

Tetanus and Occam's Razor: Almost Forgotten but Not Gone: A Case Report

Stephanie O. Skuby, MD,^{a,b} Eunice Rhee, MD,^c Elizabeth H. Thilo, MD,^{a,b} Eric A.F. Simões, MB, BS, DCH, MD^{a,d,e}

Tetanus is a rare disease in industrialized countries, largely due to the highly protective effect of immunization. We present a case of tetanus in a formerly preterm infant with myelomeningocele repaired in utero, who presented at 44 days of age with poor feeding, lethargy, and increased tone. His symptoms progressed despite a course of antibiotics for presumed meningitis. At 73 days of age (on 29th day of hospitalization), a clinical diagnosis of tetanus was made based on the presence of risus sardonicus, trismus, and generalized hypertonicity. Consequently, tetanus immune globulin, muscle relaxants, and metronidazole were administered. Five months later, the infant has had complete resolution of the hypertonicity, has regained normal jaw movement and swallowing, and is regaining oral feeding skills. This case involved a delay in diagnosis despite clinical symptoms and signs classic, in retrospect, for tetanus, highlighting the importance of recognizing the constellation of symptoms that should lead us to consider this rare diagnosis.

Tetanus is a disease resulting from a specific toxin produced at a site of injury by the anaerobic, spore-forming organism, *Clostridium tetani*, which is found in soil and feces. The diagnosis is based on clinical signs and symptoms, as there is no routine confirmatory laboratory test.¹ Historically, tetanus has been a major cause of death worldwide, largely due to inadequate vaccination and poor wound prophylaxis. Between 1947 and 2008, reported tetanus cases and deaths in the United States declined by >95%, and 99%, respectively.² The near-elimination of neonatal tetanus due to improved childbirth practices, and heightened maternal immunity following universal vaccination, have been implicated in this decline. Only 9 cases of tetanus were reported between 1995 and 2014 in children <5 years of age in the United States (Amanda Faulkner, MPH, Centers for Disease Control and Prevention, personal communication, November

23, 2015), making it likely that most pediatricians, including pediatric infectious disease specialists, have never seen a case. Therefore, diagnosis can be delayed or missed, affecting the timeliness of treatment and the prognosis.

CASE PRESENTATION

Our patient was a 44-day-old boy admitted to the NICU for lethargy, poor feeding, and increased tone (Table 1). He was born at 32 weeks' gestational age (wGA), after 3 days of membrane rupture. The pregnancy was complicated by a fetal diagnosis of myelomeningocele with a Chiari II malformation. The myelomeningocele was repaired in utero at 25 wGA, which partially alleviated cerebellar herniation. His neonatal course was uneventful except for a 48-hour course of antibiotics for a leaking myelomeningocele patch and stable ventriculomegaly. He was discharged

abstract



^aDepartment of Pediatrics, Children's Hospital Colorado, Aurora, Colorado; ^bSections of Neonatology, and ^cInfectious Diseases, Department of Pediatrics, University of Colorado School of Medicine, Aurora, Colorado; ^dDivision of Neonatology, Kaiser Permanente, Los Angeles Medical Center, Los Angeles, California; and ^eDepartment of Epidemiology, Center for Global Health, Colorado School of Public Health, Aurora, Colorado.

Dr Skuby cared for the infant as neonatology fellow, and drafted the initial manuscript; Drs Thilo and Rhee cared for the infant as neonatology attending physicians; Dr Simões contributed his infectious disease expertise toward the care of the infant, and wrote the cover letter; and all authors reviewed and revised the manuscript, and approved the final manuscript as submitted.

DOI: 10.1542/peds.2016-0298

Accepted for publication Jul 26, 2016

Address correspondence to Stephanie Skuby, MD, Fellow, Neonatology, Mail Stop 8402, 13121 E. 17th Ave, Aurora, CO 80045. E-mail: stephanie.skuby@gmail.com

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2016 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Skuby SO, Rhee E, Thilo EH, et al. Tetanus and Occam's Razor: Almost Forgotten but Not Gone: A Case Report. *Pediatrics*. 2016;138(5):e20160298

TABLE 1 Timeline of Important Events in This Case

Date	Event Detail
2/18/15	In utero repair of myelomeningocele.
4/12/15	Birth at 32 wGA following preterm premature membrane rupture.
5/3/15	Infant discharged from the hospital with <ul style="list-style-type: none"> • Full oral feedings. • 6-h interval urinary catheterizations. • Chiari II malformation with ventriculomegaly and bulging fontanelle
5/26/15	Infant readmitted with 1-d history of poor feeding, lethargy, increased tone. <ul style="list-style-type: none"> • Intubated secondary to apnea. • Blood and urine cultures obtained. • Vancomycin and cefotaxime therapy started. • MRI: new bilateral thin subdural fluid collections, unchanged hydrocephalus, and chronic hindbrain herniation (Chiari II). • Phenobarbital load administered due to seizure concern.
5/27/15	Subdural tap performed by Neurosurgery. <ul style="list-style-type: none"> • 87 white blood cells/mm³; 8000 red blood cells/mm³; 3438 mg/dL protein; 96 mg/dL glucose. <p>EEG revealed no seizure activity despite clinical concern; however, remains on phenobarbital and intermittent lorazepam.</p>
5/28/15	Infant extubated successfully.
5/30–6/4/15	Infant working on oral feeds with bottle. Phenobarbital and lorazepam gradually withdrawn.
6/5–6/7/15	Difficulty with oral feeds. Trismus, hypertonicity, inconsolability, increased oral secretions. Clinical concern for seizure: phenobarbital reloaded and maintenance dosing started. EEG again revealed no seizure activity.
6/12/15	Phenobarbital discontinued after 5 d of improved tone, alertness, and neurologic examination.
6/16/15	Completion of 21-d course of antibiotics for presumed meningitis.
6/16–6/19/15	Again working on oral feedings with bottle.
6/22/15	Clinical examination again shows hypertonicity, trismus, inability to swallow oral secretions. Additional history revealed details of hose water supply in trailer park yard frequented by animals.
6/23/15	Infectious disease team consulted for possibility of tetanus.
6/24/15	Diagnosis of tetanus made based on ID expert review of video showing risus sardonius, trismus, and masseteric spasms. <ul style="list-style-type: none"> • Tetanus immunoglobulin administered. • 7-d course of metronidazole initiated. • Lorazepam for symptomatic muscle spasms.

at 21 days of age, feeding well by bottle, and receiving clean intermittent bladder catheterizations regularly.

At 44 days of age, he was brought to the neurosurgery clinic with a 1-day history of decreased oral intake, difficulty opening his mouth, periods of lethargy alternating with intense irritability, and episodic stiffness. Examination revealed an extremely fussy infant with normal vital signs who was difficult to console. Unchanged from his discharge examination, the anterior fontanelle was bulging and the lower back wound was healing; however, his neurologic examination was

concerning for lack of ocular fixation, absent suck reflex, and hypertonicity.

Shortly after admission to the NICU, he appeared to have tonic seizure activity with periods of whole body stiffening, apnea, and hypoxia. He was tracheally intubated for mechanical ventilation and was administered phenobarbital and broad-spectrum antibiotics for possible sepsis. MRI of the head revealed bilateral subdural fluid collections, ventriculomegaly, and vermal enhancement related to chronic hindbrain herniation, but no leptomeningeal enhancement, restricted diffusion, or thrombosis. Despite the clinical appearance

of “seizures,” 24-hour continuous EEG did not reveal electrographic seizures. An ophthalmologic evaluation and a skeletal survey were negative for signs of nonaccidental trauma. The subdural fluid was cloudy yellow with a glucose level of 96 mg/dL, a protein concentration of 3438 mg/dL, a red blood cell count of 8000/mm³, and a white blood cell count of 87/mm³. He was treated for 21 days with intravenous vancomycin and cefotaxime for presumed meningitis, although blood and subdural fluid cultures were negative. Despite this treatment, he continued to have waxing and waning hypertonicity, which was treated with phenobarbital and intermittent lorazepam for sedation and “seizure” control.

After respiratory improvement, he was extubated on the third hospital day, and oral feedings were reintroduced on the fifth day. Because seizures were not confirmed on serial EEGs, the phenobarbital and lorazepam were gradually weaned. Within several days of their discontinuation, severe diffuse hypertonicity and trismus reappeared, and he was unable to feed or swallow his secretions. Repeat EEG and cranial imaging failed to reveal any significant change that could explain the infant’s recurring symptoms. Electrolytes, blood gas, ammonia level, and C-reactive protein were reassuring, and repeat bacterial and fungal cultures remained sterile.

Given the infant’s puzzling clinical status, further history was obtained. The infant lived with his mother in a trailer in a rural area. The trailer received its water supply from the city, but it was delivered to their taps from a hose that was often dragged around the yard. This water was reportedly used for mixing formula, bathing the infant, and cleaning the skin for his intermittent bladder catheterizations. The mother had



FIGURE 1
Still frame of infant displaying the pathognomonic feature for tetanus, risus sardonicus.

received tetanus immunization 5 to 6 years earlier, but not during this pregnancy. A review of the patient by EAS, who had previously seen and managed cases of tetanus, revealed the diagnosis based on the pathognomonic features of trismus, risus sardonicus (Supplemental Video 1; Fig 1), and induced masseteric spasms (Supplemental Video 2).

Tetanus immune globulin was subsequently administered, 29 days after his initial presentation to the hospital. He was also treated with a 7-day course of metronidazole as well as muscle relaxants for the extreme hypertonicity and muscle spasms. Before discharge, he underwent placement of a feeding gastrostomy tube and a ventriculoperitoneal shunt. At follow-up 5 months later, he had resolution of his hypertonicity, with return of normal jaw movement and swallowing, as well as some oral feeding.

DISCUSSION

C tetani is a gram-positive, anaerobic bacillus typically introduced into an area of injury as a spore, which is then converted to vegetative forms that multiply and elaborate tetanus toxin. Tetanus toxin is initially taken up into motor neuron nerve terminals but, unlike Botulinum toxin, ultimately reaches the spinal cord and brainstem where it is taken up by inhibitory GABAergic and glycinergic neurons.³ Inhibition of these neurons by tetanus toxin leads

to increased muscle activity and the pathognomonic manifestations of trismus, hypertonicity, and skeletal muscle spasms.¹ Less specific symptoms include irritability, restlessness, difficulty swallowing, neck stiffness, and rigidity of thoracic and abdominal muscles.¹ The incubation period typically is 3 to 21 days, but may be longer. Although culture of *C tetani* on oxygen-reduced blood agar from entry sites and bioassay/polymerase chain reaction detection of tetanus toxin in plasma or wound exudates are possible, these are rarely available.⁴ The pathognomonic features of trismus, risus sardonicus, and skeletal muscle spasm establish the clinical diagnosis. Management of tetanus is trifold: toxin neutralization with tetanus immune globulin, bacterial elimination with antimicrobial agents (penicillin or metronidazole), and supportive care to minimize discomfort and excessive stimulation.⁴

The case presented here represents a delay in diagnosis and treatment despite the presence of the pathognomonic signs of tetanus, which were transiently masked by the episodic use of phenobarbital and benzodiazepines, standard symptomatic treatment of patients with tetanus. In retrospect, the initial presenting features of difficulty opening the mouth and episodic stiffness were symptoms of tetanus. Although this diagnosis was entertained earlier in the hospital course, it was discounted as being too unlikely due to the rarity of the disease in the United States and the lack of a clear nidus of infection. This illustrates the main point we wish to make: even rare diagnoses need to be entertained when a patient presents with classic signs of the rare disease.

We were unable to find a clear source of infection in our patient, as frequently occurs with tetanus.¹ We propose that spores in the soil-contaminated water were introduced

via any of the following routes: the gastrointestinal tract (via formula preparation), the skin (via bathing the healing myelomeningocele wound), or the genitourinary tract (via cleansing the skin for intermittent bladder drainage). A lack of passive immunity also likely contributed to his risk for tetanus, as he was born at 32 wGA, before most transplacental immunoglobulin transfer. Finally, his mother had not received tetanus immunization in 5 to 6 years and may have had waning antibody titers.

Clinically, our patient displayed generalized hypertonicity, trismus, and risus sardonicus. New-onset hypertonicity can be caused by rabies, strychnine poisoning, and phenothiazine reactions. Masseteric muscle spasms and tetany may be caused by hypocalcemia, hypoparathyroidism, hyperventilation syndrome, or hypomagnesemia. Trismus, an entity separate from both tetany and generalized hypertonicity, warrants consideration of tonsillitis, peritonsillar abscess, parotitis, temporomandibular joint dysfunction, mandibular fracture, or head/neck tumors. None of these were present in this infant. Risus sardonicus, or “sardonic smile,” is due to increased tone in the orbicularis oris muscle, and is considered pathognomonic for tetanus when present with trismus. It was this combination of signs in the absence of these other conditions that ultimately led to the diagnosis of tetanus in our patient.

Maternal tetanus immunization during pregnancy has reduced neonatal deaths from tetanus by 94% since 1988 in areas of the world in which the World Health Organization strategy has been implemented.^{5,6} In the United States, tetanus immunization during pregnancy is not routinely recommended. Importantly, the infant in this report did not have neonatal tetanus.

The limitations of our report include the lack of known tetanus antitoxin concentrations in the patient's mother or in the infant (minimal serum concentration needed for protection is 0.1 IU/mL by enzyme-linked immunosorbent assay), although these would not have been diagnostic.¹ Although we did not have any laboratory confirmation, our patient was ultimately treated for tetanus based on his classic pathognomonic signs, and has gradually improved.

Our main goal in presenting this case report is to emphasize that the diagnosis of tetanus is based on clinical findings and is made more difficult by the rarity of the disease in the United States, as well as the inexperience of most pediatricians with this disease. Our

patient's complicated medical history and other coexisting neurologic conditions also contributed to the delay in his diagnosis. We hope that this case report reminds pediatricians of the pathognomonic signs of an almost forgotten disease and can perhaps lead to earlier diagnosis and treatment in the future.

ABBREVIATION

wGA: weeks' gestational age

REFERENCES

1. Cherry JD, Harrison GJ, Kaplan SL, Hotez PJ, Steinbach WJ. *Feigin and Cherry's Textbook of Pediatric Infectious Diseases*. 7th ed. Philadelphia, PA: Elsevier/Saunders; 2014
2. Centers for Disease Control and Prevention (CDC). Tetanus surveillance— United States, 2001-2008. *MMWR Morb Mortal Wkly Rep*. 2011;60(12):365–369
3. Hassel B. Tetanus: pathophysiology, treatment, and the possibility of using botulinum toxin against tetanus-induced rigidity and spasms. *Toxins (Basel)*. 2013;5(1):73–83
4. Thwaites CL, Beeching NJ, Newton CR. Maternal and neonatal tetanus. *Lancet*. 2015;385(9965):362–370
5. World Health Organization. Tetanus vaccine. *Wkly Epidemiol Rec*. 2006;81(20):198–208
6. World Health Organization. Immunization, Vaccines and Biologicals. Tetanus. 2014. Available at: www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/passive/tetanus/en/. Accessed January 22, 2016

Tetanus and Occam's Razor: Almost Forgotten but Not Gone: A Case Report

Stephanie O. Skuby, Eunice Rhee, Elizabeth H. Thilo and Eric A.F. Simões

Pediatrics 2016;138;

DOI: 10.1542/peds.2016-0298 originally published online October 4, 2016;

Updated Information & Services

including high resolution figures, can be found at:
<http://pediatrics.aappublications.org/content/138/5/e20160298>

References

This article cites 4 articles, 0 of which you can access for free at:
<http://pediatrics.aappublications.org/content/138/5/e20160298#BIBL>

Subspecialty Collections

This article, along with others on similar topics, appears in the following collection(s):
Fetus/Newborn Infant
http://www.aappublications.org/cgi/collection/fetus:newborn_infant_sub
Neonatology
http://www.aappublications.org/cgi/collection/neonatology_sub
Infectious Disease
http://www.aappublications.org/cgi/collection/infectious_diseases_sub

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
<http://www.aappublications.org/site/misc/Permissions.xhtml>

Reprints

Information about ordering reprints can be found online:
<http://www.aappublications.org/site/misc/reprints.xhtml>

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Tetanus and Occam's Razor: Almost Forgotten but Not Gone: A Case Report

Stephanie O. Skuby, Eunice Rhee, Elizabeth H. Thilo and Eric A.F. Simões

Pediatrics 2016;138;

DOI: 10.1542/peds.2016-0298 originally published online October 4, 2016;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/138/5/e20160298>

Data Supplement at:

<http://pediatrics.aappublications.org/content/suppl/2016/10/02/peds.2016-0298.DCSupplemental>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2016 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

