Tick Toxicosis in North America

Patrick F. Mongan, MD
Gainesville, Florida

This is a case presentation and review of an uncommon disorder, tick toxicosis. The history, epidemiology, pathophysiology, and treatment are discussed. This disorder was mentioned in diaries from the early 1800s and has been reported in 18 states and the District of Columbia. A review of 70 cases reveals that the typical patient is a female child who develops leg weakness, irritability, or clumsiness. The exact site at which the toxin induces the paralysis is unknown. Removal of the tick usually reverses the paralysis within hours. Confusing tick toxicosis with other disorders may occur, and death has resulted. This article will remind physicians to consider tick toxicosis when seeing patients with acute ataxia or ascending paralysis and to, perhaps, prevent death from an easily treatable disorder.

Tick toxicosis, also known as tick paralysis, is a disorder that has been recognized since the 1800s.[1] Most cases have occurred in British Columbia, Canada, and the northwest or southeast United States.[2-5] Very little is written about this disorder in common pediatric texts,[6-9] though most cases have occurred in children. Several texts only mention the problem as part of the differential diagnosis in patients with acute ataxia,[7] or acute ascending paralysis.[6,8] The last extensive review of this disorder was a monograph by Gregson[1] in 1973. Tick paralysis is a potentially fatal disease and although not a common problem, it is one with which physicians should be familiar. Most affected patients will be seen by a family physician or pediatrician and this communication will remind them to consider tick toxicosis in any patient with an acute ataxia or ascending paralysis.

Case Presentation

A six-year, 11-month-old white female was brought to the Family Practice Center by her mother because of numbness in the arms and legs. The prior evening the mother noticed her daughter had a "dazed look." The next morning the child fell several times when getting out of bed. As she came down the stairs her knees "buckled" and she had difficulty maintaining her balance. Shortly thereafter, she complained of her legs and feet feeling "asleep." This progressed to involve her arms and hands.

The child had been well until this episode and other children in the household were not ill. There was no history of drug ingestion, recent infection, immunization, or trauma. She had a good appetite and no other symptoms were noted. The past history was remarkable for black-out spells during the second year of life which resolved spontaneously and had not recurred. Birth and developmental history were normal. The family appeared stable and appropriately concerned.

Physical examination in the Family Practice Center revealed an ataxic gait, an inability to walk heel-to-toe, and "past pointing" with the finger-to-nose maneuver. Sensation was found to be normal in spite of her feelings of numbness. (The numb feeling was most likely a result of the weakness). Deep tendon reflexes and strength were also normal. No nystagmus was noted. The

From the Department of Community Health and Family Medicine, University of Florida, Gainesville, Florida. Requests for reprints should be addressed to Dr. Patrick F. Mongan, Vernal Family Health Center, 75 North 2nd West, Vernal, UT 84078.

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patient was thought to have a cerebellar disorder and was admitted to the hospital for observation and neurologic consultation.

Approximately three hours after the first examination the patient was seen by the resident and the attending physician on call. She was noted to have normal vital signs and was in no distress. She complained of "the room spinning around" and had bilateral nystagmus on lateral gaze. Deep tendon reflexes were decreased to 1+. She had no clonus and had a negative Romberg sign. Coordination was decreased in all extremities but was worst in the lower extremities. Strength appeared normal.

It was felt by both examiners that the patient had a relatively acute onset of cerebellar dysfunction which might be the result of a toxin, drug, or tumor. The possibility of tick toxicosis was discussed with the mother. She was familiar with this disorder and remembered that the family dogs had suffered from this problem when she was a child. Unsuccessfully, the patient was searched for a tick. A complete blood count, urinalysis, and test values for electrolytes, blood urea nitrogen, glucose, calcium, and phosphorus were within normal limits. Skull x-rays were also normal.

The patient slept uneventfully that night, but on awakening the next morning she was unable to feed herself because of weakness in the arms, right greater than left. She was unable to walk without assistance. After another search, a tick was found in the occipital area and removed. By noon the patient was able to feed herself and the next morning walked with a slight ataxic gait. She was discharged from the hospital and rechecked 24 hours later in the Family Practice Center, at which time her neurologic examination was normal.

Historical Perspective

The first scientific descriptions of tick toxicosis were published in 1884 by Bancroft in the *Australian Medical Gazette* and in 1904 by Malley in the *Agricultural Journal of the Cape of Good Hope*.[10] Both articles dealt with this disorder in animals, which had been described by laymen as early as 1824.[10] In 1912, Temple [10,11] described three cases of tick paralysis he had seen in children and presented several more cases that he had learned of by surveying fellow physicians in Oregon. During the same year, Todd[1] described several cases from Canada. Finally, in 1913, Hadwen[12] wrote a review of tick paralysis in man and animals. He induced the disease experimentally by attaching ticks to sheep and then reversed the paralysis by removing the ticks. He failed to transmit the disease after injecting blood or other tissues of paralyzed animals into unaffected animals. Thus, he concluded the disorder was not infectious in origin but caused by a toxin.

Epidemiology

Tick toxicosis has been reported in the following states: Oregon, Wyoming, Washington, Idaho, Montana, Colorado, Texas, Pennsylvania, New York, District of Columbia, Virginia, Tennessee, North Carolina, Kentucky, Alabama, South Carolina, Georgia, Mississippi, and Florida. Most cases in North America have been reported in British Columbia, Canada. Dermacentor andersoni Stiles, or "wood tick," is the offending tick in the Northwest and Dermacentor variabilis Say, or dog tick, on the East Coast. The wood tick ranges as far east as the Dakotas, and to Arizona and New Mexico in the South. The dog tick is distributed mainly in the east, but is prevalent in California and present in Texas, Oklahoma, and Nebraska.[5] A more potent toxin appears to be produced by Ixodes holocyclus in Australia.[10,13] Other ticks rarely seen on humans have also been reported to cause tick toxicosis.[14,15]

Ticks prefer areas with tall grass and are attracted by animal scents. Therefore, they congregate along paths frequented by animals and as the animal brushes against the grass the tick climbs onto the animal. Apparently ticks will climb to the highest point and this explains why most ticks are found on the head and neck of man or along the spine on animals. The months between March and August are when the ticks become sexually active and are the months when most cases occur.[5] There is a 5-to-13-day period of feeding until full engorgement, at which time the female tick detaches itself and leaves the host. Four to six days of feeding are required before paralysis can be induced. All reported cases of paralysis, with one exception,[14] in which a tick was identified, involved females.

Experimental data gathered by Gregson and others[1] explain why many people are not paralyzed by ticks. Of 75 animals infested with four wild ticks each, only 52 percent developed paralysis. As the tick season advanced, the toxic-

ity of the ticks decreased and three times the usual number of female ticks were required to induce paralysis. Further work by Gregson demonstrated that mated females, which feed or engorge more rapidly, were less toxic. This contradicted work done by earlier experimenters in Germany,[1,5] who felt the eggs were the source of the toxin, and as the eggs matured toxicity increased. Other animal studies reveal them to be less sensitive to the toxin than man and usually several female ticks must feed on the animal to cause paralysis.[11, 12, 16] Most cases of tick paralysis in man involve one tick.[17-30] Animals in Australia develop antibodies to the toxin fairly quickly and become resistant to tick toxicosis.[16,31] The development of this toxin may help perpetuate the species by inducing enough paralysis to prevent removal of the tick by the animal.

These characteristics may explain why there are not more cases of tick paralysis in man, though the tick is very prevalent. First, the tick must be female and if mated, she is less toxic. Secondly, she must feed a minimum of four days to induce toxicosis. Thirdly, many people are aware of this problem in prevalent areas, and search their children for ticks when they have been outdoors.[22,32] Fourthly, there is a great deal of variability in the toxicity of each tick. And finally, the diagnosis may be missed. The peak incidence of tick toxicosis is similar to that of poliomyelitis, and the two diseases may be confused with each other.[5,33] In fact, ticks have been found during funeral preparations on people who have died unexpectedly.[1,18]

Pathophysiology

Animal studies of tick toxicosis leave little doubt that the causative agent is a toxin secreted by the tick during feeding.[1,16] The source of the toxin remains a mystery, but artificially collected tick saliva can paralyze an animal.[1] Gregson[1] discusses three possibilities as the source of the toxin. First is production of a toxin in one of the tick's organs, such as the ovaries or salivary glands, but experimental data have been controversial in locating the organ. The next hypothesis is that a substance from the tick interacts with the host's blood to form the toxin. Finally, the tick may be infested with a viral or rickettsial agent that produces the toxin. Most investigators believe the first hypothesis is the most likely, though the others have not been disproven. Autopsies performed on animals with tick toxicosis have not elucidated the pathophysiology of this disorder.[11,12] Kaire took whole body extract and fractionated it in a DEAE cellulose column.[31] Fraction 2 induced paralysis in dogs within 48 hours, and when injected in smaller amounts, it gave dogs immunity to the toxin. A tick antitoxin has been developed in Australia for use in animals, but it was also used successfully in a human.[13]

In 1956, Rose and Gregson[34] demonstrated in animals that the toxin blocks nerve conduction peripherally, but does not prevent muscle contraction with direct electrical stimulation. Since then animal studies have indicated a failure to conduct action potentials in the motor fibers, the greatest effect being in the finer fibers.[35,36] Finally, it appears that this impaired conduction results in a failure to release acetylcholine at the neuromuscular synapse.[37,38]

Several studies have been conducted with electromyogram (EMG) testing in children affected by tick toxicosis.[32, 33, 39-42] All have demonstrated a reduction in nerve conduction velocity and/or a reduced muscle action potential. Swift and Ignacio[40] believe the toxin affects the ionic fluxes which mediate both the action potential and release of acetylcholine at the end plates. Tetrodotoxin produces a similar effect. The effect on the central nervous system, if any, has not been elucidated.

Clinical Features

The case presented is typical. Most patients are female children who first become weak, restless, irritable, or drowsy in the evening. The next morning they may complain of paresthesias in the legs and have difficulty walking. They may have some improvement after arising, but are usually worse the next morning. Within 24 to 48 hours after the onset of symptoms most patients cannot walk, and the ascending paralysis will progress to involve the upper extremities and respiratory muscles. If respiratory embarrassment is present, death is much more likely, even after the tick is removed.[10,13,18,23] With modern respiratory care none of these patients should die, as they did in the past. Apparently the last patient death from this disorder in North America was in 1964.[2] If the patient is seen early, as in the present case, no objective evidence of weakness will be present and a diagnosis of

Table 1. Causes of Acute Ataxia in Children Other Than Tick Toxicosis[6]

1. Acute cerebellar ataxia of childhood
2. Drugs
   - Sedatives
   - Tranquilizers
   - Antipsychotic medications
   - Alcohol
   - Anticonvulsants (phenytoin and phenobarbital)
3. Trauma
4. Subdural hematomas
5. Hydrocephalus
6. Tumor (primarily posterior fossa)
7. Guillain-Barré syndrome
8. Fisher syndrome
9. Fever
10. Rare disorders
    - Metachromatic leukodystrophy
    - Infantile neuroaxonal dystrophy
    - Lipofuscinosis
    - Ataxia telangiectasia
    - Multiple sclerosis
    - Familial intermittent cerebellar ataxia
    - Hartnup disease
    - Pyruvate decarboxylase deficiency
    - Maple syrup disease
    - Hyperalaninemia

acute ataxia may be made. A discussion of acute ataxia by Nash points out this difficulty. She states, "sensory deficits, weakness, myoclonus, chorea, athetosis, tremor, vertigo, and *diffuse undefinable incoordination,* or *clumsiness,* may all be confused with ataxia even by well-trained experienced observers." Experimental data indicate the incoordination of tick toxicosis is due to the slowing of nerve conduction, and weakness is secondary to the failure of acetylcholine release at the neuromuscular junction.[34-42]

Physical examination usually reveals a child who is in no distress and whose vital signs are normal. Most patients are afebrile or have a low grade temperature. Physical examination, excluding neurologic, is normal. Early in the course, incoordination is usually present with deep tendon reflexes in the lower extremities decreased or absent. As the disease progresses, muscle weakness appears in the lower extremities and spreads upward to involve the upper extremities within hours. After 48 to 72 hours, swallowing and phonation become difficult, with respirations labored. From the onset of symptoms to paralysis of legs is usually 24 hours, but respiratory arrest has been described in a small child within hours,[11] and an adult had symptoms for three weeks before the tick was removed.[18]

Table 2. Causes of Acute Polyneuropathy Other Than Tick Toxicosis[44,48]

1. Poliomyelitis
2. Guillain-Barré syndrome
3. Rabies
4. Botulism
5. Tetanus
6. Diphtheria
7. Syringomyelia
8. Spinal cord tumor
9. Drugs
   - Aminoglycosides
   - Polymyxin
   - Tetracycline
   - Sulfonamides
10. Myasthenia gravis or Eaton Lambert syndrome
11. Periodic paralysis

The differential diagnosis in a patient presenting with acute ataxia or ascending paralysis is extensive (Tables 1 and 2). The obvious way of establishing the diagnosis is to find the tick, even though the patient may have paralysis after the tick has detached itself. Other distinguishing characteristics of tick toxicosis are a lack of fever, normal cerebrospinal fluid and sensory examination, no preceding infection, and a very rapid progression of signs. Cerebral cortical functions are normal.

Treatment

Treatment is simply removal of the tick. Rose[43] who has seen many cases, claims the tick should be pulled off and only rarely will the head be left behind. Many "folk" remedies which require the application of various chemicals are apparently ineffective. However, one child[18] died when the tick was pulled off, and the head left behind. Many authors emphasize the importance of a thorough examination for more ticks even after one has been found. Several authors reported difficulties similar to those of this author in locating ticks on the scalp of a young female.

Surgically excising the tick head should be done if it separates from the body. Careful observation of the patient should be continued after removal of the tick until the patient shows definite improvement. One child[18] died 12 hours after the tick was removed, and it is common for symptoms to progress after removal of the tick Ixodes.[10,13] After the tick is removed, patients are usually completely normal in 24 to 48 hours, but some patients with severe paralysis have taken two weeks to return to normal. Improvement is usually noted within hours after tick removal. The possibility of contracting other tick-borne diseases also exists in these patients.

Summary

Tick toxicosis is a disease characterized by a rapidly ascending paralysis which may end in respiratory arrest and death. It may occur in all ages but more commonly in children. The patients are usually not ill and have only mild constitutional symptoms. Simply removing the entire tick will resolve the paralysis. All general/family physicians and pediatricians should be aware of this problem, especially if they practice in rural areas. Physicians in tick infested areas can stress the importance of searching each family member's body for ticks when they have been outdoors. Early diagnosis and prompt therapy will prevent death (Table 3).

Table 3. Mortality of Tick Toxicosis

Conditions	Schmitt et al (%) (N=305)	Case Review (%) (N=70)
Deaths	9.8	14
<15 years old	79	91
Deaths<15 years old	12.8	6.2
Female<15 years old	67	80
Tick on head and neck	70	90

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