The Journal of Laryngology & Otology (2008), ***122***, *1389–1391*.

doi:10.1017/S0022215107001223

Clinical Record

Ketamine in the management of generalised cephalic tetanus

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Abstract

Background: Tetanus is a fatal infection caused by the neurotoxin tetanospasmin released by the vegetative spores of *Clostridium tetani*. The high mortality rate is related to frequent tetanic fits with laryngeal spasm and airway obstruction. Numerous anticonvulsants are in use, with varying efficacy in controlling fits. This case report highlights the use of ketamine as adjunctive therapy in the management of tetanus.

Case report: A 20-year-old woman was admitted with a history of recurrent left ear pain, with bloody, purulent discharge, following a self-inflicted injury. She developed tetanic spasms 24 hours after admission. She had received no immunisations. A tracheostomy was established to relieve airway obstruction, and ketamine was added to the medication when breakthrough seizures were refractory to diazepam.

Conclusion: Ketamine is of proven safety as an anaesthetic agent, especially in cases in which an anaesthetist is not readily available. Its effectiveness in this case, in combination with diazepam, warrants further evaluation.

Key words: Clostridium Tetani; Tetanus; Airway Obstruction; Ketamine

Introduction

Tetanus is a life-threatening infection characterised by painful muscle spasms, hypertonia and autonomic instability.[1] It is caused by *Clostridium tetani*, a spore-forming, Gram-positive, non-encapsulated, obligate anaerobic bacteria. Its spores remain viable at ambient oxygen concentration; they are highly resistant to extremes in temperature and humidity and can survive indefinitely. Spores are ubiquitous in soil and in animal and human faeces. When conditions occur which favour anaerobic proliferation, such as gross contamination of tissue injury, *C tetani* spores germinate into mature bacilli which form the toxins tetanolysin and tetanospasmin. Tetanospasmin accounts for the clinical manifestations of tetanus.[2,3] Tetanospasmin enters the peripheral nerves and travels via axonal retrograde transport to the central nervous system. It then enters presynaptic neurons and disables neurotransmitter release, mostly of the inhibitory neurotransmitter gamma-aminobutyric acid and glycin. This results in the inhibition of end-organ neurons, such as motor neurons and those of the autonomic nervous system, accounting for the muscle spasm and autonomic instability seen in severe disease.[4]

Despite being easily preventable by a highly effective vaccine, tetanus remains a significant public health problem, especially in developing countries. The true incidence is unknown, but it is estimated to be between 500 000 and 1 000 000 cases yearly worldwide. The majority of these cases occur in developing countries, where 50 per cent of cases occur in neonates. Cephalic tetanus is an uncommon variant, with an incidence of 1–3 per cent and a short incubation period of one to two days. Otitis media and head injury are frequently implicated.[5,6] The commonest presenting symptom is trismus with dysfunction of one or more cranial nerves, often the VIIth nerve, resulting in facial hemi-paresis and ptosis (Figure 1).[7] Over 60 per cent of cases will become generalised, with the onset of broader symptoms such as restlessness, irritability, headache, risus sardonicus, opisthotonus and (typically violent) tetanic spasm.[8] Laryngeal spasms may produce upper respiratory obstruction, while sphincteric dysfunction in the gastro-intestinal and urinary systems manifest as faecal and urinary incontinence.

Diagnosis is clinical and straight-forward when trismus, muscle stiffness and tetanic spasm occur in the presence of a clear sensorium. The spatula test is 100 per cent positive (Figure 1). However, clinical tetanus should be differentiated from alveolar, parapharyngeal and retropharyngeal abscess.

The principles of care are to remove the source of tetanospasmin, to neutralise circulating toxins and to provide supportive care until the toxins fixed to the neural tissues are metabolised.[9] A variety of drugs have been used, such as diazepam, chlorpromazine and phenobarbitone to control fits; however, magnesium sulphate, although having a narrow therapeutic window, is increasingly preferred.[10] Diazepam is widely used in our environment, but refractory or breakthrough fits can become a problem.

We present a case of generalised cephalic tetanus, a rare diagnosis, in which we resolved to prevent imminent death by introducing intravenous ketamine, a previously undescribed intervention, which resulted in effective seizure control.

Case report

A 20-year-old female patient was referred to the ENT clinic from the out-patient department in severe distress, with a history of recurrent left ear pain and bloody, purulent discharge following a self-inflicted injury to the ear.

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Accepted for publication: 28 August 2007. First published online 26 November 2007.

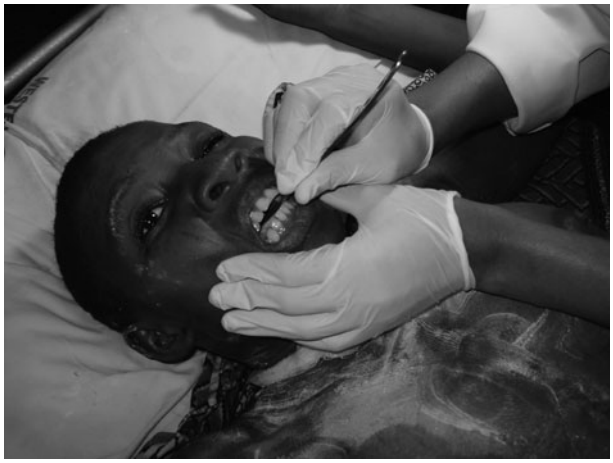

FIG. 1
Illustration of a positive spatula test and left ptosis (published with patient's permission).

A diagnosis of left otitis media and otitis externa was made, and the patient was commenced on intravenous ceftriaxone (1 g daily), oral sodium diclofenac (50 mg twice daily) and oral bromelain 40 mg/crystalline trypsin 1mg (one thrice daily). At this stage, the patient was conscious and alert and her vital signs were normal.

The following morning, the patient complained of a sensation of chest tightness with back pain. On examination, she had difficulty in opening her jaw and had nuchal and abdominal muscle rigidity, although her vital signs were still stable. Left facial palsy with ptosis of the left eyelid was noticed (Figure 1). The patient was diagnosed with generalised cephalic tetanus and was moved to a quiet, dark room. Intravenous metronidazole (500 mg 8 hourly) and diazepam (50 mg in 500 ml 5 per cent dextrose/saline 4 hourly) were added to her treatment. She was given anti-tetanus serum (10 000 IU) after a negative test dose. Ear toilet was performed with dilute metronidazole solution and ofloxacin ear drops, applied thrice daily.

Two days later, pyrexia was still persistent and there was a fleshy growth in the ear canal.

A week after admission, the patient developed severe laryngospasm with apnoea lasting about five seconds, for which cardio-pulmonary resuscitation and oxygen administration by face mask were required. A second dose of anti-tetanus serum (10 000 IU) was given. An emergency tracheostomy was performed with intravenous ketamine and local anaesthetic (1 per cent xylocaine) infiltrated into the surrounding skin.

Thereafter, muscle spasm remained frequent and severe in spite of the diazepam infusion. A decision was taken to include intermittent ketamine infusion (2 mg/kg body weight) in the patient's treatment, because of its anaesthetic properties and safety profile. The hyperalimentation started following tracheostomy was continued because a nasogastric tube was not tolerated.

The patient's clinical condition improved. On the 15th day of admission, she was clinically stable enough to undergo excision of the aural polyp in the left ear. A tissue sample was sent for histopathological assessment.

The patient's frequency of spasms progressively reduced, and she was gradually commenced on monitored oral sips on the 23rd day of admission. She was gradually weaned off intravenous medication. Facial palsy and ptosis resolved spontaneously. The patient was given tetanus toxoid injection (0.5 ml statum). She became ambulatory, and was discharged home on the 28th day of admission, after tracheostomy tube removal.

At a follow-up appointment, the patient had no complaints. An audiogram revealed some conductive deafness of the pathological ear.

Discussion

Tetanus remains a significant public health problem in developing countries. In such countries, the true incidence is unknown, although it is apparent that up to 50 per cent of cases occur in neonates, in whom the mortality rate is disproportionately high.[11,12] The majority of adult cases occur in those who have not completed the three dose primary tetanus toxoid vaccination or whose vaccination histories are uncertain. In this case report, the patient had not been vaccinated.

The progression of tetanus symptoms follow a well documented pattern. Our patient had a chronic suppurative otitis media and otitis externa as a result of trauma, and she subsequently developed trismus, left facial palsy and ptosis of the left eyelid. Her spasms became progressively more violent and were easily provoked by the slightest stimulus.

Various drugs have been used in the control of tetanus-induced muscle spasm and rigidity, which represents a major challenge to the physician in low- and middle-income areas, and even in developed countries, as there is no standard drug regimen for treating such patients.[13]

- **Tetanus is a fatal infection caused by the neurotoxin tetanospasmin released by the vegetative spores of *Clostridium tetani***
- **The high mortality rate is related to frequent tetanic fits with laryngeal spasm and airway obstruction**
- **Numerous anticonvulsants are in use, with varying efficacy in controlling fits**
- **This case report highlights the use of ketamine as adjunctive therapy in the management of tetanus**

Diazepam, a benzodiazepine, is a gamma-aminobutyric acid agonist with a long history as an effective drug in the treatment of tetanus. Its benefits are attributable to a combined anticonvulsant and muscle relaxant action on muscle spasm and rigidity. Its anxiolytic effect, with little respiratory depression, enhances its suitability.[14] It was our first line drug, but in spite of high doses, seizures were frequent and severe, with airway obstruction necessitating a tracheostomy. The urgent need to introduce complementary therapy for seizure control led to the addition of ketamine, an intravenous anaesthetic agent, which resulted in effective control without the need for artificial ventilatory support, as airway and chest compliance were maintained. Ketamine is classified as an NMDA receptor antagonist (2-(-2chlorophenyl)-2-methylaminicyclohexane-1-1), which opens in response to binding of the neurotransmitter glutamate. This NMDA receptor mediates the analgesic effects of ketamine. This drug is unique because it also has hypnotic and amnesic effects, while at the same time preserving the airway. Its onset of action after an intravenous dose is approximately 30–60 seconds for anaesthesia, with effects lasting for 10–15 minutes. It is metabolised in the liver.[15]

Our patient was adequately sedated and her spasms and rigidity controlled with alternating doses of intravenous diazepam and ketamine. Ketamine has been documented to have mild stimulatory effects on the

https://doi.org/10.1017/S0022215107001223 Published online by Cambridge University Press

cardiovascular system, causing blood pressure rises of about 25 per cent and heart rate increases of about 20 per cent, with maintenance of pharyngeal and laryngeal reflexes. It also causes an increase in muscle tone and salivation.[16,17] In our case, autonomic instability was not worsened by ketamine. Our patient's tracheostomy tube received daily suctioning and cleaning of the inner tube in order to reduce accumulation of secretion. Our patient was successfully managed in a dark room without the need for artificial ventilation.

This fascinating experience of ketamine used in combination with diazepam in the treatment of generalised cephalic tetanus indicates the need for further evaluation, especially in poorly resourced clinical environments.

Conclusion

Cephalic tetanus is a rare variant of tetanus which can become generalised, with poor prognosis. It should be considered when patients develop facial palsy with spasm following head and neck injuries. The need for better management of tetanus has lead to the use of various drugs to control spasm and rigidity. In the presented case, ketamine was successfully used to treat frequent spasm cycles; its use in this clinical scenario warrants further evaluation.

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Dr J E O Amadasun takes responsibility for the integrity of the content of the paper.
Competing interests: None declared