A case of lockjaw in the emergency department

Giulia Marullo,[1] Giulia Maria Bottani,[1] Rossella Guerrieri,[2] Adriano Basile,[2] Paolo Aseni,[2] Andrea Bellone[2]

[1]Emergency Department, Bicocca University of Milan; [2]Emergency Department, Niguarda Hospital, Milan, Italy

Abstract

Tetanus with cephalic involvement is not a typical presentation of the disease; characteristic signs and symptoms are strictly localized in cranial district, although it could frequently progress to the classical generalized form. Tetanus is still spread worldwide, especially in particular subgroups as elderly and newborn babies and in countries with an inadequate vaccine coverage. We report a case of an adult man with generalized tetanus with cephalic presentation in Emergency Department. We aim to outline how difficult it was to diagnose in an adult patient without apparent exposition of previous minimal trauma or injury because of a lot of confusing factors and slow progressing clinical signs. Prompt recognition of signs and symptoms, opportune target therapy and supportive care, in association with correct vaccination schedule, are paramount to determine the prognosis for affected patients.

Case Report

A 58-year-old man presented himself to our Emergency Department reporting progressive speech impairment caused by bilateral pterygoid and masseter muscles contraction since about one week, accompanied by dysphagia with some episodes of fluids and saliva inhalation.

He had no history of smoking or chronic disease or medications. He worked as a Forest Ranger and practiced jogging regularly. He was affected by chronic sinusitis so he performed a surgical intervention of Functional Endoscopy Sinus Surgery about one month before (33 days before). His last tetanus boosting dose was 13 years before but he had no recent history of wounds or animal bites.

On physical examination vital signs were normal, the patient was afebrile and revealed a strong and painful contracture of masseterine, pterygoids and platysma muscles bilaterally allowing a maximum mouth opening of about 1 cm. He had sialorrhea but his cough reflex was preserved. Any attempt to drink water elicited spasms and a choking sensation. There wasn't any evidence of local infection or cutaneous wounds and blood exams were in the normal range (Table 1). The neurologic examination did not reveal any focal features, sensory changes or abnormalities in coordination.

Differential diagnosis

The differential diagnosis in a case of isolated lockjaw and difficulty swallowing is a challenging trial to face for the Emergency Physician.

Since symptoms were strictly localized in the cranial district, with a history of a recent procedure in the same area involving implantation of a surgical prosthesis, we initially suspected a surgical complication (infective or nervous and muscular impairment). As a consequence we asked for a Ear Nose and Throat consult in the Emergency Department. At the specialist's evaluation there were no signs of infection of oral mucosa or teeth, no lesions or pain on the site of intervention, no bleeding or wounds in the oral cavity, no abscess in the cervical or facial area; so probabilities of a surgical complication seemed to diminish.

Moreover, the absence of malocclusion or joint clicking on examination ruled out the hypothesis of a temporomandibular joint dysfunction causing the symptoms.[1]

Hypocalcemic tetany could be quickly ruled out by detection of normal serum levels of total and ionized calcium.[1]

Among other conditions associated with muscle spasms, there are also Malignant Neuroleptic Syndrome, Serotonin Syndrome, Dystonic reactions and Stiff-Man Syndrome, but none of these seemed likely because the patient's history was negative for taking of medications and the overall clinical presentation didn't suggest any of these diseases.[1,2]

Some features of this case could remind of Rabies presentation, such as excess salivation and spasms triggered by attempts to drink water, which could be interpreted as hydrophobia. However, a history of animal bite was lacking and the integrity of neurological status was not consistent with rabies encephalitis.[3-5]

The remaining most likely hypothesis was tetanus, in which sensorium is unimpaired while trismus and spasms of deglutition muscles may result in difficulty with swallowing and verbal expression. However, a history of infection was lacking and the subacute onset of the symptoms wasn't typical for the disease. In this case, the localization of symptoms in the cranial district could depend either on a subacute form of cephalic presentation or, even more uncommon, on a localized form of post-surgical

Correspondence: Giulia Marullo, Emergency Department, Bicocca University of Milan, ASST Grande Ospedale Metropolitano Niguarda, Piazza Ospedale Maggiore 3, 20161, Milano.
Tel.: +39.02.64447433.
E-mail: giulia.marullo@gmail.com

Key words: Lockjaw; Tetanus; Emergency department.

Contributions: the authors contributed equally.

Conflict of interest: the authors declare no potential conflict of interest.

Funding: none.

Received for publication: 10 March 2018.
Revision received: 25 June 2018.
Accepted for publication: 29 June 2018.

Emergency Care Journal 2018; 14:7410
doi:10.4081/ecj.2018.7410

tetanus. The latter is linked to an exogenous contamination of spores in the site of surgery (favoured by necrotizing tissues or presence of foreign bodies such as prosthesis) or to an endogenous transmission by the use of contaminated equipment. Moreover, post surgical tetanus develops quickly, usually within 24 hours.[3,6]

Perfectly mimicking tetanus, strychnine poisoning could be another possible causative agent of muscle spasms and trismus in the absence of alteration of mental status but this condition is characterized by an acute onset, a generalized spread of the spasms and a rapid, often fatal course of the disease if not treated.[1]

Clinical course

During some hours of observation in the Emergency Department the patient remained symptomatic for painful contractions of facial muscles and strong lockjaw.

Even if an early expert opinion from an Infectious Diseases clinician couldn't rule out or confirm our main suspicion of tetanus, we finally agreed upon a broad spectrum strategy, to protect the patient from common infective agents and tetanus risk. A dose of 500 UI Human Tetanus Immunoglobulin (HTIG) was given intramuscularly along with a single dose of tetanus vaccine with tetanus toxoid. We started an antibiotic coverage with metronidazole 500 mg tid and ampicillin 3 g qid. An early inten-

Table 1. Test results in the emergency department.

Laboratory data at presentation		
Variables	Patient	Reference Range
Hematocrit (%)	40.6	42.0 - 52.0
Hemoglobin (g/dl)	13.5	14.0 - 18.0
Mean corpuscular volume (fl)	95.3	82.0 - 97.0
White-cell count (per mm3)	10930	4.00 - 10.00
Platelet count (per mm3)	256000	140 - 440
C-reactive protein (mg/dl)	0.1	0.0 - 0.5
Sodium (mmol/liter)	142	132 - 143
Potassium (mmol/liter)	3.99	3.40 - 5.20
Calcium (mg/dl)	9.3	8.50 - 10.50
Urea nitrogen (mg/dl)	52	18 - 48
Creatinine (mg/dl)	0.82	0.70 - 1.20
Glucose (mg/dl)	93	70 - 100
Total Bilirubin	1.22	0.25 - 1.00
Alanine aminotransferase (U/liter)	18	3 - 45
Creatine phosphokinase (U/liter)	152	30 - 200
Protrombin Time – INR (ratio)	1.04	0.86 - 1.13
Activated partial-thromboplastin time (sec)	27.7	24.0 - 38.0
Further test results in the ED		
Electrocardiogram	Sinus rhythm, HR 66, normal findings	
Chest X-ray	Normal findings	
Head CT scan	Normal findings	
Maxillofacial CT scan	Outcomes of Functional Endoscopy Sinus Surgery with maxillary antrostomy, normality of the facial soft tissues	

Table 2. Differential diagnosis of tetanus.

Differential Diagnosis of Tetanus		
Disease	Features	Diagnosis
Strychnine poisoning	Acts as a glycine inhibitor causing tetanic seizures, overpowering of the extensor muscles, hyperthermia. Rapid onset, course of 1-3 days leading to autolimitation or death	Hystory, Clinical; Strychnine detection on urine or gastric content
Dystonic reaction	Extrapyramidal Symptoms such as akathisia, parkinsonism or tardive dyskinesia	History, Clinical
Hypocalcemic tetany	Muscle spasms, flushing, positive Chvostek and Trousseau sign	Clinical; Low serum calcium levels
Malignant neuroleptic syndrome	Hyperthermia, rigidity, altered consciousness, and autonomic dysfunction	History of antipsychotic drugs use (onset 45mins to 2 months after 1st dose, average 7 days); Clinical
Serotonin syndrome	Altered mental status, autonomic instability, neuromuscular hyperactivity with clonus	History of serotonergic agent taken within past 5 weeks; Clinical
Stiff man syndrome	Autoimmune disorder of the CNS (Ab anti - glutamic acid dehydrogenase, Ab anti -glycine, Ab anti – amphiphysin) characterized by increased muscle activity due to decreased inhibition of the CNS, with progressive rigidity and muscle spasms beginning with axial muscles and progressing to limbs	Clinical, positive serology for antibodies, electromyography
Ludwig's Angina	Infection of the submental, sublingual, and submandibular Spaces, possibly complicating a superficial odontogenic abscess. Findings are poor dental hygiene, dysphagia and odynophagia, trismus and edema of the entire upper neck and floor of mouth. Airway compromise	Clinical, laboratory, Imaging (CT scan)
Meningeal irritation (Meningitis, subarachnoid hemorrhage)	Nucal rigidity, fever, altered sensorium, photophobia, neurologic deficits	Clinical, Neuroimaging (CT/RMN), Lumbar puncture, Laboratory
Rabies	Viral encephalitis caused by Rhabdovirus. Transmission by bite or contact with fluids belonging to dogs, foxes or bats. Symptoms include fever, itching in the inoculation area, hyperexcitability and muscle spasms, agitation, hydrophobia, neurologic deficits. Nearly always fatal.	Clinical, History, RT-PCR in saliva and biopsy samples, Immunohistochemistry, Direct fluorescent antibody test on biopsy samples.
Temporomandibular joint disease	Pain and limitation in the range of motion of the mandible, rigidity of the muscles of mastication, temporomandibular joint clicking	Clinical, Imaging (X-ray, CT scan)

sivist evaluation suggested starting with intravenous benzodiazepines and baclofen.

The patient was admitted to Emergency Medicine Unit for a strict hemodynamic and respiratory observation. The results of plasmatic tetanus immunoglobulin levels revealed to be insufficient for an appropriate tetanus coverage (IgG: 0,01 UI/mL). Electromyography (EMG) was performed and showed a bilateral absence of physiologic answers (Sp1 and Sp2) of masseterine inhibitory reflex. This exam consists of an electric stimulation during massive masseterine contraction; Sp1 is a silent inhibitory period that lasts about 10-15 seconds, Sp2 is the following inhibitory one of 40-50 seconds. This neurophysiological result suggested cephalic tetanus.[7]

In the meantime, on the second day from admission, we observed a rapid worsening of lockjaw and sialorrhea a progression of muscular contractions with the involvement of thoracic muscles, a consequent onset of respiratory distress, hypoxic-hypercapnic acute respiratory failure and respiratory acidosis.

At this stage, the clinical course along with laboratory and neurophysiological findings were all consistent with a diagnosis of generalized tetanus with a cephalic onset.

Hence, a second dose of 5500 UI intravenous HTIG was administered, reaching a total of 6000 UI.

A maxillofacial surgeon's evaluation excluded any possibility for surgical debridement in the absence of even minimal wound infection.

Hence, our patient underwent curarization and oro-tracheal intubation and was transferred to Intensive Care Unit (ICU), where he was treated with mechanical ventilation for 17 days. Antibiotic therapy was continued. After a few days, a tracheostomy was performed, and the man underwent progressive respiratory weaning until reaching of complete normal breathing pattern. In that period enteral nutrition by nose-gastric tube was started; benzodiazepines and baclofen therapy was continued with a progressive and gradual dosage reduction according to patient improvement.

Table 3. Treatment.

Therapy	Dose	Route of administration	Start	End
Specific therapy				
HTIG	500 UI	IM	26/06/2017	-
	5500 UI	IV	27/06/2017	-
Metronidazol	500 mg qid	IV	26/06/2017	05/07/2017
Ampicillin	3 g qid	IV	26/06/2017	05/07/2017
OTI Induction				
Propofol 1%	100 mg	IV	28/06/2017	-
Atropin	0,3 mg	IV	28/06/2017	-
Fentanyl	100 mcg	IV	28/06/2017	-
Cisatracurium	20 mg	IV	28/06/2017	-
Sedation and Muscles Relaxants				
Propofol 2%	600 mg/die ic	IV	28/06/2017	09/07/2017
	200 mg/die	IV	10/07/2017	11/07/2017
Midazolam 5 mg/50 mL	4.2 mL/h ic	IV	28/06/2017	11/07/2017
Diazepam 5mg/mL	5 gtt + 10 gtt	OS	26/06/2017	28/06/2017
	5 gtt + 20 gtt	SNG/OS	12/07/2017	03/08/2017
Clonazepam	2,5 mg tid	SNG	10/07/2017	14/07/2017
MgSO4 5 mg/NaCL 50 mL	2,1 mL/h ic	IV	28/06/2017	17/07/2017
Baclofen	10 mg tid	SNG	08/07/2017	10/07/2017
	20 mg tid	SNG	10/07/2017	17/07/2017
	10 mg tid	OS	17/07/2017	20/07/2017
	5 mg tid	OS	20/07/2017	03/08/2017
Supportive Therapy				
Nadroparin calcium	0,6 mL qd	SC	28/06/2017	17/07/2017
Morphine	10 mg tid	SNG	28/06/2017	04/07/2017
	10 mg bid	SNG/OS	05/07/2017	13/07/2017
Reidratante III	80 mL/h	IV	28/06/2017	13/07/2017
Nutrison Standard Fibre	2000 mL/die	SNG	28/06/2017	13/07/2017

After seven days in ICU, the clinical course was complicated by MSSA nosocomial pneumonia, treated with levofloxacin and amoxicillin/clavulanate with a good response. The patient started physical rehabilitation of swallowing, oral and full motor movements with intensive muscular physiotherapy obtaining an excellent global recovery in two months. We then performed a second dose of vaccine with tetanus toxoid. Two months later, a second EMG was performed showing a weak silent masseterine time after mandibular nerve stimulation (Sp1 inhibitory reflex), while a Sp2 answer absence. The patient returned home after two months of stay in good general conditions; our final diagnosis was general tetanus with cephalic onset (Table 2).

Tetanus: clinical outline of the disease

Tetanus is a toxin-mediated disease produced by the bacterium *Clostridium tetani* characterized by generalized rigidity and muscle spasms that may cause respiratory arrest and death. It is characterized by various forms and presentations, even though it would be entirely preventable by a specific vaccine.[3,8] Nowadays it is still spread worldwide, especially in South East Asian and African countries, reaching a maximum in regions as Nigeria and India, where population's vaccine coverage is still inadequate. However, cases are diminishing in these regions as well. Incidence in Europe and USA is 0.01/100.000 inhabitants,[9,10] mostly in the elderly. With increasing age, the human immune system undergoes immunosenescence, which leads to insufficient protection following vaccination; response to tetanus vaccination in the elderly was evaluated in a study on people over 60 years old demonstrating that single shot vaccinations did not lead to long-lasting immunity.[11-13] The higher incidence of tetanus in the elderly seems to be mainly due to the lack of tetanus toxoid boosting doses. There is little literature about this topic; an Italian study showed a progressive rise in uncovered population in elderly, reaching about 80% in people ove 80 years old. Incidence was higher in females; the most probable explanation for this phenomenon is that males are usually vaccinated during the military service and/or receive booster vaccination after injury more frequently. Similar results are showed in a European study; available data, for a few number of countries, demonstrates an insufficient seroprotection in oldest groups.

The causative agent of tetanus is *Clostridium tetani*, a Gram-positive anaerobic bacillus. It is a common host of the gastrointestinal tract of many animals (like sheep, horse, cow, cat) and in the soil in the form of spores. It represents a continuous threat especially for more vulnerable subgroups, like elderly or newborns. Around the world, there are many cases of neonatal tetanus for delivery from non-immune mothers, umbilical cord's cut and perinatal care in non-sterile conditions.[3,14]

Transmission is from continuous cutaneous solution, there is not an inter-human transmission. Infection is strictly localized in entrance site as a wound, burned tissue or umbilical cord. Source is not always identifiable, with rates of cryptogenic tetanus as high as 23%.[3] Anaerobic conditions allow spore germination with production of tetanic toxins as tetanospasmin. Toxin's targets are central inhibitory interneurons, glycinergic and GABAergic: the interruption of release of these neurotransmitters determines an uncontrolled activity of motoneurons (alpha and gamma) and autonomic nerves. It follows muscular spasms, hypertonic muscle activity and disregulation of the autonomic system.[3,14]

Clinical presentation can be generalized, neonatal and localized cephalic form with an incubation period in adults is 3-21 days, median 8 days. A progression of respiratory failure and hemodynamic instability is frequently observed.[1,3,8]

Diagnosis relies on clinical diagnosis. Determination of plas-

ma Immunoglobulin levels (IgG) is useful for defining vaccine status and possible susceptibility to disease; generally, a plasmatic concentration above 0,1 UI/mL is considered to be protective.[3] Microbiological culture is insensitive and unspecific with positivity in about 30% of cases.[3,8] The EMG can be helpful to support clinical diagnosis.[7]

Standard therapy requires Intravenous 6000UI HTIG, or a first intramuscular 500 UI HTIG dose near the site of infection and an intravenous 5500 UI one. However, according to some authors, a dose of 500 units IM appears as effective as larger doses;[15,16] literature is still debated. Antibiotic coverage is usually recommended. Supportive care with antispastic agents (benzodiazepines and baclofen), magnesium sulfate, adequate airway management by orotracheal intubation and mechanical ventilation, neuro-muscular blocking drugs, and hemodynamic support are often required. Early wound debridement is recommended after prophylactic HTIG administration, in order not to diffuse a bigger amount of circulating toxin. Appropriate tetanus prophylaxis should be administered as soon as possible following tetanus-prone wounds injury with HTIG 250 UI IM. However, a dose of HTIG 500 UI should be given also to late presenting patients and to penetrating trauma victims because incubation period is quite variable. For patients who have been previously vaccinated against tetanus but are not up to date there is little benefit in administering human tetanus immune globulin more than one week after the injury. However, for patients thought to be completely unvaccinated, human tetanus immune globulin should be given up to 21 days following the injury and tetanus toxoid should be given to such patients. All affected patients should receive a complete immunization cycle, regardless of previous immunization history. The amount of pathogenetic toxin during the disease is not sufficient to elicit a long lasting immune response.[3,8]

A detailed table (dose, route of administration, length of therapy) with therapy (immunization, benzodiazepines/ Propofol/baclofen, Magnesium infusion, Vecuronium/cisatracurium/pancuronium) it would be helpful (Table 3).

Prognosis: We couldn't find reliable data about mortality rates. This could be due to tetanus's rapid onset and highly lethal consequences, justifying the absence of randomized controlled trials ethically unacceptable and observational studies in a patients with or without symptomatic and specific therapy.

Conclusions

Treating patients with tetanus is a rare event in industrialized countries and awareness is needed to recognize early signs of this serious disease. Our patient's case was unusual because he had a history of previous immunization and at presentation he had vague symptoms and no defined portal of entry. However, his levels of tetanus antibodies were undetectable. This finding reflects the particular risk for tetanus in adult patients who could have been vaccinated many years before and outlines the importance of renewing adequate tetanus immunization to the whole population. We hypothesize that the subacute course of the disease in our patient could be partly justified by the previous immunization. Tetanus can present with unusual clinical forms and therefore, this diagnosis should be taken into consideration in the Emergency Department even in poorly symptomatic patients and in acute dysphagia. Management should be focused on early administration of tetanus immunoglobulin (500 UI IM as initial dose), early wound debridement and supportive care. All affected patients should receive a complete immunization cycle, regardless of previous immunization history.

References

1. Tintinalli J. Tintinalli's Emergency Medicine. 8th ed. New York, NY: McGraw-Hill; 2015.
2. Bhatti AB, Gazali ZA. Recent advances and review on treatment of stiff person syndrome in adults and pediatric patients. Cureus 2015;7:e427.
3. Mandell G, Bennett J, Dolin R. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. London, UK: Churchill Livingstone; 2009.
4. Greer DM. Case 1-2013: A 63-year-old man with paresthesias and difficulty swallowing. NEJM 2013;36:172-80.
5. Centers for Disease Control and Prevention. Rabies. Available from: https://www.cdc.gov/rabies/index.html
6. Dhalia S. Post surgical tetanus. Canad J Surg 2004;47:375-9.
7. Neumann B. Misleading bilateral blink reflex loss in a severe tetanus case. Clin Case Rep 2017;5:85-8.
8. Centers for Disease Control and Prevention. Tetanus disease (Clostridium Tetani infection). Available from: www.cdc.gov.
9. World Health Organization. Tetanus vaccines: WHO position paper - February 2017. Weekly epidemiological record 2017;92:53-76.
10. Filia A. Tetanus in Italy 2001-2010: a continuing threat in older adults. Lancet 2014;32:639-44.
11. Weinberger B. Biology of Immune response to vaccines in elderly persons. Vaccines 2008;46:1078-84.
12. Weinberger B. Adult vaccination against tetanus and diphtheria: the European perspective. Clin Exp Immunol 2016:187:93-9.
13. Weinberger B, Schirmer M, Matteucci Gothe R, et al. Recall responses to tetanus and diphtheria vaccination are frequently insufficient in elderly persons. PLoS One 2013;8.e82967.
14. Cook T, Protheroe RT, Handel JM. Tetanus: a review of the literature. Br J Anaesth 2001:87:477-87.
15. Blake PA. Serologic therapy of tetanus in the United States. JAMA 1976:235:42-4.
16. Bleck TP. Intravenous immune globulin for passive tetanus prophylaxis. J Infect Dis 1993:167:498-9.