Case Report

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Tetanus in an Intravenous Drug User

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Abstract

Tetanus is the only vaccine-preventable disease that is infectious but is not contagious. The diagnosis is based on the presentation of tetanus symptoms and does not depend upon isolation of the ubiquitous bacteria, which is recovered from the wound in only 30% of cases and can be isolated from patients who do not have tetanus.

In the United Kingdom, 5 doses of tetanus toxoid–containing vaccine at appropriate intervals are considered to provide lifelong protection, as long as tetanus-prone wounds are treated with tetanus immunoglobulin but the immunity wanes over time particularly in elderly.

Recent experience has pointed to Intravenous Drug Users (IVDUs) as being at significant risk of tetanus. Awareness of the risk and value of vaccination in this group, and awareness among those working with them, is extremely important. The reasons for emergence of *Clostridium* infections in IVDUs in the United Kingdom include an increase in contamination of heroin and an aging cohort of heroin users who are more likely to use "popping" as the mode of injection.

Most patients with tetanus lack a history of receipt of a full series of tetanus toxoid immunization and receive inadequate prophylaxis following a wound. Approximately three-fourths of the patients who acquired tetanus recalled an acute injury prior to the onset of their symptoms, but approximately two-thirds of these individuals did not seek medical care. Tetanus is a clinical diagnosis and must be considered in patients with muscle spasms and an inadequate vaccination history. 'Confirmed cases' of tetanus need to meet the laboratory criterion.

Keywords: Magnesium and Tetanus; IVDUs and Tetanus; "Skin Popping" and Tetanus; Tetanus Immunoglobulin Vs Human Immunoglobulin.

Learning Points

- Clostridium tetani (C. tetani) can be isolated from patients who do not have tetanus and no cause can be identified in a small percentage of "cryptogenic" patients with classic signs and symptoms of tetanus.
- Penicillin G is no longer used as it is a known antagonist of GABA, like tetanus toxin, Metronidazole is preferred.
- Since IVDUs are at risk for *Clostridium* infections, drug action teams, needle exchange programs, prison staff, and clinicians should ensure that IVDUs are vaccinated against tetanus and educated about signs and symptoms of soft tissue infections that require prompt medical intervention.
- All patients with tetanus should receive active immunization with a total of three doses of tetanus and diphtheria toxoid spaced at least two weeks apart, commencing immediately upon diagnosis.
- Health Protection Agency (HPA) in UK has approved batches of normal human immunoglobulin with sufficient tetanus antitoxin levels if there is a problem obtaining the specific tetanus immunoglobulin, only IM formulation is available.
- Tetanus is mainly a clinical diagnosis. Although a serum sample should be taken before administering immunoglobulin, treatment of tetanus should never be delayed to wait for the laboratory result.

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Epidemiology of Tetanus in England and Wales

In England and Wales, the annual incidence of tetanus was 0.2 cases/million population with the highest incidence in patients above the age of 64 years[1]. The widespread distribution and temporal clustering [2] of cases in the United Kingdom suggest that its cause was contamination of heroin rather than changes in injecting practices. This finding is consistent with results of a similar investigation of a cluster of *C. botulinum* in IVDUs in California.

In 2000, an outbreak of serious illness and death occurred among IVDUs in Scotland, Ireland, and England, associated with *Clostridium novyi* infection, a particular supply of heroin, and a particular method of preparation and injection called 'popping' (subcutaneous and/or intramuscular injection). A total of 108 cases and 44 deaths were reported in this outbreak. Female IVDUs were shown to be at increased risk, possibly due to the higher prevalence of subcutaneous or intramuscular injection.[3]

Twenty five cases of tetanus were reported in injecting drug users (IVDUs) between July 2003 and February 2004. Thirteen (50%) were women, seventeen of 21 patients with information reported having injected heroin intramuscularly or subcutaneously or having missed veins. Two patients died (case fatality of 8%), of 23 survivors, 2 had mild disease and 21 required intensive treatment for a median of 40 days. Tetanus immunization status available for 20 case-patients and only 1 patient had received the 5 doses necessary for complete coverage. Nine patients were never completely vaccinated [4].

Since this cluster in 2003/4, only seven sporadic cases of tetanus were reported in IVDUs until the end of 2012. The overall case-fatality rate among reported cases of tetanus in England and Wales between 1984 and 2000 was 29% [1]. The severity of illness may be decreased by partial immunity

Case Report

A 38 year old IVDU on methadone replacement therapy was brought by ambulance to the emergency department with 'seizures', dysarthria, dysphagia, jaw spasms, excessive sweating and drooling of saliva. He was also noted to be incontinent of urine and faeces, the body tone in between 'seizures' was increased and the tonic posturing was worsened by any sort of sensory stimulus. There was no clonic phase to the 'seizures' and they can be better described as 'spasms'.

A Glasgow Coma Scale was 15 and he was oriented to time, place and person. Pupils were small but regular and reactive. His vitals showed a tachycardia of 124, blood pressure of 170/94 mm Hg and a temperature of 38.4 degree Celsius but no evident focus of infection on clinical examination.

Initial differential included: encephalitis, alcohol withdrawal, methadone withdrawal, neuroleptic malignant syndrome and drug withdrawal states (cocaine/ amphetamines).

His bloods were notable for a mild increase in white cell count and mildly increased Creatine Kinase.

His awake, alert and oriented state between the 'spasms' did not support an '*ictal/ postictal*' or '*encephalitic*' phenomenon; 'alcohol *withdrawal*' was a possibility with his history of excess alcohol intake but his last drink was a week ago. His clinical presentation could be explained by '*methadone withdrawal*' alone but he admitted taking 60 mg methadone in the morning. There was a possibility of '*neuroleptic malignant syndrome*' but he was not on any anti-psychotics, Creatine Kinase was only mildly elevated and urine had no hematuria.

The focus shifted on the powerful muscle spasms involving the whole body and jaw (trismus). These spasms were sudden onset, painful and affected his breathing. He was restless and occasionally arched his back with the spasms (*Opisthotonus*) which is classically described in tetanus; although extra-pyramidal syndromes, cerebral palsy and traumatic brain injury can also cause it.

He admitted injecting cocaine in his groin 2 weeks ago and he had a small groin lump to prove it, incidentally there was an Health Protection Agency alert a few weeks ago regarding the circulation of a contaminated cocaine batch in the area.

After the initial dilemma of a '*Methadone withdrawal*' and poor response to small dose morphine he was clinically diagnosed with tetanus (HPA grade 2) [1] linked to his groin injection of contaminated cocaine and was treated with metronidazole, diazepam and magnesium infusions. Tetanus Immunoglobulin (TIG) was used at 150 IU/Kg intramuscular as the intravenous preparation was not available.

The patient stayed in the 'Medical Admission Unit' side room to avoid any sensory stimuli that could worsen his spasms, intensive care team was involved due to periods of apnoea following chest muscle spasms but the patient never developed airway compromise needing intubation.

The spasms slowly settled over the next day. Patient had red eye and blurring of vision in right eye and on

call ophthalmologist was contacted and examination showed subconjunctival haemorrhage with no signs of inflammation inside eye secondary to his IVDU. A soft tissue ultrasound suggested that the groin lump was 2 X 3 cm but a little deep to contemplate any easy surgical drainage and obtain a tissue sample. He was discharged day 4 post admission with a 10 day course of antibiotics and 'alcohol and drug abuse service' follow up. A three dose tetanus immunisation schedule was commenced with the first toxoid injection given before discharge.

The tetanus immunoglobulin levels in the patient's blood taken prior to treatment were found to be low (<0.1IU/ml), in agreement with the diagnosis. A sample for specific tetanus toxin was not sent to the Respiratory & Vaccine Preventable Bacterial Reference Unit (RVPBRU), Public Health England.

Table 1: Tetanus-prone wounds

Wounds or burns that require surgical intervention that is delayed for more than six hours
Wounds or burns that show a significant degree of devitalized tissue or a puncture-type injury, particularly where there has been contact with soil or manure
Wounds containing foreign bodies
Compound fractures
Wounds or burns in patients who have systemic sepsis.

Discussion

Tetanus is a life-threatening disease caused by the bacterium *Clostridium tetani* which usually enters the body through an acute wound. It is characterized clinically by rigidity, muscle spasms and autonomic instability. Mortality is high (20–50%) with sympathetic over activity being the major cause [5].

The goals of treatment include:

- Halting the toxin production and neutralization of the unbound toxin (Table 1).
- Airway management
- Sedation and control of muscle spasms
- Management of dysautonomia

In these wounds IM human tetanus immunoglobulin should be given for immediate protection, irrespective of the tetanus immunization history of the patient. Tetanus vaccine is not considered adequate for treating a tetanus-prone wound since tetanus vaccine given at the time of a tetanus-prone injury may not boost immunity early enough to give additional protection within the incubation period of tetanus. However, giving a dose of vaccine at the time of injury provides the opportunity to ensure that the individual is protected against future exposure.

Tetanus, arguably the oldest infection associated with IVDU and potential sources for tetanus infection are contaminated drugs (spore contamination during production, distribution, storage, cutting, and reconstitution), paraphernalia, and contaminated skin. Intramuscular and subcutaneous drug use (popping), in particular, are associated with tetanus infections in IVDUs [6].

The key aspect of treatment is the provision of adequate sedation, provided by benzodiazepines in combination with opiates. Additional benefit may be provided by anticonvulsants, (particularly phenobarbitone), chlorpromazine, clonidine or dantrolene. If the control of rigidity and muscle spasms is inadequate, then neuromuscular blocking agents and mechanical ventilation are often necessary.

Magnesium sulphate may offer another treatment modality acting as a presynaptic neuromuscular blocker and vasodilator, reducing catecholamine release and catecholamine receptor responsiveness and antagonize the effects of calcium in the myocardium [7].

Magnesium infusion significantly reduced the requirement for other drugs to control muscle spasms and patients treated with magnesium were 4.7 times [8] less likely to require verapamil to treat cardiovascular instability than those in the placebo group. However, magnesium sulphate infusion did not reduce the need for mechanical ventilation.

The dose of tetanus immunoglobulin for intravenous use is 5000–10,000 IU by infusion. If intravenous administration is not possible, 150 IU/kg of the intramuscular preparation may be given in multiple sites. In one study of 64 patients with tetanus, serum obtained prior to the institution of treatment contained detectable levels of antibody in 35 percent of patients, and the severity of tetanus in these patients appeared to be inversely related to the level of pre-treatment anti-tetanus toxin antibody [9].

An intake of 3500-4000 calories, and at least 150 gm of protein per day, is often given via percutaneous endoscopic gastrostomy or total parenteral nutrition. This high-caloric diet maintenance is required because

of the increased metabolic strain brought on by the increased muscle activity. Full recovery takes 4 to 6 weeks because the body must regenerate destroyed nerve axon terminals. Tetanus is a notifiable illness. In March 2013, the Health Protection Agency (HPA) convened an expert working group to review the published evidence on the use of Tetanus Immune Globulin (TIG) for the treatment of clinically suspected tetanus and now only tetanus immunoglobulin (TIG) for IM use is now available from Bio Products Laboratory (020 8258 2342). An IV tetanus immunoglobulin product is no longer available [10].

Appendix 1: Algorithm 1 for the diagnosis of tetanus

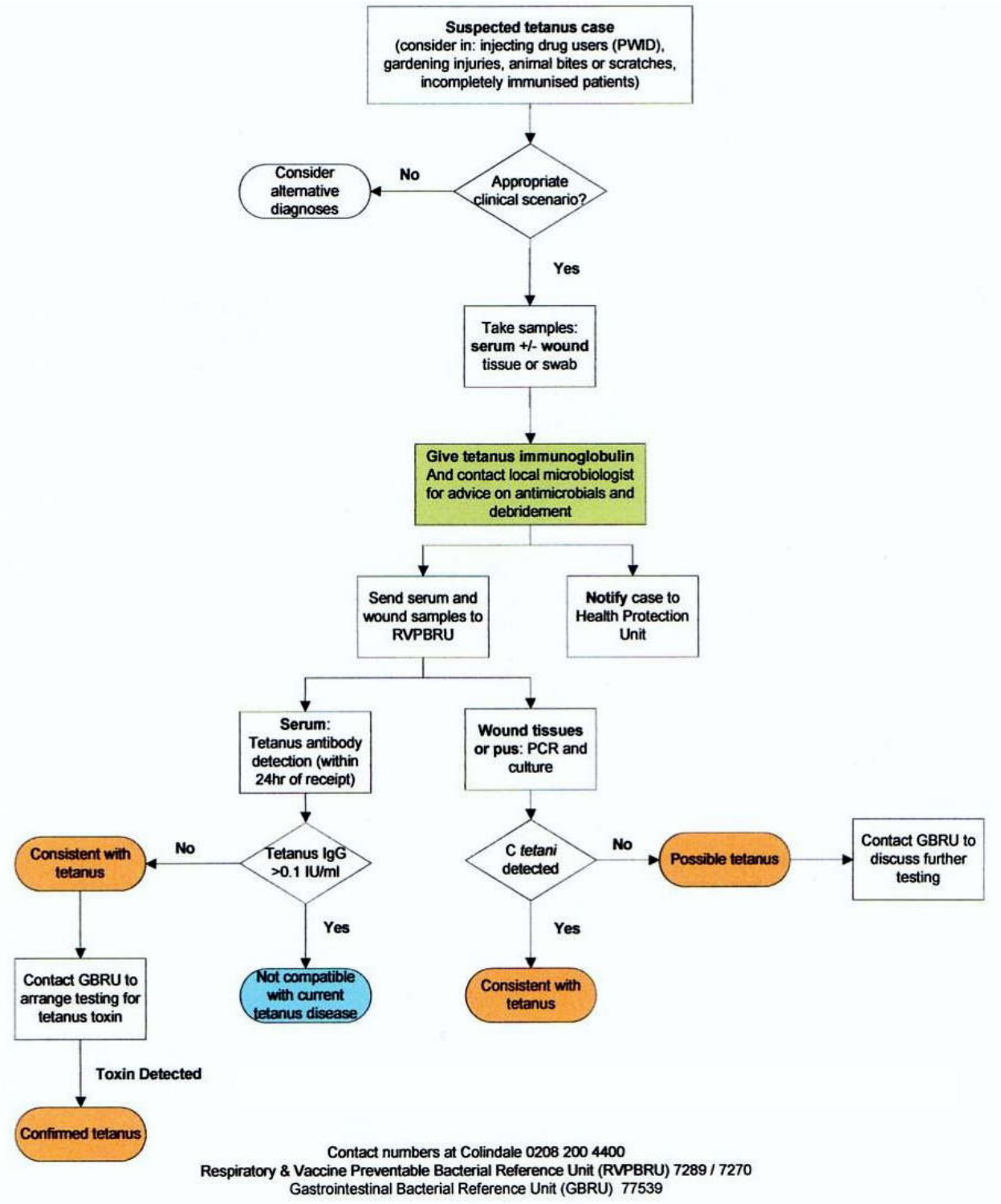

Table 2: Laboratory confirmation of tetanus infection [13]

1. **Detection of IgG against tetanus in serum**. If the antibody level is **above** the protective threshold (>0.1 IU/ml) in a sample taken before the administration of immunoglobulin, this excludes current tetanus infection. An antibody level **around or below** the threshold supports, but does not confirm, a diagnosis of tetanus.
2. **Detection of toxin in serum**. This is a bio-assay and is only performed if the antibody level is below the protective threshold. Absence of toxin does not exclude tetanus.
3. **Detection of C. tetani** in wound material or from a pure isolate, by direct Polymerase Chain Reaction (PCR) and culture methods. A negative result does not exclude tetanus

Conclusion

Lack of tetanus immunity is the main cause of the persistence of tetanus. According to a study, 25.9% of patients with a tetanus-risk wound had no protective antibody level and the incidence of the disease rises with increasing age [11,12].

Because the spores of *Clostridium tetani* are ubiquitous, exposure is frequent and difficult to prevent. Passive or active immunisation by immunoglobulin or vaccine, respectively, is the most efficient way to prevent the disease. Early recognition and treatment may be life saving (Table 2 and Algorithm 1) [13].

Treatment of tetanus is best performed in the intensive care unit in consultation with an anaesthesiologist and includes early and aggressive airway management. Unfortunately, little evidence exists to support any particular therapeutic intervention in tetanus. There are only nine randomized trials reported in the literature over the past 30 years [14].

Primary prevention of tetanus among IVDUs is possible through changing drug practices: smoking heroin rather than injecting it, and where injecting cannot be avoided it should be advised not to inject into the muscle or under the skin [15].

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