

**The Editorial Board encourages all readers to submit an interesting case to the "Clinician's Corner"**

The case presentation should not exceed 200 words and should give the reader enough information to suspect the diagnosis without making it obvious. The discussion should not exceed 600 words and should be followed by a couple of 'clinical pearls'. A maximum of two references may be included, if helpful. The submitted cases will undergo peer review and revision at the discretion of the editors. Priority is given to cases illustrating an approach to common problems or important clinical clues to less common diagnoses that should not be missed. The Editorial Board hopes that this provides an opportunity for trainees and paediatricians practising outside of the teaching hospitals to share their clinical experiences and to publish in *Paediatrics & Child Health*. If you have a case to submit, contact Dr Friedman by e-mail at [jeremy.friedman@sickkids.ca](mailto:jeremy.friedman@sickkids.ca).

## Case 1: Pneumonia with hypotension and a rash

A four-year-old boy presented to a secondary level centre in transfer from a small community hospital. He had been unwell for six days. His initial problem was abdominal pain, but on day 3 of his illness he developed fever and diarrhea. He had no specific respiratory complaints, but nevertheless, a chest x-ray (CXR) was performed and was normal. His symptoms persisted and he began developing respiratory distress. One day before transfer, he was admitted to the community hospital with a diagnosis of pneumonia confirmed on CXR and was started on intravenous cefuroxime. No blood culture was performed. He continued to have fever and required oxygen to maintain oxygen saturation above acceptable levels. Furthermore, he experienced significant hypotension (70/50 mmHg), which was treated with normal saline boluses.

On initial evaluation, he had a temperature of 38.7°C, a heart rate of 150 beats/min, a respiratory rate of 60 breaths/min, a blood pressure of 100/60 mmHg and an oxygen saturation of 97% in 1 L of oxygen by nasal prongs. He looked unwell and was in moderate to severe respiratory distress. He had bilateral nonpurulent conjunctivitis, and some tender anterior and posterior auricular nodes. There was pain and decreased air entry over the right chest. He also had a diffuse maculopapular rash and red, swollen lips and hands.

Initial laboratory investigations in the referral hospital indicated a hemoglobin of 129 g/L, white blood cell count of  $2.3 \times 10^9/L$ , platelets of  $187 \times 10^9/L$ , erythrocyte sedimentation rate of 39, urea of 10.6 mmol/L, creatinine of 82  $\mu\text{mol/L}$  and normal liver function tests.

A repeat CXR in the secondary hospital revealed a worsening right-sided pneumonia and pleural effusion, despite being on antibiotics. The patient was started on cefuroxime, vancomycin and clindamycin. Culture performed on the chest tube drainage revealed the etiology of his symptoms.

## Case 2: An infant with hypotonia and constipation

A five-month-old female infant was brought to the emergency department with a three-day history of poor feeding and a one-week history of constipation. There was no history of fever, irritability, vomiting, breathing difficulty, or exposure to sick contacts or medications. She was born after an uncomplicated full-term pregnancy and delivery, and her developmental milestones were attained appropriately. She was breastfed, and three weeks before admission, the parents introduced fruits and vegetables made by pureeing organic produce in a blender.

On physical examination, she was afebrile, alert and in no respiratory distress. The neurological examination was notable for ptosis, decreased facial expression, weak cry, diffuse hypotonia, reduced muscle power and absent deep tendon reflexes. Initial investigations revealed normal serum electrolytes, calcium, magnesium, phosphate, venous blood gas, complete blood count, ammonium, lactate and creatine kinase. Cultures of blood, urine and cerebrospinal fluid were performed (and subsequently found to be negative), and a computed tomography scan of the head was normal.

The infant required nasogastric tube feeding and suctioning of her oral secretions due to poor swallowing. An electromyogram was performed demonstrating an abnormality at the level of the neuromuscular junction; no improvement occurred with a dose of pyridostigmine bromide. Three days after presentation, increasing respiratory distress and right upper lobe collapse developed, requiring intubation, ventilation and transfer to the critical care unit. The clue to her diagnosis was found in her stool specimen.

**TABLE 1**  
**Staphylococcal toxic shock syndrome: Clinical case definition**

- Fever >38.9°C (>102°F)
- Presence of diffuse macular rash (sunburn appearance)
- Desquamation one week to two weeks after onset of illness
- Hypotension
- Involvement of three or more of the following systems:
  - gastrointestinal: history of vomiting or diarrhea
  - musculoskeletal: severe myalgia, increased creatine phosphokinase
  - mucous membranes: hyperemia of conjunctiva, oropharyngeal or vaginal mucosae
  - renal: abnormal results of renal function/urinalysis
  - hepatic: elevated transaminases and bilirubin levels
  - hematological: thrombocytopenia
  - central nervous system: altered consciousness or disorientation

*In addition, normal results of blood, cerebrospinal fluid and throat cultures (although blood may be positive for staphylococci in less than 5% of cases). Toxic shock syndrome is probable when at least four of five criteria are fulfilled. Data from recommended reading 2*

**CASE 1 DIAGNOSIS:  
TOXIC SHOCK SYNDROME**

At the tertiary care centre, 680 mL of purulent fluid was drained from the pleural space; a culture of the fluid was positive for *Streptococcus pyogenes* (group A streptococcus). The patient was diagnosed with group A streptococcal toxic shock syndrome. He received a 14-day course of intravenous penicillin and clindamycin, and made a full recovery. Kawasaki syndrome was considered as a possible diagnosis due to conjunctivitis, pyrexia, rash (ultimately desquamation of hands and feet), thrombocytosis and an erythrocyte sedimentation rate of 130. However, no coronary ectasias were visualized by echocardiography and the patient responded appropriately to intravenous antibiotics.

Toxic shock syndrome (TSS) can result from infection with either *Staphylococcus aureus* or *S pyogenes*. Staphylococcal toxic shock was first described in menstruating teenagers and young women who were using high-absorbency tampons. Changes in the absorbency of tampons in recent decades have led to a substantial reduction in the incidence of such cases. The major risk factor for group A streptococcal toxic shock in children is varicella zoster virus infection. Both forms of toxic shock are more common in children, presumably due to an absence of adequate superantigen neutralizing antibodies.

TSS is thought to be mediated by toxins known as superantigens. These antigens bind to T-cell receptors, resulting in massive proliferation and activation of T-cells, leading to the production of large quantities of cytokines including tumour necrosis factor and interleukin-1. This nonspecific immunostimulatory process causes a 'cytokine storm', which in turn leads to the development of TSS.

The criteria established for the diagnosis of staphylococcal and streptococcal TSS are listed in Tables 1 and 2.

In general, it is not possible to differentiate between staphylococcal and streptococcal TSS based on clinical manifestations or laboratory features. Confirmation of the diagnosis rests on the detection of the organism in culture. Blood cultures are positive in 50% or more of streptococcal TSS cases, but in less than 5% of staphylococcal TSS cases.

**TABLE 2**  
**Streptococcal toxic shock syndrome: Clinical case definition**

1. Isolation of group A streptococcus
  - A. From a normally sterile site (blood, cerebrospinal fluid, peritoneal fluid, tissue biopsy specimen)
  - B. From a normally nonsterile site (throat, sputum, vagina)
2. Clinical signs of severity
  - A. Hypotension, and
  - B. Two or more of the following signs:
    - renal impairment
    - coagulopathy (platelets <100×10<sup>9</sup>) or disseminated intravascular coagulation
    - liver involvement (increased transaminases or total bilirubin)
    - adult respiratory distress syndrome
    - generalized erythrodermatous macular rash that may desquamate
    - soft tissue necrosis, including necrotizing fasciitis or myositis

*An illness fulfilling criteria 1A, 2A and 2B can be defined as a definite case. An illness fulfilling criteria 1B, 2A and 2B can be defined as a probable case if no other etiology for the illness is identified. Data from recommended reading 2*

Treatment of TSS includes supportive therapy (fluid resuscitation, inotropic agents), anticipatory management of multisystem organ failure and parenteral antibiotics. Intravenous penicillin and clindamycin is the preferred treatment option for culture-confirmed group A streptococcal TSS. If a specific etiologic diagnosis has not been established, treatment should include a lactamase-resistant antistaphylococcal agent such as cloxacillin or cefazolin.

Intravenous immunoglobulin (IVIG) is recommended for the treatment of group A streptococcal TSS. Pathophysiologically, the rationale for using IVIG is that invasive group A streptococcal infections may be associated with inadequate levels of neutralizing antibody against streptococcal superantigens and other important antigens such as the M protein. There is evidence from a comparative observational study that treatment with IVIG may be lifesaving in patients with streptococcal TSS (5). In addition, a recent randomized, double-blind, placebo-controlled trial was conducted in Europe to determine if IVIG is beneficial in treating this condition. The results were inconclusive because of the small sample size, but the study did provide further support for IVIG as an adjunctive therapy in streptococcal TSS. Other adjunctive treatments have included steroids, plasmapheresis and monoclonal antibodies, although the indications for use of these therapies are controversial.

The incidence of invasive group A streptococcal disease among household members of cases is between 18 and 122 times that of the general population. At the present time, most public health authorities in Canada recommend that all household contacts receive chemoprophylaxis with penicillin, amoxicillin, a first-generation cephalosporin, clindamycin or erythromycin for a period of 10 days. All household contacts of our patient received appropriate chemoprophylaxis and none developed invasive group A streptococcal disease.

**CLINICAL PEARLS**

- Clinicians should be aware of the clinical manifestations of TSS and consider this diagnosis when faced with a patient with pneumonia or other focal infections who also has hypotension and/or multisystem involvement.

- TSS can be caused by *S aureus* or group A streptococcus infection.
- Adjunctive IVIG therapy should be considered for all patients with suspected or proven group A streptococcal TSS.
- Chemoprophylaxis is recommended for all household contacts of a patient with invasive group A streptococcal disease.

### RECOMMENDED READING

1. Canadian Paediatric Society, Infectious Diseases and Immunization Committee ID 98-05. Invasive group A streptococcal infections. *Paediatr Child Health* 1999;4:73-6.
2. American Academy of Pediatrics. Toxic shock syndrome. In: Pickering LK, ed. *Red Book*: 2003, 26th edn. Elk Grove Village, Illinois: American Academy of Pediatrics, 2003:624-30.
3. Davies HD, Schwartz B. Invasive group A streptococcal infections in children. *Adv Pediatr Infect Dis* 1999;14:129-43.
4. Darenberg J, Ihendyane N, Sjolín J, et al. Intravenous immunoglobulin G therapy in streptococcal toxic shock syndrome: A european randomized, double-blind, placebo-controlled trial. *Clin Infect Dis* 2003;37:333-40.
5. Kaul R, McGeer A, Norrby-Teglund A, et al. Intravenous immunoglobulin therapy for streptococcal toxic shock syndrome – a comparative observational study. The Canadian Streptococcal Study Group. *Clin Infect Dis* 1999;28:800-7.

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### CASE 2 DIAGNOSIS: BOTULISM

One week after admission, a stool specimen obtained on admission was reported to be positive for botulinum toxin. Samples of the puréed foods given to the infant were negative for the toxin. There was no history of corn syrup, canned food or honey ingestion. She required mechanical ventilation for seven weeks and was discharged home three months after presentation. At one year of age, her neurological examination was normal, but insertion of a gastrostomy tube was required for a pronounced feeding aversion.

Infant botulism is a neuroparalytic disorder that occurs after ingested spores of *Clostridium botulinum* multiply and produce toxin in the intestine, most likely during a period of alteration of the intestinal microflora. *C botulinum* spores exist worldwide in soil and dust, but cases often occur in clusters; approximately 100 cases are reported annually in the United States.

The incubation period is estimated at three days to 30 days from the time of exposure to spore-containing material. Although honey ingestion is a known risk factor, the source of the spores in the majority of cases is unknown. The median age of presentation is between two months and four months; 95% of affected infants are between three weeks and six months old. The most common initial symptom is constipation, followed by weakness, hypotonia and lethargy. Loss of head control can be a prominent sign. Bulbar palsies subsequently develop, leading to a weak cry, poor feeding, ptosis, an expressionless face and swallowing impairment. Fatigability with repetitive muscle activity may be observed. The spectrum of severity can range from constipation and mild

weakness to rapidly progressive respiratory failure. The differential diagnosis of infantile botulism includes sepsis, drug or toxin ingestion, metabolic disorders, central nervous system infection, myasthenia gravis and spinal muscular atrophy.

Diagnosis requires detection of botulinum toxin in stool or serum by mouse neutralization assay or isolation of toxigenic *C botulinum* in feces. Suspected foods should also be tested. Electromyographic studies can provide supportive evidence, but infants can lack the characteristic findings and their absence cannot exclude the diagnosis. Treatment is primarily supportive with particular attention to respiratory and nutritional care. Over 50% of affected infants require assisted ventilation, but the case fatality rate is less than 1% with most affected infants making a full recovery. Intravenous human-derived botulinum antitoxin (BIG-IV) has been shown to reduce recovery time if initiated early. In a placebo-controlled trial, the mean hospital stay in infants was reduced from 5.6 weeks to 2.6 weeks (3). BIG-IV can be obtained through the California Department of Health Services, Infant Botulism Treatment and Prevention Program. In our case, permission to release the treatment was not authorized. The case occurred during the conflict in Iraq and the reasons for the lack of release of BIG-IV remain speculative. Treatment with equine botulinum antitoxin is associated with hypersensitivity reactions and its use is generally not recommended. Antimicrobial agents should be avoided because of their potential to increase the toxin available for absorption through lysis of intraluminal *C botulinum*.

### CLINICAL PEARLS

- Infant botulism should be suspected in any infant less than one year of age (particularly if between the ages of two months to four months), presenting with acute hypotonia/weakness especially if constipation and difficulty in sucking, swallowing, crying or breathing are present.
- Diagnosis requires detection of botulinum toxin in stool or serum, or isolation of toxigenic *C botulinum* in stool.
- Avoid feeding honey to infants younger than one year old.

### RECOMMENDED READING

1. Woodruff BA, Griffin PM, McCroskey LM, et al. Clinical and laboratory comparison of botulism from toxin types A, B, and E in the United States, 1975-1988. *J Infect Dis* 1992;166:1281-6.
2. Schreiner MS, Field E, Ruddy R. Infant botulism: A review of 12 years' experience at the Children's Hospital of Philadelphia. *Pediatrics* 1991;87:159-65.
3. Arnon SS. Infant Botulism. In: Feigin RD, Cherry JD, eds. *Textbook of Pediatric Infectious Diseases*, 4th edn. Philadelphia, PA: WB Saunders Company, 1998.

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