

Tetanus in an Injecting Buprenorphine Abuser

Felicia SW Teo,¹*BMedSci (Hon), BM BS (Engl), MRCP (UK)*, Li Yang Hsu,²*MBBS, MRCP (UK), DTMH (Gorgas)*,
Khim Nian Sin Fai Lam,³*MB BCh BAO (Belfast), FRCP (Ire), FCCP*, A Johan,³*MBBS, FCCP*

Abstract

Introduction: Injecting drug abusers are vulnerable to many infectious complications. We describe a case of tetanus in a Singaporean who regularly abused buprenorphine. **Clinical Picture:** A 49-year-old male was hospitalised for progressive generalised spasms associated with dysarthria and opisthotonus. Tetanus was diagnosed clinically. **Treatment:** Supportive management was instituted in the intensive care unit (ICU). Toxicology samples tested positive for buprenorphine. **Outcome:** He recovered rapidly and was transferred out of the ICU after 8 days. Retrospective questioning confirmed parenteral abuse of buprenorphine. **Conclusion:** This case highlights an uncommon and potentially lethal complication of parenteral drug abuse.

Ann Acad Med Singapore 2007;36:1021-3

Key words: Clostridia, Buprenorphine, Drug abuse

Introduction

Problems with parenteral drug abuse with opioids and infectious complications have been well-described in medical literature.¹⁻³ Substitution drugs such as buprenorphine (Subutex) have been used as an adjunct to manage intractable opioid dependence. Buprenorphine, a partial opioid agonist, has been shown in previous trials to reduce heroin use, with a low potential for dependence and a high safety profile in the case of overdose.³⁻⁵

However, this pharmacological advantage, coupled with the legal status of the drug (it is not a controlled drug and can be freely prescribed in many countries), was quickly recognised by injecting drug users (IDUs) as ideal for producing analgesia and euphoria. Although buprenorphine diversion and injection was not found to be significant in some countries,^{5,6} it has become a growing problem in Singapore.⁷ On 14 August 2006, as part of enhanced efforts to restrict its access, the status of buprenorphine in Singapore was changed from being a licensed drug to a Class A Controlled Drug under the Misuse of Drugs Act (MDA).⁸ We present a case of tetanus in an injecting abuser of buprenorphine.

Case Report

A 49-year-old Singaporean of Chinese ethnicity was admitted with a history of functional decline over the

preceding 5 days. His symptoms, which began with vague generalised weakness on the first day, progressed the next day to that of difficulty swallowing and episodic stiffness of his back and limbs, which were noticed by his relatives at home. He was finally brought to hospital after he became unable to walk or speak clearly.

His medical history was initially ascertained from his son. He had a long history of polysubstance abuse which included oral and intravenous opiates and benzodiazepines. Since his early 20s, he had been imprisoned several times for drug-related offences, including a period in Thailand 4 years ago where he had sustained a gunshot wound to his right foot requiring debridement while he was in police custody. Buprenorphine was introduced to him a few weeks prior to admission to help wean him off opiate dependence.

On clinical examination, he was alert and oriented but had an anxious disposition. He had a low-grade temperature of 38°C, but his vital signs were otherwise normal. He was able to obey all commands but had difficulty verbalising due to an inability to part his upper and lower incisors beyond 2 cm of his mouth opening. His pupils were of normal size and reactive to photo-stimuli. There was no ophthalmoplegia or diplopia. His neck muscles were tense but Brudzinski's sign was not elicited. During the examination, recurrent episodes of tonic rigidity involving

¹ Department of Respiratory and Critical Care Medicine, Singapore General Hospital, Singapore

² Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

³ Department of Medicine, Alexandra Hospital, Singapore

Address for Correspondence: Dr Felicia Teo Su Wei, Department of Respiratory and Critical Care Medicine, Singapore General Hospital, Singapore 169608.

Email: felicia.teo.s.w@singhealth.com.sg

the limbs, neck and back were observed, lasting a few minutes each time, with marked opisthotonus and carpopedal spasms. Chvostek's sign was not elicited. In between these episodes, tone and deep tendon reflexes were equal and brisk, plantar reflexes normal. Extensive tattoos were noted over his abdomen and forearms, and numerous old venepuncture marks were noted, but his skin was otherwise intact with no signs of an open wound.

Preliminary investigations which included a chest X-ray, electrocardiogram, full blood count, liver function tests, calcium and magnesium levels and other electrolytes were normal.

A clinical diagnosis of generalised tetanus was made and he was transferred to the intensive care unit (ICU), where prophylactic tracheostomy was arranged. He was given a dose of intramuscular anti-tetanus immunoglobulin and tetanus toxoid, and started on a course of metronidazole for 10 days. He was sedated with intravenous propofol and paralysed with atracurium over the next few days to control his frequent spasms. Intravenous fentanyl was given as analgesia. As an adjunct, intravenous magnesium sulphate was loaded at 5.0 g, then continued using an infusion pump at 2.0g/h for about 48 h, with frequent monitoring of serum magnesium and calcium concentrations and appropriate replacement if calcium levels were low.

An electroencephalogram performed while he was in ICU merely showed a sleep pattern consistent with the effects of sedation. Samples of his blood and urine sent for toxicological screening were positive for buprenorphine but not for strychnine or other toxins tested.

By the third day, his spasms had improved significantly and intravenous magnesium was stopped. He was weaned off ventilatory support by the 8th day in intensive care.

Prior to his discharge, further questioning revealed that the patient had abused buprenorphine parenterally. He described how he prepared and administered his drugs: tablets would be crushed by pounding or biting and dissolved in warm water, which would then be syringed and injected parenterally. Like most seasoned injecting drug abusers, he admitted to having attempted subcutaneous and intramuscular routes of injection when intravenous access became more difficult. The patient was unable to recall if he had received a tetanus vaccination after his wound debridement in Thailand. Due to his frequent convictions and imprisonment, he had not served in the military since his early twenties and was therefore not vaccinated where most other males performing national service would have been.

Conclusions

To our knowledge, this is the first reported local case of tetanus acquired through the parenteral abuse of

buprenorphine. The diagnosis was made solely on clinical grounds as laboratory confirmation of tetanus is not routinely available in Singapore. Differentials considered and discarded while managing the patient include strychnine poisoning, dystonic reaction, status epilepticus and a conversion disorder.

Strychnine, a natural product of the plant *Strychnos nux vomica*, is uncommonly mixed with “street drugs” like heroin, cocaine and LSD.⁹ Its clinical effects are very similar to that of tetanus and only small amounts are needed to cause severe effects. However, the negative toxicology screen and patient history effectively exclude this possibility. Acute dystonia was considered in the light of a history of polysubstance abuse with neuroleptic drugs. The patient's clinical features, however, were too extensive to be accounted for by an oculogyric crisis; his preserved mentation and ability to fully cooperate similarly made the differentials of neuroleptic malignant syndrome, status epilepticus or a conversion disorder unlikely.

A wide spectrum of infectious complications arising from parenteral drug abuse have been increasingly described in literature, including that of infective endocarditis, cutaneous abscesses, meningitis, bone and soft tissue infections.¹ Notably, the incidence of anaerobic bacterial infections, including tetanus, has risen dramatically amongst IDUs towards the end of the last century in many parts of the developed world.¹⁰ This was accompanied by a dramatic shift in demographics: where most reported cases had initially been accounted for by older individuals not previously covered under national immunisation programmes, cases had later shifted to a younger age distribution of IDU.³ The reason was partly related to an increased number of young IDUs engaged in alternative routes of drug administration which bred ideal conditions for anaerobic bacterial inoculation.³ In particular, skin and muscle “popping” was popular in the late 1990s^{3,10} when venous access became difficult.

Most cases of tetanus occurred in IDUs who had low serum antitoxin antibody levels and no documented history of complete tetanus vaccination. Possible sources of contamination by spores of *Clostridium tetani* include:¹

1. Contaminated needles;
2. Injection paraphernalia;
3. Injecting practices: deep inoculation via subcutaneous and intramuscular routes optimise the growth of anaerobic species such as *Clostridium* in a relatively anaerobic environment;
4. Preparation of the drug: use of a mild acid such as quinine used to dilute heroin, as well as dissolution of the concoction by heating in a spoon at about 65°C to 75°C kills non-spore-forming bacteria and favours the

growth of spore-forming bacteria such as *Clostridia*.

The diagnosis is made on clinical grounds since the organism is rarely cultured and in 14% to 30% of patients, no portal of entry is defined.¹¹ However, 3 diagnostic laboratory tests for tetanus have been employed, where the first 2 may confirm the diagnosis but the third only supports it:¹²

1. Tetanus toxin in serum sample: failure to detect toxin, however, does not exclude the diagnosis.
2. Isolation of tetanus bacillus from an infection site: unfortunately the recovery of this is exceedingly rare.
3. Tetanus toxin antibodies in serum: this is the most widely used of the 3 tests. Low or absent levels of antibody (<0.01 IU/mL) may provide laboratory evidence to support the clinical diagnosis.

Principles of management for tetanus have been detailed in many review articles.¹³ They include: airway management, control of spasms and autonomic instability, prevention of further neuromuscular toxicity, supportive care and immunisation. Early recognition of the disease presentation is paramount.

The most effective way to reduce infection is to stop the injection of drugs, particularly via cutaneous or intramuscular routes.¹ Other steps which may be taken include education of high-risk groups against needle-sharing and re-use, minimising the amount of citric acid used in drug preparation, and alternative modes of drug use (e.g., smoking rather than injecting) for recalcitrant abusers.

Although parenteral drug abuse with buprenorphine has been curtailed, its occurrence with benzodiazepines is still common among drug addicts in Singapore. Hence, there is a need to be aware of the various complications that may arise from this practice among substance abusers in Singapore.

Acknowledgements

The authors would like to thank the medical and nursing staff of the Medical Intensive Care Unit, Alexandra Hospital, Drs Pavanni and Liow PH for their care of our patient during his hospitalisation.

REFERENCES

1. Brett MM, Hood J, Brazier JS, Duerden BI, Hahne SJ. Soft tissue infections caused by spore-forming bacteria in injecting drug users in the United Kingdom. *Epidemiol Infect* 2005;133:575-82.
2. Calder KK, Severyn FA. Surgical emergencies in the intravenous drug user. *Emerg Med Clin of North Am* 2003;21:1089-116.
3. Barsam A, Kerins M, Jaye P. Tetanus and intravenous drug use. *Eur J Clin Microbiol Infect Dis* 2005;24:497-8.
4. McGovern MP, Carroll KM. Evidence-based practices for substance use disorders. *Psychiatr Clin North Am* 2003;26:991-1010.
5. Jenkinson RA, Clark NC, Fry CL, Dobbin M. Buprenorphine diversion and injection in Melbourne, Australia: an emerging issue? *Addiction* 2005;100:197-205.
6. Cicero TJ, Inciardi JA. Potential for abuse of buprenorphine in office-based treatment of opioid dependence. *N Engl J Med* 2005;353:1863-5.
7. Ministry of Health issues guidelines on the prescription and use of buprenorphine (subutex). Available at: <http://www.moh.gov.sg/corp/about/newsroom/pressreleases/details.do?id=34668568>. Accessed 4 June 2006.
8. Ministry of Home Affairs. Tougher action against Subutex abuse. Available at: <http://www2.mha.gov.sg/mha/detailed.jsp?artid=2050&type=4&root=0&parent=0&cat=0>. Accessed 6 March 2007.
9. Centers for Disease Control and Prevention. Chemical Emergencies. Facts about Strychnine. Available at: <http://www.bt.cdc.gov/agent/strychnine/basics/facts.asp>. Accessed 4 June 2006.
10. Beeching NJ, Crowcroft NS. Tetanus in injecting drug users. *BMJ* 2005;330:208-9.
11. Farrar JJ, Yen LM, Cook T, Fairweather N, Binh N, Parry J, et al. Tetanus. *J Neurol Neurosurg Psychiatry* 2000;69:292-301.
12. Health Protection Agency. Cluster of cases of tetanus in injecting drug users in England: update. *Commun Dis Rep (CDR) Weekly [serial online]* 2003;13(48). Available at: <http://www.hpa.org.uk/cdr/PDFfiles/2003/cdr4803.pdf>. Accessed 19 October 2005.
13. Bassin SL. Tetanus. *Curr Treatment Options Neurol* 2004;6:25-34.