

Tetanus - A Case Report with Severe Autonomic Instability and A Review of the Literature.

¹ALAGBE-BRIGGS OT; ²TINUBU SA

¹Department of Anaesthesia and Intensive Care. ²Critical Care Unit. Lagos State University Teaching Hospital, Ikeja, Lagos.

ABSTRACT

BACKGROUND: Tetanus is an infection that can be associated with a high mortality especially in developing countries. Critical care which may include artificial control of respiration is crucial in survival, but cardiovascular complications from autonomic instability remains an important cause of death. The objective of this report is to highlight this important cause of mortality despite artificial control of ventilation to prevent respiratory arrest.

METHOD: The medical record of the patient and relevant literature were reviewed.

RESULT: A 29-year old male following a wound on the lower limb presented with clinical features suggestive of tetanus. Incubation period was short and immunization history was uncertain. Basic treatment directed at removing source of infection and neutralisation of unbound toxin was however commenced. Following signs of imminent respiratory failure due to severe uncontrollable spasms, controlled mechanical ventilation was instituted in the critical care unit (CCU). However, the patient succumbed to cardiac arrest as a result of severe autonomic instability, despite aggressive cardiopulmonary resuscitation.

CONCLUSION: Cardiovascular arrest from severe autonomic instability remains an important cause of mortality in tetanus despite artificial ventilation. Early management with appropriate therapy is advisable to prevent its occurrence.

KEY WORDS: Tetanus, Artificial ventilation, Autonomic instability.

Date Accepted for Publication: 9th August, 2012

NigerJMed 2012;353-356

Copyright ©2012. Nigerian Journal of Medicine

INTRODUCTION

Tetanus is an acute, toxin-mediated bacterial infection caused by *Clostridium tetani*, a gram positive, motile, endospore forming bacillus and obligate anaerobe.¹ With natural habitat in the soil, it is widespread in domestic animals and human faeces, with abundant spores in the environment. Being preventable, it is now rare in developed countries, but mortality remains high especially in developing countries due to ineffective immunisation practices. Infection usually follows contamination of deep penetrating wounds by soil, manure or rusty metal where anaerobic growth is facilitated.^{2,3} Incubation period averages 7-10 days (range: 1-60 days), but may be <72 hrs.

Two exotoxins are subsequently secreted: tetanolysin

that causes local tissue damage, optimising conditions for further multiplication; and tetanospasmin an extremely potent neurotoxin, that is transported to the axon terminals of peripheral nerves producing the clinical syndrome. This acts pre-synaptically blocking inhibitory neurotransmitters in the CNS (glycine and GABA-gamma-aminobutyric acid), causing failure of inhibition of motor reflex responses to sensory stimulation, and affecting motor nerves first with resultant muscular stiffness and typical spasms, then sensory and autonomic nerves.^{3,4}

It can affect any age group with reported mortality of 15-40% depending on the availability and quality of intensive care, and case-fatality rates of 10-80% even with modern intensive care.^{5,6,7}

Usually, there is evidence of a wound within the last 2 weeks, with no clear history of immunization; but in about 15-25%, there is no evident wound. Wounds may be trivial, 50% occurring indoors and not considered serious enough for treatment.³ Any type of wound can be affected but usual ones are those of the lower limbs, childbirth, septic abortion, ulcers, compound fractures and nonsterile intramuscular injections.

Three types are known^{3,4} - local, cephalic and generalized; approximately 80% being generalized in nature, with characteristic signs of trismus due to spasm of the masseter muscles, neck stiffness, dysphagia, dyspnoea and fever. In severe cases, there is *risus sardonicus*, opisthotonos and board-like rigidity of the abdomen. Later, uncoordinated widespread muscle spasms occur which may be spontaneous or provocative, continuous or intermittent, painful and exhausting, with possible musculoskeletal injuries, and lasting from a few seconds to minutes. Pharyngolaryngeal spasms, aspiration of secretions, respiratory obstruction, renal failure and even sudden death can result. Artificial ventilation may be required to prevent hypoxaemia, while autonomic disturbances when present, can be life-threatening with poor prognosis.⁶

Diagnosis is usually made following clinical than bacteriologic findings.^{3,6}

However, laboratory studies may reveal moderate leukocytosis, normal CSF but elevated pressure due to muscular contractions, and ECG findings of sinus tachycardia or T-wave inversion with cardiac involvement.

Recommended guidelines in management^{3,4} which may involve critical care prevents death from respiratory failure,⁷ but other causes of death including cardiovascular complications from autonomic disfunction(AD) remain problematic.⁴

Neuronal binding is irreversible, complete recovery occurring 25 weeks after toxin destruction and regrowth of axon terminals, which explains the long duration. Infection however confers no immunity as recurrence can occur.^{3,4,6}

CASE REPORT

A 29-year old male presented at the medical emergency unit of the Lagos State University Teaching Hospital with a 3day history of restricted mouth opening, chest pain, neck stiffness and spasms of 1day duration. There was a 1week history of fever, headache and left ankle wound treated in a private hospital, but nature of treatment was unknown and history of antitetanus prophylaxis was uncertain. On general examination patient was warm to touch, mildly pale, anicteric, not dehydrated, but had trismus and intermittent spasms. The chest was clear with good air entry bilaterally. The cardiovascular system findings were P.R.-104b/min, B.P.-110/70mmHg and normal heart sounds I&II. The abdomen was rigid but bowel sounds were normal. The patient was admitted following a diagnosis of tetanus, nursed in a quiet room with close monitoring of vital signs and spasms, and daily open wound dressing. Investigations ordered included FBC, ESR, CXR and urinalysis.

Other management instituted were ATS 10,000IU(IM) and 10,000IU(IV) after a test dose; IM tetanus toxoid-0.5mls stat, IV crystalline penicillin 3MU 6hrly, IV metronidazole 500mg 8hrly, IV diazepam 40mg 6hrly by slow infusion and 20mg bolus 6hrly.

Two days later, spasms became continuous and uncontrollable with imminent respiratory arrest. He was therefore transferred to the CCU where monitors were attached with baseline arterial O₂ saturation (SaO₂) of 43-65%; HR-92b/min; NIBP- 140/80mmHG; T^oC-36.8^oC and ECG showed a sinus rhythm. Controlled mechanical ventilation was therefore commenced following a rapid sequence induction (RSI) with IV propofol 150mg, and tracheal intubation with a #7 COTT facilitated by IV suxamethonium 100mg. Sedation was continued with diazepam and muscle paralysis with an infusion of pancuronium (2mg/hr) and later atracurium (30mg/hr).Ventilator settings were SIMV mode; TV-700mls; RR-14cycles/min; FiO₂-50%. Tracheobronchial toileting was done to clear excessive secretions, while bladder was catheterized for urine output monitoring. The SaO₂ subsequently increased to 99% and arterial blood gas values were pO₂ -205.9mmHg, pCO₂-

22.4mmHg, HCO₃⁻-18.6mmol/L and pH-7.53.

Results of PCV and E/U were normal, but WBC count was 12.2 x 10⁹/L.

Approximately 24hrs post ICU admission, patient became restless, pyrexic (38.3^oC), with desaturation (SaO₂-33%) and sinus tachycardia(118b/min). Latter worsened, progressing to dysrhythmia, severe bradyarrhythmia (<30-40/min) and finally asystole. Cardiopulmonary resuscitation was commenced with cardiac compressions, atropine-3mg(x3), adrenaline-1mg(x3) and defibrillation; but was discontinued after about 45min of failed resuscitation.

1. Table 1: Ablett classification of tetanus severity¹⁰

| Grade | Clinical features |
|------------------|---|
| I (mild) | Mild trismus, general spasticity, no spasms, no dysphagia. no respiratory embarrassment. |
| II (moderate) | Moderate trismus, rigidity, short spasms, mild dysphagia, moderate respiratory involvement, respiratory rate > 30. |
| III (severe) | Severe trismus, generalized spasticity, prolonged spasms, pulse > 120, respiratory rate > 40, severe dysphagia, apnoeic spells. |
| IV (very severe) | Grade 3 + severe autonomic disturbances involving the cardiovascular system. |

DISCUSSION

Tetanus is still a major health problem in our environment,^{8,9} severity being related to a short incubation period and onset time, inadequate treatment and immunization⁶ and nearness of entry site to CNS.^{3,4} Though entry was remote, these factors produced a very severe form using Ablett's grading¹⁰ (Table 1). With the advent of ICU's, Trujillo⁷ has reported a decline in deaths from respiratory complications from 80% to15%, while AD became apparent with 40% of deaths caused by sudden cardiac death. Suggestive signs of AD in this patient were excessive secretions, pyrexia, tachy and bradyarrhythmias and hypertension. Komolafe and colleagues⁸ in their study also found AD as the commonest complication and a cause of death. It is postulated to result from brain stem damage by exotoxin,¹¹ myocardial disfunction from high levels of catecholamines or widespread disinhibition of autonomic nervous system discharge with sympathetic and/or parasympathetic overactivity.^{3,4,12}

Management of tetanus includes removal of exotoxin source by debridement, open dressing and antibiotic therapy. Metronidazole known to lower mortality and reduce requirements for sedatives and muscle relaxants^{3,13,14} was used. Neutralization of unbound circulating toxin was late due to patients delayed arrival. Supportive care includes spasm control by sedation, muscle paralysis and avoiding unnecessary stimulation (gentle nursing care in a quiet, dark room). Sedation can

be with diazepam (used in this patient), phenobarbitone, phenothiazines, morphine, remifentanyl, midazolam, propofol, dantrolene and baclofen.^{4,6,15} With this case of uncontrollable spasms, risk of aspiration and imminent respiratory arrest, muscle paralysis with tracheal intubation (TI) was instituted. Pancuronium was employed for continued muscle paralysis as vecuronium which offers cardiostability though short acting, is expensive and not available.¹⁶ Tracheostomies have been recommended for long term use, better toileting, and when there is opisthotonos as TI can stimulate spasm.¹⁷ Control of AD involves sedation, α and/or β -adrenergic blockade, use of α_2 -adrenergic agonist and neuraxial bupivacaine.³ With parasympathetic excess, adrenaline and anticholinergics have been used, tetanus being regarded as a disease of acetylcholine excess.^{4,6,18} ACE inhibitors, dexmedetomidine sodium valproate and adenosine^{19,20,21,22} have also been considered for use.

In the search for drugs that can control spasms and AD without heavy sedation or artificial ventilation; IV magnesium sulphate 5g stat, then 1-2.5g/hr has been used successfully.⁵ It acts as a presynaptic neuromuscular blocker and blocks release of catecholamines. It lowers serum calcium, so toxicity is prevented by monitoring patella tendon reflex and keeping serum Mg^{+} at 2-4mmol/L.⁵ But our patient could not benefit from it due to rapid progression.

Investigations also showed leukocytosis,³ hypoxia and blood gas disorders for which mechanical ventilation was instituted.

Other supportive management include physiotherapy, fluid and nutritional balance, prevention of pressure sores, stress ulcers, thromboembolism, urinary and respiratory infections.^{3,4,23,24} Psychological support is also essential.²⁵

Though outcome depends on the centre and disease severity,^{4,7,26} early therapy with magnesium sulphate has yielded better results from reports by Attygalle and Rodrigo.⁵ It is easy to administer and cost effective, and by avoiding the need for heavy sedation and ventilatory support, it simplifies nursing care and reduces respiratory and thromboembolic sequelae: these being major advantages in resource poor settings.⁵

CONCLUSION

Tetanus is a major health problem associated with high mortality, but preventable with adequate vaccination and appropriate wound care.^{3,27} Challenges from respiratory compromise and cardiovascular instability can be life threatening,⁴ so critical care is crucial in survival. However, being a third world disease that requires first world technology limited in endemic areas,²⁸ there is

urgent need for new treatments.^{3,5} Therapy with magnesium sulphate therefore remains promising.

REFERENCE

1. Farrar JJ, Yen LM, Cook T, Fairweather N, Binh N, Parry J, Parry CM. Tetanus. *J Neurol Neurosurg Psychiatry* 2000; 69:292-301.
2. Centers for Disease Control and Prevention. Tetanus Puerto Rico, 2002. *MMWR* 2002; 51:613-615.
3. Edlich R. F. et al. Management and Prevention of Tetanus. *J Long Term Eff Med Implants*, 2003; 13:139-154.
4. Cook TM, Protheroe RT, Handel JM. Tetanus: a review of the literature. *Br J Anaesth* 2001; 87:477-87.
5. Attygalle D, Rodrigo N. Magnesium sulphate for control of spasms in severe tetanus: can we avoid sedation and artificial ventilation? *Anaesthesia* 1997; 52:956-962.
6. Current recommendations for treatment of tetanus during humanitarian emergencies. WHO Technical Note January 2010. (WHO/HSE/GAR/DCE/2010. 2)
7. Trujilo MH, Castillo A, Espana J, Manzo A, Zerpa R. Impact of intensive care management on the prognosis of tetanus. Analysis of 641 cases. *Chest* 1987; 92:63-65
8. Komolafe MA, Komolafe EO, Ogundare AO. Pattern and outcome of adult tetanus in Ile-Ife Nigeria. *Nig J Clin Pract* 2007; 10:300-303.
9. Talabi OA. A 3 year review of neurologic admissions in the University College Hospital Ibadan Nigeria. *West Afri. J Med.* 2003; 22:150-151.
10. Ablett JLL. Analysis and main experiences in 82 patients treated in the Leeds Tetanus Unit. In: Ellis M, ed. *Symposium on Tetanus in Great Britain*. Boston Spa, UK: National Lending Library, 1967; 1-10.
11. Tsueda K, Oliver PB, Richter RW. Cardiovascular manifestations of tetanus. *Anesthesiology* 1974; 40:588-591.
12. Wright DK, Lalloo UG, Nayiager S, et al. Autonomic nervous system dysfunction in severe tetanus: current perspectives. *Crit Care Med* 1989; 17:371-375.
13. Ahmadsyah I, Salim A. Treatment of tetanus: an open study to compare the efficacy of procaine penicillin and metronidazole. *BMJ* 1985; 291:648-650.
14. Yen LM, Dao LM, Day NPJ, et al. Management of tetanus: a comparison of penicillin and metronidazole. *Symposium of antimicrobial resistance in southern Viet Nam*, 1997.
15. Beecroft CL, Enright SM, O'Beirne HA. Remifentanyl in the management of severe tetanus. *Br J Anaesth* 2005; 94:46-8.
16. Powles AB, Ganta R. Use of vecuronium in the

- management of tetanus. *Anaesthesia* 1985; 40:879-81.
17. Mukherjee DK. Tetanus and tracheostomy. *Ann Otol* 1977; 86:67-72.
 18. Dolar D. The use of continuous atropine infusion in the management of tetanus. *Intensive Care Med* 1992; 18:26-31.
 19. Wright DK, Laloo UG, Nayaiger S, Govender P. Autonomic nervous system dysfunction in severe tetanus: current perspectives. *Crit Care Med* 1989; 17:371-5.
 20. Girgin NK, Iscimen R, Gurbet A, Kahveci F, Kutlay O. Dexmedetomidine sedation for the treatment of tetanus in the intensive care unit. *Br. J. Anaesth.* 2007; 99:599-600. doi: 10.1093/bja/aem251
 21. Pinder M. Controversies in the management of severe tetanus. *Intensive Care Med* 1997; 14:129-43.
 22. Foca A, Rotiroti D, Mastroeni P, Nistico G. Effects of tetanus toxin after intracerebral microinjection are antagonised by drugs enhancing GABAergic transmission in adult fowl. *Neuropharmacology* 1984; 23:155-8.
 23. World Epidemiological Record. Tetanus vaccine: WHO position paper. 2006; 81:197-208.
 24. Edmondson RS, Flowers MW. Intensive care in tetanus: management, complications, and mortality in 100 cases. *BMJ* 1979; 1:1401-4.
 25. Towey R. Tetanus: a review. Update in *Anaesthesia*. 2005; 19:43-48.
 26. Sanford JP. Tetanus- forgotten but not gone. *N Eng J Med* 1995; 332:812-3.
 27. Izurieta HS, Sutter RW, Strebel PM, et al. Tetanus surveillance United States, 1991-1992. In: *CDC Surveillance Summaries (February 21)*. *MMWR* 1997; 46 (No. SS-2).
 28. Delport SD. Neonatal tetanus - an opportunity for prevention. *SAfr Med J* 1990; 77:78-9.