainstem. Once within the CNS, the toxin can be taken up by inhibitory GABAergic or glycinergic neurons or both, where the tetanus toxins can cleave VAMP and inhibit release of GABA and glycine [5].This results in rigidity and spasms of hyperactive muscles. The toxin irreversibly binds to tissues and thereby cannot be neutralized by TIG once bound. However, TIG can be administered to prevent toxin binding in the CNS if toxin binding has begun in the periphery [6], but not yet progressed to the CNS.

Diagnosis

There is no existing laboratory test for tetanus, thus the diagnosis is based purely upon clinical presentation. In 2009, the Council of State and Territorial Epidemiologists published a case definition, which stated: "in the absence of a more likely diagnosis, an acute illness with muscle spasms or hypertonia and diagnosis of tetanus by a health care provider." Cases are classified as probable provided they are clinically compatible with tetanus presentation and are reported by a healthcare professional. There is no definition for confirmed tetanus [7]. A case suggestive of tetanus should be reviewed for immunization status, history of injury, duration before a patient develops signs and symptoms, specific patient signs and symptoms and progression of patient signs and symptoms in order to make a diagnosis. Disease severity can be predicted by assessing the incubation period [6].

Epidemiology

Since 1947 when tetanus became a nationally reportable disease in the United States, the number of cases has declined by > 95% and the number of deaths by > 99%. Between 2001 and 2008, the Centers for Disease Control received 233 tetanus case reports, with 197 reported patient outcomes. The case - fatality rate for the period analyzed was 13.2%, with an annual incidence of 0.10 per 1 million and 0.23 for those ≥ 65 years of age. Tetanus-toxoid (TT) containing vaccination status was known for 92 patients, of which 37 (40.2%) had received no doses of TT vaccination. Appropriate prophylaxis was not administered in 49 of 51 (96.1%) of patients who presented with an acute wound [8].

Treatment

According to the CDC, tetanus treatment includes the administration of TIG, a tetanus toxoid booster, agents to control muscle spasms (benzodiazepines), and antibiotics (metronidazole). Aggressive wound care measures should also be initiated [9]. TIG confers passive immunity to the toxin produced by the tetanus pathogen, *C.tetani,* through neutralization of the exotoxin produced by the bacterium. TIG is indicated for prophylaxis in patients whose immunization status against tetanus is incomplete or uncertain. TIG is also indicated as a component of the regimen for treatment of active cases of tetanus. Standard dosing, per the package insert, for routine prophylaxis of adults and children seven years of age or older is 250 units given by deep intramuscular injection. Children less than seven years can receive prophylactic doses of either 4 units/kg or the entire contents of the vial 250 units. Treatment of active cases should be implemented immediately, with the dosage adjusted according to the severity of the infection [10]. Currently, the recommended dosage range is 500 - 6,000 units, with no optimal range clearly defined. A study conducted by Nation et al [11] enrolled 20 patients with active tetanus and treated them each with a single dose of between 3,000-6,000 units. The authors of this study noted that the serum levels of TIG obtained through this dosing regimen were well in excess of recommended therapeutic levels and resulted in an observed mortality of 30%, which was approximately half of the observed national average of 60% for the time period evaluated (1951-1954). In an analysis conducted by Blake et al. [12], of 545 patients who received TIG in the United States from 1964 through 1971, no difference in mortality was observed between dosing ranges of 500 - 8,000 units, thus no optimal dose could be determined.

Patient Discussion

The patient presented with trismus due to an upper extremity injury and an open wound. The differential diagnosis was indicative of probable tetanus. Upon administration of TIG, TDap, antibiotics, and antispasmodics the patient experienced rapid clinical and symptomatic improvement. The wide dosing range recommended within the TIG package insert leaves room for clinical judgment in terms of the appropriate dosing regimen. An initial dose of 5,000 units of TIG was ordered, however with uncertain evidence supporting this dosing regimen, the dose was reduced to 500 units and administered. Dosing regimens documented in published case studies range from 500 to 10,000 units [13-27]. Based on the symptomatic resolution observed in this patient with low-dose therapy and the evidence presented herein, it seems likely that the lowest recommended dose may be sufficient to provide optimal patient outcomes.

The patient reported an uncertain vaccination status, and self-reported a history of not receiving any vaccinations within the previous ten years. Despite this the patient's tetanus antibody immunoglobulin assay demonstrated a protective immunity level (> 7.00 IU/mL). It is possible that the efficacy of the lower dose was a result of this protective immunity level. Several case reports of tetanus have been reported in patients with antibody levels ranging from 0.04 IU/mL to 8.4 IU/mL [22-33]. Regardless of the patient's antibody level, he still developed trismus due to tetanus and responded well to treatment with appropriate agents. It is possible the patient had received the appropriate booster and could not recall. Regardless, the development of tetanus symptomatology following acute injury despite adequate serum immunity is not well documented. Based on this and other published reports, a reevaluation of the antibody level deemed protective may be warranted.

Conclusion

In summary, this case of a 33-year-old Hispanic male with trismus as a result of tetanus was successfully treated with 500 units of TIG, vaccination, and antibiotics. The result was resolution of the patient's trismus and underlying tetanus. The administration of low dose, 500 units, of TIG appeared to be sufficient in the treatment of this patient. Based on these results as well as the existing literature, lower doses of TIG appear to be sufficient to resolve tetanus symptoms.

IRB Statement

Exemption - Approval; "[H]ave determined that this DUE project is exempt from IRB review."

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The authors do not have any conflict of interest to declare.

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