

Reminder of important clinical lesson

A minor wound with a fatal course

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The authors report on a fatal case of severe tetanus in a 74-year old woman. Despite comprehensive intensive care management they could not achieve a satisfying control of the autonomic dysfunction caused by tetanus. By now there is no established therapy for the treatment of the autonomic dysfunction. This report demonstrates the dismal prognosis of severe tetanus in the older people, which is often complicated by cardiovascular comorbidity and underlines the importance of tetanus prevention by sufficient vaccination.

BACKGROUND

Tetanus is nowadays a rare disease in developed countries, but mortality still remains high. Patients aged over 60 years are at greatest risk for tetanus infection. This increased risk results from inadequate immunity due to the vaccination status with advanced age: some of these patients might never have been vaccinated at all while others missed their vaccination boosters. Subsequently, a considerable part of the older people does not have a protective antibody level against tetanus.¹ The increased presence of cardiovascular diseases in the older people complicates the treatment of the autonomic dysfunction, which has become the main cause of death since respiratory failure can be prevented by mechanical ventilation.

Because of its poor outcome, the prevention of tetanus by sufficient vaccination is without choice.

As the disease and its vaccination are frequently forgotten, we think it is important to present our experience to a large number of physicians.

CASE PRESENTATION

A 78-year-old woman presented at our ENT outpatient department with an increasing lockjaw since the previous day. She was known to suffer from a renal insufficiency that required chronic dialysis, from paroxysmal atrial fibrillation as well as from a pre-existing coronary artery disease. Initially, the patient was clinically stable and fully responsive.

A prior tetanus vaccination was not memorable to the patient.

INVESTIGATIONS

Fiberoptic pharyngo-laryngoscopy indicated no signs of injuries or an inflammation in the upper airways. Particularly noticeable was an increase of the tonus of the masseter muscle as the cause of the lockjaw but also a mild generalised muscle rigidity. On inquiry, the patient

reported about an injury of the left lower leg sustained while gardening 1 week before. The skin lesion presented reddened with a seropurulent exudate (figure 1).

DIFFERENTIAL DIAGNOSIS

Laboratory investigations are not revealing except for negative findings, so the diagnosis of tetanus has to be made based on the typical clinical findings with increased muscle tone of the head and neck region due to spasms. Strychnine poisoning is the only differential diagnosis because it may mimic the initial clinical picture of tetanus, but not the autonomic dysfunction.

Tetanus is unlikely if a vaccination has been completed previously and protective serum antitoxin levels are found. Nevertheless there are case reports of tetanus in immune competent individuals with 'protective' antibody levels.^{2 3} The isolation of *Clostridium tetani* from the patient's wound is unreliable and typically not positive.⁴

TREATMENT

Within hours, the patient developed respiratory failure requiring emergent nasotracheal intubation. Furthermore, as a sign of autonomic dysfunction, the patient showed a fluctuating blood pressure and tachycardia that could barely be controlled by sophisticated medication based on invasive monitoring of circulation. We performed a prompt wound debridement and administered tetanus antitoxin subcutaneously. Further on, a high-dose antibiotic therapy with metronidazole was initiated. To control persistent generalised spasms, benzodiazepines and propofol were given. Magnesium was given intravenously for the additional control of spasms and cardiovascular stabilisation. Initially, these measures were sufficient. However, during the further course of the disease, severe cardiovascular instability and recurrent spasms occurred. The latter required intermittent application of muscle relaxants.



Figure 1 An injury of the left lower leg sustained while gardening was the portal of entry for the generalised tetanus infection.

OUTCOME AND FOLLOW-UP

With repeated episodes of profound hypotension, the patient deceased on the 28th day of treatment on cardiac failure. Serological findings confirmed a missing immunity against tetanus.

DISCUSSION

The treatment aims at the binding of circulating toxin, prevention of further toxin production, and minimising its effects on the central and peripheral nervous system. Toxin already bound to the central nervous system cannot be neutralised by antitoxin.

Antitoxin

Human tetanus immunoglobulin of 500–6000 units should be applied immediately. The optimal dosage and duration of antitoxin therapy is not known, recommendations are inconsistent in literature.^{5 6}

Prevention of toxin production

Wounds as being the entry side for *C tetani* should be explored, debrided and thoroughly cleaned.¹ Antibiotic therapy improves survival rate and reduces the need for muscle relaxants.⁷ Penicillin as a γ -aminobutyric acid (GABA) antagonist may counteract the therapy with benzodiazepines so metronidazole seems to be the antibiotic of choice. Clindamycin, tetracyclin and erythromycin are acceptable alternatives.¹

Minimising the toxin effect

The patient should be taken to an intensive care unit. Early intubation and mechanical ventilation is necessary to minimise the risk of pulmonary complications.¹ Some authors favour early elective tracheotomy as laryngeal spasms or aspiration may occur unexpectedly at any time even in mild forms of the disease.⁸

To control the spasms and muscle rigidity benzodiazepines are the standard therapy. Also, the patient should be protected from unnecessary stimulation. If adequate sedation could not be achieved by this regimen, propofol and neuromuscular blocking agents (particularly vecuronium with low side effects on the cardiovascular system) can be administered.¹

The use of intrathecal baclofen, a GABA antagonist, that does not penetrate the blood–brain barrier, has been described in case series.^{5 9} Because of high invasiveness, varying outcome and induction of deep coma, Baclofen cannot be recommended as a standard therapy of tetanus.¹

Autonomic dysfunction

Since mechanical ventilation and effective control of muscle spasms avoid respiratory failure, cardiac arrest due to the autonomic dysfunction has become the main cause of death.¹⁰ Most authors attribute the autonomic dysfunction to an overactivity of the sympathetic nervous system with elevated serum catecholamine level.¹¹

Treatment of the autonomic dysfunction remains challenging. Although a variety of case reports with different treatment strategies can be found, improvement of mortality is often inconsistent.

Sedation is the primary therapy to reduce sympathetic activity. Benzodiazepines are useful for sedation and muscle relaxation, but have little effect on sympathetic activity.¹² Morphines lower the sympathetic overactivity and stabilise the cardiovascular status.¹²

Epidural blockades with local anaesthetics are reported to lower the sympathetic tonus and stabilise the cardiovascular situation.^{13 14} As continuous infusion may be required the possibility of infectious complications at the catheter site limits the use of epidural blockade.¹⁴

Several studies describe the use of adrenergic blockade to attenuate the effect of the elevated catecholamine levels.

While some authors describe adequate control of tachycardia and hypertension with an α/β -adrenergic blockade¹⁵ several authors associate these agents with acute cardiac failure when sympathetic tone reverses.¹ Edmondson and Flowers report on sudden bradycardia and cardiac arrest of two young and previously fit patients during tracheal suction.¹⁶ These agents cannot be recommended as a standard therapy of autonomic dysfunction because of dangerous unpredictable effects when sympathetic activity suddenly declines.

Clonidine lowers sympathetic activity by stimulating α_2 -adrenergic receptors in the brain stem.¹¹ It also inhibits catecholamine release from the adrenal medulla and norepinephrine release from peripheral prejunctional endings.¹ After the administration of clonidine Sutton *et al* found a decrease in plasma norepinephrine associated with a reduction of cardiovascular instability in a patient with severe tetanus.¹¹ Gregorakos *et al* even demonstrated in a small randomised study a decrease in mortality in cardiovascular unstable patients treated with clonidine compared to patients, who did not receive clonidine.¹⁷ In contrast two case reports describe the failure of clonidine to control blood pressure and lower catecholamine excesses.^{18 19}

Several studies recommend the administration of magnesium sulphate to attenuate catecholamine levels and receptor responsiveness. In vitro studies show a reduction of catecholamine release from both the adrenal medulla and peripheral nerve endings.¹ In patients with pheochromocytoma, magnesium sulphate reduces the release of epinephrine,²⁰ so magnesium sulphate seems an interesting option for reducing the autonomic dysfunction in severe Tetanus caused by elevated catecholamine levels. In a placebo controlled study with 195 patients in total, Thwaites *et al* showed a significant reduction of the requirement of drugs to control muscle spasms and cardiovascular stability in patients with magnesium infusions but no difference in survival and requirement for mechanical ventilation.²¹ James and Manson described an improvement of haemodynamic parameters during infusion of magnesium in 9 subjects with persistent autonomic dysfunction despite heavy sedation.²² Lipman used magnesium sulphate in a case report during a sympathetic crisis. He achieved a stabilisation of cardiovascular function as well as a decrease in catecholamine levels, but also found that magnesium without other sedatives was not effective.²³

However, in our case we could not achieve a satisfying control of the sympathetic overactivity by magnesium sulphate.

Due to the progressive heart failure with episodes of severe hypotension, we did not use clonidine.

This case demonstrates the dismal prognosis of severe tetanus in the older people. Cardiovascular comorbidity complicates the treatment of sympathetic overactivity. In our case, the patient developed a fatal cardiac deterioration that could not be prevented with comprehensive intensive care management.

Because tetanus still has a poor outcome, its prevention by sufficient vaccination is mandatory.

Learning points

- ▶ Tetanus is a clinical diagnosis, because laboratory findings are non-contributory except for negative findings.
- ▶ Today mechanical ventilation and improved control of muscle spasms avoid respiratory failure, so cardiac arrest due to a concomitant autonomic dysfunction has become the main cause of death in tetanus.
- ▶ Insufficient seroprotection is common among the older people in industrial countries.
- ▶ The prevention of tetanus by sufficient vaccination is mandatory since Tetanus has a dismal prognosis among the older people.

Competing interests None.

Patient consent Obtained.

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