

Tetanus

A clinical review

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ABSTRACT

Objectives: Although tetanus is now uncommon in Oman (The Expanded Program on Immunization was introduced in 1981), patients continue to present from time to time at an average rate of 6 cases per year. Worldwide, the mortality rate for tetanus remains high (ranging from 15-20% in developed countries). At the Sultan Qaboos University Hospital, Muscat, Oman, prolonged Intensive Care Unit treatment and multi-disciplinary management is invariably required for tetanus patients. This study was carried out to evaluate our results over the past decade.

Methods: All tetanus patients admitted to the Sultan Qaboos University Hospital from 1991 up to the end of 1999 were retrospectively reviewed. Patients were diagnosed early, and aggressive treatment in the Intensive Care Unit was instituted, with a coordinated multidisciplinary management.

Results: Ten cases were identified and included in the review, comprising 9 adults and one infant aged 2 weeks. Adult patients were aged 36-75 years (mean 59 years), and the average Intensive Care Unit stay of the 9 surviving patients was 5.5 weeks (range 3-7 weeks). All patients

presented with severe generalized tetanus. Two patients with traditional cautery marks developed tetanus. A focus of infection could not be found in 2 patients. All patients had early tracheostomy and assisted ventilation with appropriate sedation. One patient required almost 45 gm of diazepam throughout his Intensive Care Unit stay. One adult patient died on the 6th day of admission following myocardial infarction. The neonatal case survived after 35 days care in the Intensive Care Unit. The mortality rate for our patients was therefore 10%.

Conclusion: Tetanus in Oman remains an infrequent but important disease requiring costly and prolonged Intensive Care Unit treatment. We attribute the comparatively low mortality rate (10%) in this study, to early diagnosis, institution of aggressive treatment, good nursing as well as a well-coordinated multi-disciplinary management.

Keywords: Tetanus, tetanus management, cautery burns, immunization, Risus Sardonius.

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Tetanus is a potentially preventable disease caused by a potent neurotoxin produced by *Clostridium tetani*. The disease was first described in the 14th century by John of Arderne.¹ Tetanospasmin is responsible for its pathogenesis. After the toxin of botulism, it is the most potent neurotoxin known to man, with an estimated lethal dose of 2.5 ng/kg body weight.² Tetanus is one of the target diseases of the

World Health Organization (WHO) Expanded Program on Immunization (EPI). The overall annual incidence worldwide is 0.5-1 million cases. It is estimated that there are 140,000 fatal neonatal cases per annum. The disease is more common in tropical and developing countries, where immunization is deficient and opportunities for penetrating contaminated wounds is higher.³ In Oman, tetanus

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toxoid was first included in the EPI in 1981 and accordingly the majority of adults are not immunized. Most Omanis live in rural areas and are involved in subsistence agriculture and livestock farming, subsequently, exposure to tetanus is common. Sultan Qaboos University Hospital (SQUH) is a tertiary care teaching hospital in Muscat and patients with tetanus are referred from regional and district hospitals.

Methods. All patients referred to, or presenting at, the SQUH from 1991 to 1999 were included in this study. One or more of the authors had treated each patient. A retrospective evaluation of all the patients was undertaken to determine the results of treatment during this time. Medical records were reviewed to collect demographic information, circumstances of injury, anatomic site and type of injury, treatment and outcomes. Ten cases were identified including a neonate, 9 males and one female (Table 1). All but one patient, a Bangladeshi, were Omanis. All patients had full clinical examinations, including identification of the focus of infection. Severe generalized tetanus was the main diagnosis in all the cases thus early ventilatory support and tracheostomy together with intensive nursing care, were instituted. The diagnosis of tetanus is purely clinical, as there are no specific laboratory tests. However, the basic initial investigations have included full blood count, erythrocyte sedimentation rate, serum glucose, serum

calcium, arterial blood gases, urea and electrolytes, electrocardiogram, chest x-ray and wound cultures. All the patients received antibiotics, anti-tetanus toxoid and human tetanus immunoglobulin (TIG). Generalized muscle spasms, which occurred in all patients, were well controlled with a combination of sedative drugs and muscle relaxants. Initially parenteral then enteral nutrition was instituted in all patients.

Results. Most patients presented with progressive difficulty in swallowing, back pain and stiffness of the back and neck, of 2 days to one-week duration. Tetanic spasms were observed in only one patient. On admission, all patients were alert, agitated, had trismus, generalized rigidity associated with hyperreflexia and exhibited plantar withdrawal, their sensorium was otherwise normal. A focus of infection could not be found in 2 patients. Risus sardonicus and opisthotonos were noted in 2 patients. Two patients with traditional cautery burns developed tetanus. One of them was a female patient with an unreported, infected cautery lesion on her scalp, which was found by chance by the nursing staff when being washed. The other one had multiple traditional cautery marks on the neck and the trunk. We obtained only one positive culture out of the 8 cases with a known focus of infection and the basic initial investigations were unremarkable. Our neonatal case was delivered by an old blind woman at home in a remote village (mother Gravida 7, Para

Table 1 - Tetanus cases admitted to the Intensive Care Unit at Sultan Qaboos University Hospital during the period from 1991 to 1999.

Case Number	Patient Age/Sex	Year of admission	ICU stay (days)	Source of tetanus infection	Incubation period (days)	Significant complications	Outcome
1	59/M	1991	41	Unknown	NA**	Pneumonia, UTI	Recovered
2	66/M	1992	6	Left big toe	10	MI, cardiac arrest	Died
3	67/M	1992	50	Right thigh	7	2 x pneumonia	Recovered
4	63/M	1993	19	Left neck cautery	4	Pneumonia	Recovered
5	47/M	1993	31	Unknown	NA**	Myoclonic epilepsy, pneumonia	Recovered
6	6 days/M	1995	35	Umbilical cord	5	Pneumonia	Recovered
7	75/F	1996	51	Small scalp cautery	6	Pneumonia	Recovered
8	36/M	1997	52	Left ear	8	DVT, Pneumonia, VT, SVT, arrhythmia	Recovered
9	68/M	1998	41	Right foot	12	UTI, pneumonia, asystole, SVT	Recovered
10	52/M	1999	35	Right breast*	15	Pneumonia	Recovered

* Two weeks postoperative for abscess ** NA: Not available as the wound or the history of penetrating injury have not been found.
M - Male F - Female ICU - Intensive Care Unit UTI - Urinary Tract Infection MI - Myocardial infarct
DVT - Deep vein thrombosis VT - Ventricular tachycardia SVT - Supraventricular tachycardia

6 and sera confirmed non-immunized state). An unsterile knife cut the umbilical cord. On the 5th day the baby showed failure of sucking, vomiting and looked unwell. On the 6th day, he presented to the nearest hospital. He was dehydrated, showing tetanic spasms, risus sardonicus, opisthotonos with an infected umbilical cord. As the tetanus diagnosis was evident, the neonate was sedated, intubated and transferred to our hospital. All patients had early tracheostomy and assisted ventilation with appropriate sedation. It has been noted generally, the further distant the focus of infection from the central nervous system (CNS) the longer the incubation period. The average Intensive Care Unit (ICU) stay of the 9 surviving patients was lengthy, 5.5 weeks (range 3-7 weeks). In this small sized sample the mortality rate of our patients was therefore 10%. The following major complications were encountered. All patients developed multiple chest infections (pneumonia) and 2 patients contracted urinary tract infections. One patient developed right subclavian vein thrombosis probably secondary to continuous diazepam infusion. One patient with severe aortic stenosis (pressure gradient across the aortic valve 70-80mmHg) was revived from cardiac arrest (asystole) and underwent a successful aortic valve replacement after a full recovery from tetanus. Unsuccessful resuscitation of cardiac arrest occurred in a patient with non-insulin dependent diabetes mellitus who sustained myocardial infarction on the 6th day of his admission. Myocardial infarction is a rarely observed complication of tetanus.⁴ All patients showed one or more manifestations of autonomic dysfunction e.g. hypertension, hypotension, tachycardia, bradycardia and dysrhythmias particularly in the 2nd and the 3rd week. On discharge there were no major sequelae to any patient and outpatient follow-up showed no major long-term complications.

Discussion. Tetanus remains an important cause of morbidity and mortality despite the wide implementation of the EPI. The WHO estimated in 1990 that worldwide, there were about 715,000 deaths from neonatal tetanus.² In Oman, tetanus is a notifiable disease, and there were 2 neonatal and 52 adult cases (on average 6 cases per year) reported over the period from 1991 up to the end of 1999. Tetanus is primarily a disease of the elderly in developed countries. Active immunization and better hygiene, wound care and management of childbirth have diminished its incidence. Mortality has been reduced to 15% with the active employment of intensive care facilities for the treatment of this condition.⁵ Our mortality rate is comparatively low at 10%. The diagnosis of tetanus is purely clinical, as there are no specific laboratory tests. It has been estimated that wound cultures are positive in only 32% of cases.⁶ Only one positive culture was

obtained. A simple bedside test, the "spatula test" (a reflex spasm of the masseters on touching the posterior pharyngeal wall leading to biting of the spatula rather than a gag reflex), was described by Apte et al. In 400 patients, this test had a sensitivity of 94% and a specificity of 100%.⁷ Pain and stiffness of the back are the most common presenting symptoms, followed by trismus and dysphagia. Spasms may be precipitated by minimal stimuli such as noise, light or touch and may last from seconds to minutes. They can be painful or dangerous, causing apnea, fractures or rhabdomyolysis and thus our patients were kept in a quiet room and stimuli kept at a minimum until satisfactory sedation was achieved. Sera can be analyzed for tetanus antitoxin, the presence of more than 0.01 antitoxin unit per ml is regarded as protective against clinical tetanus, although cases have occurred in patients with antibody concentrations at least 10-fold higher than this. In this study, tetanus serology was only performed for the mother of the neonatal case, which confirmed her non-immunized state.

The major differential diagnoses which were excluded in our cases are hypocalcemia, meningitis, encephalitis, subarachnoid hemorrhage, peritonsillar abscess, dystonic reactions, rabies, spider envenomation (widow), strychnine poisoning and hysteria. There are 4 clinical forms of tetanus: neonatal, localized, cephalic and generalized. All the adult tetanus cases studied were of the generalized form. In the literature, the source of infection is from an obvious injury in 58% of cases (8 out of 10 in our series). Two patients with traditional cautery remedy developed tetanus. It is probable, that the source of tetanus in these cases was ash applied by the traditional healer to accelerate the wound healing.

Our treatment followed the recommended guidelines: Neutralization of the toxin and elimination of the source of infection by careful surgical excision and wound care. As soon as the diagnosis of tetanus was made, Human TIG 1000 units were given and repeated for an additional 2 days in most patients. This at best neutralizes only circulating toxins, but does not affect toxins already fixed to the CNS. Intrathecal administration of antitetanus toxin has not been used as large meta-analyses reported it to be ineffective in reducing the morbidity and mortality.⁸ Once the Human TIG has been given, the infected site should be thoroughly cleaned and all the necrotic tissue extensively debrided. Antibiotics destroy tetanus spores. The favorite choice was Metronidazole 500mg intravenously (IV) 8 hourly for 10 days as the drug has a spectrum of activity against anaerobes, it is able to penetrate necrotic tissue and has been shown to be more effective than penicillin in this situation.⁹ However, penicillin or a 3rd-generation cephalosporin have also been used in a few patients. Natural immunity to tetanus does not occur, tetanus

may both relapse and recur, so victims of tetanus must be actively immunized. Immunization with tetanus toxoid was given at the time of the diagnoses. A 2nd and 3rd toxoid injection were given one and 2 months later, with planned booster injections one-year later and then 10 yearly intervals. In the case of a neonate, the mother also was given the vaccine.

The main aims of treatment are to relieve the patient's distress, controlling the spasms and rigidity and to maintain adequate respiration. If endotracheal intubation was necessary, tracheostomy was performed within 10 days. As the endotracheal tube seems to be a strong stimulus for spasms, in the last 3 patients a tracheostomy was carried out earlier, on the 2nd day of ventilation. Benzodiazepines reduce anxiety, induce amnesia, sedation and muscle relaxation as well as being anticonvulsant.¹⁰ These drugs are GABA-amniobutyric acid A (GABA-A) agonists, thereby functioning as indirect antagonists of the effect of the toxin on inhibitory systems. Diazepam or midazolam by continuous infusion have been used. Diazepam is less expensive compared to other benzodiazepines. The disadvantages of diazepam include slow onset, prolonged action, and irritation to tissues and thrombophlebitis (one patient developed subclavian vein thrombosis). Most of our patients received diazepam IV infusions ranging between 10 to 60 mg/hr. One of our patients required 4500 ampoules of 10 mg diazepam (45000 mg) throughout his ICU stay. Other antispasmodics used included magnesium sulphate, morphine and muscle relaxants.

It is known that the mortality in tetanus associated with autonomic dysfunction is as high as 50%. Unexpected cardiac arrest is the most common cause of death in patients with tetanus admitted to the ICU and no obvious cause of death can be found at autopsy in up to 20% of deaths. It is general consensus that no drug singly, or in combination, has proved consistently effective in the control of autonomic disturbances. The armamentarium of drugs used in our patients included benzodiazepines, morphine,¹¹ alpha blockers, beta blockers, or agents with both properties, calcium antagonists, magnesium sulphate,¹² and atropine. Physiotherapy and nursing played a major role in preventing contractures and deep vein thrombosis in ICU and were the mainstay of rehabilitation in the ward. Other factors known to contribute to morbidity and mortality in tetanus were also prevented. These include hypoxia, malnutrition, and complications of mechanical ventilation (barotrauma), fluid and electrolytes disturbances. Bed sores and embolic phenomena were avoided thanks to excellent nursing care. Supportive psychotherapy was offered to both patient and family. Prevention of tetanus is the key

to its elimination and loss of life in an easily preventable disease is unacceptable. Primary care and emergency physicians can reduce the morbidity and mortality of tetanus through proper immunization. As a patient's tetanus immunization history is often unreliable in routine wound management, liberal use of tetanus toxoids and appropriate TIG is recommended.³

In conclusion, tetanus is a potentially preventable disease. However, it remains a frequent cause of death and hospitalization in most developing countries. Proper attention, strict adherence to immunization schedules and appropriate wound care will reduce the incidence of this potentially fatal disease. Active immunization is the clear solution. Early recognition of tetanus and early use of intensive care facilities can reduce the mortality considerably.

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