Glandular tularemia with typhoidal features in a Manitoba child

Pierre J. Plourde,* MD; Joanne Embree,* MD; Frank Friesen,† MD; Gary Lindsay,‡ MD; Trevor Williams,§ MB, BCh

Tularemia, a zoonotic infectious disease, is uncommon in Canada. In Manitoba the first reported case occurred in a trapper in 1950.[1] In 1978 an outbreak in a monkey colony at the Assiniboine Park Zoo, Winnipeg, killed several animals and resulted in transmission of the disease to a veterinarian.[2]

The disease manifests itself in six clinical syndromes: ulceroglandular, glandular, typhoidal, oropharyngeal, oculoglandular and pneumonic. In Canada 50% of cases are ulceroglandular and 30% typhoidal or pneumonic.[3] In children glandular disease is more common.[4] This report of glandular tularemia with typhoidal features in a child is presented to alert Canadian physicians to the treatment difficulties associated with this more aggressive form of the disease.

Case report

A previously healthy 6-year-old girl was admitted to a community hospital with a 3-day history of fever, shaking chills, headache and vomiting that had begun 8 days after she was bitten by an unidentified insect over her left scapula.

The girl appeared ill. Her temperature was 40.3°C, pulse rate 144 beats/min and blood pressure 95/70 mm Hg. She had severe gingivostomatitis without pharyngitis or oral ulceration. No cervical lymph nodes were palpable, but inguinal lymph nodes were enlarged bilaterally and were quite tender. Her abdomen was diffusely tender without localizing signs. There was no evidence of the insect bite. The other physical findings were normal.

The leukocyte count was 13.1 × 10^9/L (47% mature and 32% band neutrophils and 21% lymphocytes), the hemoglobin level 114 g/L, the platelet count 144 × 10^9/L and the erythrocyte sedimentation rate 14 mm/h. Bacterial cultures of a throat swab and of urine, cerebrospinal fluid and blood samples were negative, as were bacterial and viral cultures of stool samples.

The patient was given cefuroxime intravenously. On the third day in hospital excision of an enlarging, fluctuant right inguinal lymph node revealed necrotizing, suppurative, nongranulating lymphadenitis with multiple abscesses. Blood and chocolate agar cultures of the node yielded *Haemophilus* species. The following day watery, nonbloody diarrhea developed and was associated with increasingly painful abdominal distension. A computed tomogram of her abdomen was unremarkable, and laparotomy did not reveal any abnormalities. Intravenous metronidazole therapy was added. Because of her deteriorating condition she was transferred to a university teaching hospital.

Pertinent serum levels were as follows: aspartate aminotransferase 1120 U/L, alanine aminotransferase 540 U/L, alkaline phosphatase 174 U/L, γ-glutamyl transferase 95 U/L and total bilirubin 31 μmol/L (direct fraction 30 μmol/L). Ultrasonography of the abdomen revealed a distended gallbladder filled with sludge and surrounded by fluid; these findings were consistent with cholecystitis. The levels of immuno-

*From the departments of *Medical Microbiology and †Pediatrics, University of Manitoba, Winnipeg, Man., ‡Western Medical Clinic, Brandon, Man., and §Cadham Provincial Laboratory, Winnipeg, Man.*

Reprint requests to: Dr. Pierre J. Plourde, Department of Medical Microbiology, Rm. 544, Basic Sciences Building, University of Manitoba, 730 William Ave., Winnipeg, MB R3E 0W3

globulin, rheumatoid factor, antinuclear factor and anti-DNA antibody were all within normal limits. The results of serologic tests for adenovirus, respiratory syncytial virus, parainfluenza viruses, influenza viruses, Epstein–Barr virus, cytomegalovirus, hepatitis A virus, hepatitis B surface antigen, *Mycoplasma pneumoniae* IgM, *Coxiella burnetii* and *Borrelia burgdorferi* were negative. Two sets of aerobic and anaerobic blood cultures yielded negative results, as did repeat stool and throat cultures for bacteria and viruses.

The organism previously described as *Haemophilus* was ultimately identified as *Francisella tularensis* and was found to be sensitive to gentamicin, streptomycin and cefotaxime but resistant to cefuroxime. The identity of the organism was confirmed through biochemical tests and slide immune agglutination.

Therapy was changed to gentamicin, 1.5 mg/kg intravenously every 8 hours. However, the patient's temperature continued to spike dramatically, to nearly 41°C, and the shaking chills persisted; the watery diarrhea worsened, as did the inguinal adenitis. After 5 days streptomycin, 7.5 mg/kg intramuscularly every 12 hours, was substituted. Although the fever began to subside, therapy was switched to gentamicin, at the same dosage as before, and cefotaxime, 50 mg/kg intravenously every 8 hours, because of intolerance to the streptomycin injections. Defervescence occurred 17 days after the start of antibiotic therapy (Fig. 1). The antibiotic therapy was continued for a total of 28 days. The patient was fully recovered at the time of discharge and remained well during the 12 months of follow-up.

Comments

F. tularensis has been isolated from many animals, including muskrats,[5] rabbits[6] and beavers.[7]

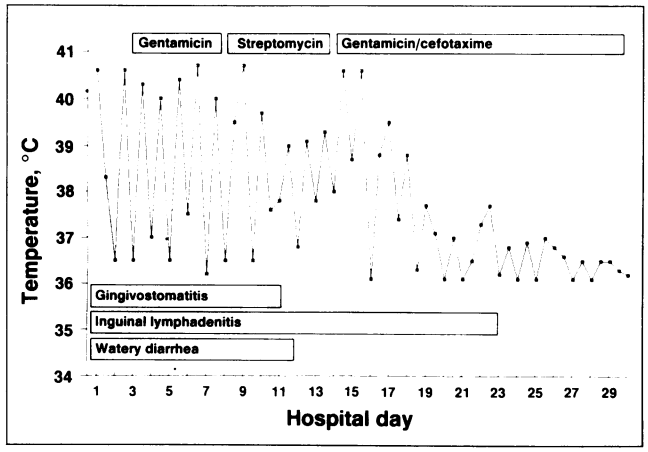

Fig. 1: Temperature and clinical features during aminoglycoside and combination antibiotic therapies in 6-year-old girl who had glandular tularemia with typhoidal features.

Transmission to humans has occurred directly through contact with animals or bites by insect vectors such as wood ticks, dog ticks, deer flies and mosquitoes.[8–10] Airborne and waterborne routes of transmission have also been described.[11,12] Tularemia is endemic in the south-central region of the United States; in Canada isolated outbreaks have been reported only from Quebec during the past 25 years.[5,7]

The case we have described was an atypical one of presumed insect-borne tularemia. The diagnosis was difficult because of a rarely reported combination of glandular and typhoidal features. The abrupt onset of illness with dramatic fever spikes and chills, headache, vomiting and diarrhea is consistent with typhoidal disease.[13] Diarrhea is seen solely in cases of typhoidal tularemia.[14] Lymphadenopathy is very unusual in typhoidal tularemia and is most often observed in cases of ulceroglandular or glandular disease. The regional lymph nodes nearest the site of the insect bite are usually affected.

One of the most dramatic initial clinical findings in our case was severe gingivostomatitis without pharyngitis. This is the first report of gingivostomatitis associated with tularemia. Other unusual features included diarrhea, which is observed in only 4% of pediatric cases,[4] inguinal adenopathy, which is rarely seen in children,[4] the lack of evidence of an insect bite on the girl's legs to explain the inguinal adenopathy, and cholecystitis, which has never been reported in association with tularemia or cefuroxime therapy.

Standard therapy for tularemia is streptomycin given intramuscularly for 7 days. Defervescence usually occurs within 24 to 72 hours after the start of therapy.[15] A poor response is associated with typhoidal disease, a positive culture for *F. tularensis*, a delay of more than 1 month in antibiotic treatment and a lack of aminoglycoside use.[16] The delay of only 12 days from the onset of symptoms to the start of aminoglycoside therapy in our case should have been followed by rapid defervescence. However, the typhoidal features and the positive culture may have been predictors of a slower response to therapy. Also, fever may persist for 1 to 40 days during streptomycin therapy, more persistent fevers being associated with suppurative lymph nodes.[14] Because of the rarity of this disease no properly controlled antibiotic trials have been performed. Thus, there is a paucity of knowledge concerning therapy with other aminoglycosides, there is almost no experience with third-generation cephalosporins, and the usefulness of combination antibiotic therapy is unknown.

Because tularemia rarely occurs in Canada, its diagnosis is very difficult. The disease should be considered in the differential diagnosis of any febrile illness associated with lymphadenitis or typhoidal

enteritis in children who have a history of recent contact with animals or recent insect bites.

References

1. Molgat AL: Tularemia in Manitoba. *Man Med Rev* 1950; Nov: 630
2. Preiksaitis JK, Crawshaw GJ, Nayar GSP et al: Human tularemia at an urban zoo. *Can Med Assoc J* 1979; 121: 1097-1099
3. Martin T, Holmes IH, Wobeser GA et al: Tularemia in Canada with a focus on Saskatchewan. *Can Med Assoc J* 1982; 127: 279-282
4. Jacobs RF, Condrey YM, Yamauchi T: Tularemia in adults and children: a changing presentation. *Pediatrics* 1985; 76: 818-822
5. Ford-Jones L, Delage G, Powell KR et al: "Muskrat fever": two outbreaks of tularemia near Montreal. *Can Med Assoc J* 1982; 127: 298-299
6. Black DM, Thomson JAC: Tularaemia in British Columbia. *Can Med Assoc J* 1958; 78: 16-18
7. Tularemia — Quebec. *Can Dis Wkly Rep* 1982; 8: 1-3
8. Wright SW, Trott AT: North American tick-borne diseases. *Ann Emerg Med* 1988; 17: 964-972
9. Klock LE, Olsen PF, Fukushima T: Tularemia epidemic associated with the deerfly. *JAMA* 1973; 226: 149-152
10. Uhari M, Syrjälä H, Salminen A: Tularemia in children caused by *Francisella tularensis* biovar *palaearctica*. *Pediatr Infect Dis J* 1990; 9: 80-83
11. Dahlstrand S, Ringertz O, Zetterberg B: Airborne tularemia in Sweden. *Scand J Infect Dis* 1971; 3: 7-16
12. Lindsay WRN, Scott JW: Oculoglandular tularemia transmitted from contaminated sewer water. *Can J Public Health* 1951; 42: 146-151
13. Jacobs RF, Narain JP: Tularemia in children. *Pediatr Infect Dis J* 1983; 2: 487-491
14. Dienst FT Jr: Tularemia: a perusal of three hundred thirty-nine cases. *J La State Med Soc* 1963; 115: 114-127
15. Sanford JP: Tularemia. *JAMA* 1983; 250: 3225-3226
16. Penn RL, Kinasewitz GT: Factors associated with a poor outcome in tularemia. *Arch Intern Med* 1987; 147: 265-268

Conferences

continued from page 1952

June 10-13, 1992: ISPRAD VI — 6th International Symposium on the Planning of Radiological Departments (in conjunction with the International Meeting on Hospital Economy [IMHE])
Grieg Hall, Bergen, Norway
Official language: English
IMHE/ISPRAD VI, c/o Lilly Hausberg, PLUSreiser, PO Box 946, N-5001 Bergen, Norway; fax 011-47-5-475-90-20-91

June 14-20, 1992: International Society of Technology Assessment in Health Care (ISTAHC) 8th Annual Meeting
Waterfront Centre Hotel, Vancouver, and Whistler Resort Conference Centre, Whistler, BC
Karen Cardiff, ISTAHC Conference coordinator, University of British Columbia; (604) 822-5059

June 16-18, 1992: Health Care '92 Exhibition and Lectures
National Exhibition Centre, Birmingham, England
Trinity Healthcare Exhibitions Ltd., Times House, Station Approach, Ruislip, Middlesex, England HA4 8NB; telephone 011-44-21-0895-677677, fax 011-44-21-0895-676027

June 17-19, 1992: Health Care: Innovation, Impact and Challenge
Queen's University, Kingston, Ont.
Dr. S. Mathwin Davis; (613) 545-6486, fax (613) 545-2135

June 17-19, 1992: 6th Annual Forensic Conference — The Roots of Violence: Implications for Interventions with Adults (sponsored by the Mental Health Centre, Penetanguishene)
Highland Inn, Midland, Ont.
Margaret Milligan, conference coordinator, Mental Health Centre, PO Box 5000, Penetanguishene, ON L0K 1P0; (705) 549-3181, ext. 2204

June 17-20, 1992: Society for Scholarly Publishing Annual Meeting
Chicago
Society for Scholarly Publishing, 304-10200 W 44th Ave., Wheat Ridge, CO 80033; (303) 422-3914

June 18-20, 1992: 3rd World Congress of Endoscopic Surgery
Bordeaux Convention Centre, Bordeaux, France
Third World Congress of Endoscopic Surgery, scientific secretary, BCS, Palais des congrès de Bordeaux, 33300 Bordeaux Lac, France; telephone 011-33-1-56-50-84-49, fax 011-33-1-56-43-17-76

June 21-24, 1992: 4th Symposium on Violence and Aggression
Saskatoon
Registration Office, Rm. 105, Kirk Hall, University of Saskatchewan, Saskatoon, SK S7N 0W0; (306) 966-5539, fax (306) 966-5567

June 25-27, 1992: National Pro-Life Conference — Save the Planet's People (sponsored by Alliance for Life and Campaign Life Coalition)
Toronto
Campaign Life Coalition, 305-53 Dundas St. E, Toronto, ON M5B 1C6; (416) 368-8479

July 3-6, 1992: LifeCycle Learning Workshops
Regal Constellation Hotel, Etobicoke, Ont.
Guest speaker: John Bradshaw
Continuing education study credits may be available.
LifeCycle Learning, PO Box 400, Newton, MA 02159-0004; fax (617) 965-5054

continued on page 1974