Intrathecal baclofen in management of a patient with very severe tetanus

Madhusudan R. Jaju1, M. Goverdhana, Pavan Kumar Reddy N.1, Sirisha Rao Muttavarapu2, V. Chandra Sekhar2, Siddharth Bandla3, Srikanth Ram Mohan2, Shashank Kumar Srivastav1*

1Department of Critical Care Medicine, CARE Hospital, Nampally, Hyderabad, Telangana, India
2Department of Internal Medicine, CARE Hospital, Nampally, Hyderabad, Telangana, India
3Department of Anesthesiology, Critical Care Medicine, CARE Hospital, Nampally, Hyderabad, Telangana, India

Received: 08 February 2017
Revised: 02 May 2017
Accepted: 03 May 2017

*Correspondence:
Dr. Shashank Kumar Srivastav,
E-mail: dr.shashanksrivastava@gmail.com

ABSTRACT

Tetanus is uncommon in developed countries. The majority of tetanus cases occur in third world countries and 50% of these cases occur in neonates. There are more than 800,000 deaths due to tetanus each year in the world. We present a case of 40-year-old male patient diagnosed to have very severe tetanus - Grade IV as per Ablett classification of severity, managed in our hospital with aggressive treatment for 27-days and use of intrathecal baclofen he showed drastic improvement in this status. He was discharged in neurological intact conditions with hemodynamic stability.

Keywords: Autonomic instability, Intrathecal baclofen, Very severe tetanus

INTRODUCTION

Tetanus disease is caused by Clostridium tetani which is an obligate anaerobic gram-positive organism. Its spores are in soil and in the feces of humans and animals. Despite the passive and effective immunisation since 1893 and 1923, tetanus is still significant health problem in the developing world and is encountered in the developed world such as the United States. There are more than 800,000 deaths due to tetanus each year in the world. The incidence of tetanus is between 500,000 to one million cases per year worldwide. The majority of cases of tetanus occur in developing countries, which involve 50% of neonates. The most cases in developed countries happen in older adults.

We present a case of 40-year-old male patient brought to our out-patient department with chief complaints of jaw pain, unable to open mouth, unable to speak properly, difficulty in swallowing and hiccups since two days. He had history of injury to the right sole of the foot with a nail (nail prick) at construction site during the night time 8 days before presentation for which he took tetanus toxoid injection. He was diagnosed to have severe tetanus with continuous deterioration of health. He was managed with extreme medications in Medical ICU for about 27-days there after he was discharged with fair general condition and hemodynamic stability.

CASE REPORT

A 40-year-old male patient advocate by occupation was brought to our out-patient department with chief complaints of jaw pain, unable to open mouth, unable to speak properly, difficulty in swallowing and hiccups since two days. He
hypertension and was on medication since 2-years- tablet metoprolol 25mg once daily and tablet amlodipine 5mg once daily. He underwent open reduction and internal fixation for fracture of tibia 10 years back. He was non-smoker, non-alcoholic and non-vegetarian. On examination he was found to be hemodynamically stable, well-nourished and moderately built. No pallor, oedema, icterus, cyanosis, clubbing and no lymphadenopathy. His systemic examination- CVS, CNS, respiratory and per abdomen to be normal with inability in speaking, chewing and trismus present. He was admitted in the ward.

Day to day events, investigation and management with protocols are mentioned below:

**Day 1**

In the view of inability to speak, chewing and trismus, wound site is clean without pus or cellulitis, no active intervention for the wound.

In night, patient was having persistent hiccups. In view of progression of trismus, persistent hiccups and back rigidity he was shifted to MICU.

**Management**

- Injection human tetanus Ig 3000U i.m. stat
- Injection metronidazole 500mg i.v. 6th hourly.
- Injection pantoprazole 40mg i.v. Once daily
- Tablet amlodipine 5mg p.o once daily
- Tablet diazepam 2mg p/o thrice daily
- Tablet metoprolol 25mg once daily

**Day 2-4**

**Day 2**

Difficulty in opening mouth further progressed, drooling of saliva, elective intubation planned with difficult airway cart ready. Injection diazepam 5mg i.v. given and oral endotracheal intubation was done. According to WHO guidelines patient was kept in an isolation room with minimal light, vocal and tactile stimulations.

**Investigations**

- CPK- 497
- 2D ECHO- Normal

**Management**

- Injection benzyl penicillin 2 Lach IU i.v. 6th hourly
- Injection metronidazole 500 mg i.v. 6th hourly
- Intrathecal tetanus immunoglobulin 1500 units stat
- Sedation with midazolam and dexmedetomidine was started and continued as infusion.
- RT feeding 60 ml/hour.

- i.v. fluid plasmalyte was also continued.

**Day 3**

Patient on ventilator support-40% FiO2. CVS and respiratory system- normal, CNS-sedated, intake/output: 1958/1360.

**Investigations**

TLC: 14,800

**Management**

- Injection crystalline penicillin 2 lakhs IU 6th hourly
- Injection metronidazole 500 mg 6th hourly
- Injection diazepam 10 mg 6th hourly
- Injection fentanyl i.v. infusion
- Injection midazolam i.v. infusion
- IVF plasmalyte 60 ml/hour
- RT Feed 100 ml/hour

**Day 5-8**

**Day 5**


Percutaneous tracheostomy was done in view of prolonged need of ventilation. Patient had one episode of GTCS. Neurology opinion was taken and patient was started on injection levipil 1gm stat followed by 500 mg twice daily. Patient had autonomic instability with HR ranging between 100 to 180 and BP fluctuations even though on continuous vasopressor support.

**Management**

- Injection crystalline penicillin 2 Lacs IU 6th hourly
- Injection metronidazole 500 mg 6th hourly
- Injection diazepam 10 mg 6th hourly
- Injection MgSO4 i.v. infusion
- Injection atracurium i.v. infusion
- Injection midazolam i.v. infusion
- Injection fentanyl i.v. infusion
- Injection pantoprazole 40mg OD
- IVF RL/plasmalyte
- Injection nootropil 3gms TID
- Injection levipil 500mg BD

**Day 6**

2nd day after tracheostomy. Patient in Septic Shock due to ventilator acquired pneumonia, BP-110/70 on vasopressor support, SpO2-96% on FiO2 40%. Patient under sedation with intake/output=3384/2055. Patient
was having persistent fever; continuous cold sponging was given. Blood culture were sent. Injection vancomycin 1gm IV BD started.

Management
- Injection piperacillin tazobactam 4.5 gms i.v. TID
- Injection vancomycin 1 gm i.v. BD
- Injection metronidazole 500 mg 6th Hourly
- Injection pantoprazole 40 mg OD
- Injection nootropil 3 gms TID
- Injection levipil 500 mg BD
- Injection heparin 5000U S/C thrice daily
- Injection MgSO4 i.v. infusion
- Injection atracurium i.v. infusion
- Injection midazolam i.v. infusion
- Injection fentanyl i.v. infusion
- Injection noradrenaline and injection vasopressin

Day 8

Patient under midazolam sedation plus atracurium-paralysis for convulsive spasms. He had convulsive spasms frequently in spite of midazolam and atracurium. Febrile spikes were present. He was on noradrenaline support, PCV mode SpO2 96% on FiO2 30%. Systemic examination respiratory system- bilateral basal crepts positive right>left and rest other systemic examination was normal. Was continued on RT feed. Urine output- good amount and dark colored urine. Liver and renal functions- normal. Increased CPK. X-ray chest- right lower lobe consolidation. Mini BAL- klebsiella sensitive to piptaz.

Investigations

Hb: 11

Overall assess till day 8
- Severe tetanus with autonomic instability
- Tracheostomy with post CPR status
- Ventilator acquired pneumonia
- Neurostatus unclear because of continuous sedation and paralysis to control spasms
- Planned for intrathecal baclofen injection incremental doses as day 1-50 mcg, day 2-75 mcg, day 3-100 mcg
- If positive response then intrathecal infusion to be started

Day 9-12

Day 9

Hemodynamic fluctuations still present. Intake/output-1379/1530. On trying to withhold midazolam and atracurium convulsive spasms present. Injection meropenem started in view of the blood cultures- Klebsiella positive.

PLT: 8000

Management
- Injection baclofen 50mcg (0.1ml) intrathecal stat by Barbotage method.
- Inj meropenem 2 gm i.v. Stat- 1gm i.v. TID
- Inj metronidazole 500 mg 6th hourly
- Inj pantoprazole 40mg OD
- Tab nootropil 3gms TID
- Tab levipil 500mg BD
- Inj heparin 5000U s/c thrice daily
- Inj MgSO4 i.v. infusion
- Inj atracurium i.v. Infusion
- Inj midazolam i.v. Infusion
- Inj fentanyl i.v. Infusion
- Inj Potassium Phosphate i.v. infusion
- Tab Tolperisone 150 mg BD

Day 12

No spasms. Patient hemodynamically stable with input/output of 1490/1180.

Investigations

Hb: 10.5

Management

Inj baclofen intra thecal i.v/ infusion 50mcg/hour.

Day 13-17

Day 13

Patient with no spasms after intrathecal baclofen, hemodynamically stable. On CNS examination pupils-NS, RL responding to DPS, intermittent spontaneous eye-opening present. Input/output: 1490/1185. SpO2-96% on 30% FiO2 on intermittent PS/CPAP.

Investigations

TLC: 13100

Management
- Inj Baclofen intra thecal i.v. infusion 50mcg/hour.
- Rest same treatment.

Day 15

MRI with no hypoxic damage. CNS- spontaneous movement of UL++, convulsive spasms + when
intrathecal baclofen decreased. Febrile spikes present with of temperature-101°F.

Investigations

Hb: 8.3

Management

- Inj baclofen Intra thecal Infusion 100 mcg/hour (0.2 ml/hour)
- Rest same treatment

Day 17

Patient responding to verbal commands. Fever +, antibiotics changed to Inj Polymyxin B in view of VAP -- pneumonic patch at left lower lung.

Management

- Tab risperidone was started as patient was restless.
- Inj baclofen Intra thecal Infusion 100 mcg/min (0.2 ml/hour)
- Inj polymyxin B 7.5Lacs U IV BD
- Inj meropenem 1 gm IV TID
- Inj clexane 60 mg S/C OD
- Tab levipil 500 mg BD
- Tab nootropil 1600 mg TID
- Tab sodium acid phosphate 2 sachet TID
- Powder soya milk and kabipro
- Midaz, dexim i.v. infusion

Day 18-21

Day 18 and 19

Investigations

- HB-8.5
- CT SCAN CHEST- Ground glassing with air bronchogram- consolidation patches in Right upper lobe, middle lobes and bilateral lower lobes.

Management

- Inj Baclofen 100 mcg/hour intrathecal infusion.
- Inj Polymyxin B 7.5 Lac U i.v. BD
- Inj Minocycline 200 mg stat-100 mg i.v. BD
- Inj Enoxaparin 60 mg SC BD
- Tab Risperidone BD
- Syp Orofer XT 10 ml TID
- Inj Dexim and Inj Midaz i.v. infusion

Day 20 and 21

X-RAY chest showed increasing infiltrates left lung. Antibiotic added. Mini BAL- Acinetobacter sensitive to colistin and tigecycline. Colistin Nebulization started 1MU BD for 3 days. Bronchoscopy done- citrobacter growth. CNS- No FND, moving all 4 limbs.

Investigations

- HB-8.5
- CT scan chest- Ground glassing with air bronchogram- consolidation patches in Right upper lobe, middle lobes and bilateral lower lobes.

Management

- Inj Baclofen 100 mcg/hour intrathecal infusion.
- Inj Polymyxin B 7.5 Lac U i.v. BD
- Inj Minocycline 200 mg stat-100 mg i.v. BD
- Inj Enoxaparin 60 mg SC BD
- Tab Risperidone BD
- Syp Orofer XT 10 ml TID
- Inj Dexim and Inj Midaz i.v. infusion

Day 22-27

Day 22 and 23

Patient had severe cough and increased secretions. Chest Physiotherapy and Nebulization started. Patient Hemodynamically stable. On 20th Tracheostomy tube changed because of increased secretions and hypercarbia. Intrathecal baclofen stopped.

Management

- Inj Polymyxin B 7.5 Lac U i.v. BD
- Inj Minocycline 100mg i.v. BD
- Inj Doripenem 1 gm i.v. stat-500 mg i.v. TID infusion
- Nebulization with colistin 1 MU BD.
- Inj Enoxaparin 60 mg SC BD
- Tab Metoprolol XL 12.5 mg BD
- Tab Risperidone BD
- SypOrofer XT 10 ml TID

Day 25 to 27

Bed sore on gluteal region. Shifted out of MICU. X-ray chest- resolving pneumonia. CNS- moving all 4 limbs.

Investigations

Hb: 8.7

Management

- Inj Polymyxin B 7.5 Lac U i.v. BD
- Inj Minocycline 100mg i.v. BD
- Inj Doripenem 1 gm i.v. Stat-500 mg i.v. TID Infusion
- Inj Enoxaparin 60 mg SC BD
- Tab Risperidone BD
- Syp Orofer XT 10 ml TID

Discharged on the 27th day. Counseled about post discharge care. After one week in the follow up, he has been de-cannulated.

**Figure 1:** Showing the patient in isolated MICU dark room.

**Figure 2:** Showing patient getting stabilised by day 17.

**Figure 3:** Showing patient getting stabilised and discharged out of hospital on Day 27.

**DISCUSSION**

Tetanus is diagnosed by history and clinical signs. There are no laboratory tests for this disease. The first sign of tetanus is spasm. The muscle of jaw, neck, back and abdomen may be involved. The clinical features are related to the toxin named Tetanospasmin. Types of tetanus disease are variable. Those are generalised, Local, Cephalic and Neonatal tetanus. The manifestations of generalised tetanus include pain, stiffness, rigidity, opisthotonus, spasm which can lead to laryngeal obstruction. The spasms are painful and may be result in respiratory arrest and death. The local tetanus having low mortality. Cephalic type is an uncommon form that damages the cranial nerves. Neonatal tetanus occurs in the newborn around the first week of life.2 Our case’s chief complaint was pain and stiffness in face and back muscles. He had spasms in his jaw muscles due to which he was not able to open his mouth. Also, there was spasm in lumbar muscles occasionally.

The most cases of tetanus are as acute injury. There is non-acute injury in i.v. drug users, persons with chronic wounds and complications of diabetes.4 Treatment is neutralisation of tetanospasmin and care for muscle spasms. Human tetanus immunoglobulin (HTIG) neutralise circulating tetanospasmin. The effective dose is 500 IU IM (International Unit Intra Muscular).5

To prevent production of toxin, antibiotics are recommended. Penicillin is the standard therapy for tetanus in most countries. Its dose is 100,000-200,000 IU/kg/day intramuscularly or intravenously for 7 to 10 days. Penicillin acts as a competitive antagonist to Gamma aminobutyric acid (GABA). Metronidazole is a safe alternative drug. The dose is 400 mg rectally every 6 hours. If these were unavailable, erythromycin, and clindamycin would be alternatives.6,7

Our patient was admitted with chief complaints of jaw pain, unable to open mouth, unable to speak properly, difficulty in swallowing and hiccups since two days. He had history of injury to the right sole of the foot with a nail (nail prick) at construction site during the night time 8 days back for which he took Tetanus Toxoid injection. There were no complaints of fever, shortness of breath, etc.

In the view of inability to speak, chewing and trismus. The wound site is clean without pus or cellulitis, no active intervention for the wound. In night of admission, patient was having persistent hiccups. In view of progression of trismus, persistent hiccup and back rigidity he was shifted to MICU. He was started with medication of Inj. Human Tetanus Ig 3000U IM stat dose. Later, Intrathecal Tetanus immunoglobulin 1500 units Stat was added. Tracheostomy was done on day 5. Day 7, he had convulsive spasms on withdrawal of Midazolam.

The day 8 assessment- severe tetanus with autonomic instability.

- Tracheotomy on ventilator support.
• Cardiac arrest from autonomic instability. Post CPR status with hypothermia.
• Ventilator acquired pneumonia.
• Neurostatus unclear because of continuous sedation and paralysis to control spasms.
• Planned for Intrathecal Baclofen injection incremental doses. Day 1- 50 mcg, Day 2-75 mcg, Day 3-100 mcg.
• If positive response then intrathecal infusion to be started.

Day 11, after starting baclofen patient showed response with no further convulsive spasms, patient hemodynamically stable. Resolving pneumonia.

Day 17, Patient responding to verbal commands, moving all four limbs, intermittently on thermovent with O₂ inhalation. Mobilised on a chair.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. D. N. Kumar, Medical Director, CARE Hospital, Nampally. Dr. Venkat Raman Kola, Director, CARE Hospital, Banjara Hills. Dr. Bhavani Prasad, Director, CARE Hospital, Hi-Tech City. All the Doctors who directly or Indirectly helped them for recovery of patient. CARE Nursing Staff and Medical ICU Staff.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES