CASE REPORT

John E. Gerber,[1] M.D.; Joyce E. Johnson,[2] M.D.; Margie A. Scott,[3] M.D.; and Kunapuli T. Madhusudhan,[3] Ph.D.

Fatal Meningitis and Encephalitis Due to *Bartonella henselae* Bacteria

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ABSTRACT: Bacterial infection due to *Bartonella henselae* commonly develops in children and young adults following cat/dog contacts and/or cat/dog scratches. Regional lymphadenopathy is its most common clinical expression. However, encephalitis and Parinaud's syndrome (oculoglandular syndrome) have also been reported as has systemic illness. A review of the international literature in all languages revealed no fatal complications in immunocompetent hosts. A four-year-old white child with no underlying illness began to have seizure-like activity. She was taken to a local hospital and subsequently transferred to a medical center. The child was treated aggressively for seizures and fever of unknown origin. However, her condition rapidly declined and she died without a specific diagnosis. At autopsy there was marked cerebral edema with no gross evidence of acute meningitis. Microscopic exams revealed multiple granulomatous lesions as well as a meningitis and encephalitis. A variety of cultures and stains were negative for acid fast and fungal organisms. Warthin-Starry stains of involved tissue including brain and liver revealed pleomorphic rod shaped bacilli consistent with *Bartonella henselae.* Analysis of brain tissue with polymerase chain reaction (PCR) and Southern blot for the deoxyribonucleic acid (DNA) was definitive for DNA of *Bartonella henselae* bacteria.

KEYWORDS: forensic science, meningitis, encephalitis, *Bartonella henselae,* deoxyribonucleic acid typing, polymerase chain reaction, cat scratch, fatality

Although cat-scratch disease (CSD) was first described in Paris in 1931 by Debre et al. (1), it was not until 1950 that the first cases were reported. In the United States physicians recognized patients with CSD in 1932, but the first American case was not published until 1951 (2). The cause of CSD remained undetected until 1983 when Wear et al., at the Armed Forces Institute of Pathology used the Warthin-Starry and Brown-Hopp's tissue gram stain finding bacteria in the lymph nodes of patients with the disease (3). They demonstrated the presence of small pleomorphic, gram-negative, argyrophilic bacilli in sections of lymph nodes with CSD.

Bartonella henselae is a bacillus with a worldwide distribution and is found in all races. The bacilli are best demonstrated in tissue by the Warthin-Starry silver impregnation stain. They are fastidious and require special culture techniques which include high humidity and CO_2 of 5% (4). In addition they are slow growing with colonies first appearing 9 to 40 days after incubation (5).

Transmission and infection follow direct cat and direct or indirect dog contact including licking, biting, and scratching. The bite of an anthropod vector can also be involved in this chain; however, the domestic cat is the major persistent reservoir for the bacteria. Kittens less than 12 months of age are even more infectious than adult cats, especially ones infected with fleas. The organism has also been identified in cat fleas which have been shown to be vectors. Most animals associated with human disease are healthy and have negative skin tests for the bacteria. There are no reports of human to human transmission (5,6). It is important to note that there may be no observable lesions from the involved animals and insects.

Cat scratch disease is not a reportable one, thus the overall incidence is unknown. However, using national hospitalization databases the incidence of cat scratch disease was estimated to be between 0.77 and 0.86 per 100,000 population per year. For a similar ambulatory national database the diagnosis was 9.3 per 100,000 population per year (7). It occurs worldwide but is most commonly found in warm and humid climates.

In most instances the CSD is self-limiting, produces cutaneous lesions and infects regional lymph nodes. It also has been reported as a cause of status epilepticus due to encephalopathy and Parinaud's syndrome (oculoglandular syndrome). Systemic disease is associated with a longer duration of symptoms such as fever, malaise, and fatigue, and skin rashes. In addition, there may be generalized lymphadenopathy and weight loss. Some patients also have pleurisy, arthritis, splenic or liver abscesses, mediastinal masses, prolonged fevers, and severe weight loss. Patients with disease of varying severity recover. Fatal complications have never before been reported (8).

This paper is a case study of a four-year-old white female with fatal meningitis, encephalitis and granulomatous lesions of the lung, liver and spleen. The etiology of the lesions (*Bartonella henselae*) was documented first with Warthin-Starry silver stains and then with deoxyribonucleic acid (DNA) studies using both polymerase chain reaction (PCR) and Southern blot methods.

[1] Forensic Medical, 850 R. S. Gass Blvd., Nashville, TN.
[2] Department of Pathology, Vanderbilt University Medical Center, Nashville, TN.
[3] Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, AR.

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Such a case has never before been reported in the international literature.

Case Report

The decedent was a four-year-old white female who resided at home with her mother, three-year-old healthy sister, and her mother's fiancee (not the biological father of the case). There were no significant illnesses of any kind in the case or her sibling. Two weeks prior to the onset of her illness a visibly enlarged left neck lymph node associated with torticollis was noted by her mother. Left sided facial twitching and some dysphagia were also observed. She was taken to her local family doctor who prescribed penicillin. One week after beginning the antibiotics, she had a febrile illness and missed school. On the day of admission to the hospital she was found by her grandmother with generalized seizure activity. The day prior to the seizures she did not "act like herself and answered questions in a strange manner." During this period there were no disturbances of gait or coordination. In addition she had a fever to 104.5 F, vomited once, complained of bilateral groin pain and had one loose watery stool.

The environmental history included the following facts. The grandmother of the case, whom she had recently visited, had cats and kittens as well as dogs and sheep. The case had no known bites or scratches from them. She had no known history of exposure to ticks; however, she had recently been bitten by several mosquitos.

Her past medical history included the fact that she was delivered via emergent cesarean section at term due to failure to progress and "a wrapped umbilical cord." Subsequently the perinatal course was uneventful. Her mother reported that her daughter was "normal" until about two years of age when she began to evidence developmental delay. The mother associated this delay with an episode of prolonged otitis media requiring multiple courses of oral antibiotics.

On admission to the local hospital her temperature was 101°F. Other vital signs included a blood pressure of 104/34, heart rate of 160/min and respiratory rate on a ventilator of 25/min. She was sedated, unresponsive to pain and her eyelids were twitching. Physical exam included a 1 cm firm lymph node in the left submandibular region. She had no skin rash, scratch, or bite. The remainder of the examination was negative. The electroencephalogram confirmed the history of seizure activity. Management for her status epilepticus included mechanical ventilation, and medical therapy with dilantin, phenobarbital and pentobarbital. After cerebrospinal, blood, and urine cultures for bacteria, fungi, viruses, and mycobacteria were obtained she was placed on vancomycin, rocephin, and acyclovir.

Admission laboratory data included the following hematology data: WBC of 27.8 thousand/μL, with 83% neutrophils; Hct. 31.6%, Hgb. 11.1 g/dL and platelets of 588 thousand/μL; chemistries were total BR of 0.5 mg/dL, conjugated BR of 0.2 mg/dL, albumin 3.1 g/dL and SGPT of 30 U/L. Electrolytes, glucose, and BUN, and creatinine were unremarkable. Cerebral spinal fluid studies were unremarkable. Urinalysis revealed cloudy yellow urine with 1 plus protein. All cultures for organisms revealed no growth. She remained on ventilatory support at high pressures. A CAT scan after four days revealed severe generalized cerebral edema. Subsequently renal failure developed with a BUN of 33 mg/dL and a creatinine of 2.8 mg/dL. She remained comatose and unresponsive neurologically and died four days after admission.

Postmortem Findings

A postmortem examination revealed a normally developed four-year-old white female with no evidence of scratches or bites on the body. In addition, there was no evidence of trauma. Internally there were no congenital anomalies. The brain weighed 1224 g (normal weight for age is 1191 g) with marked flattening of the gyri. There was no evidence of herniation but bilateral uncal grooving was present. No gross evidence of an inflammatory exudate was identified. There were bilateral serous pleural effusions (100 cc on the

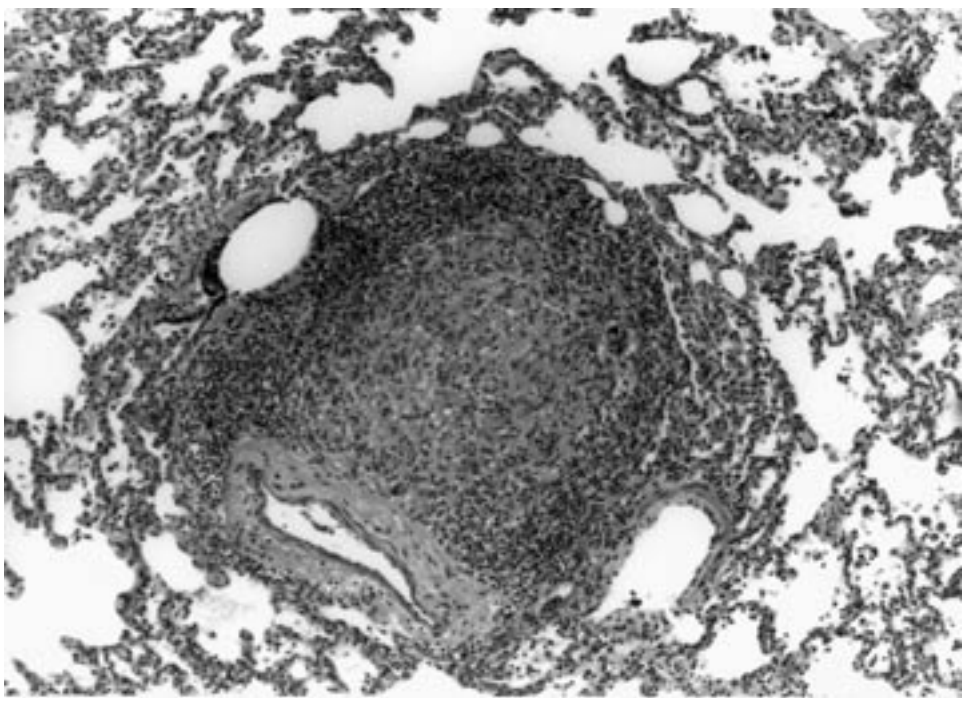

FIG. 1—*Lung section with noncaseating granulomatous lesion (10×).*

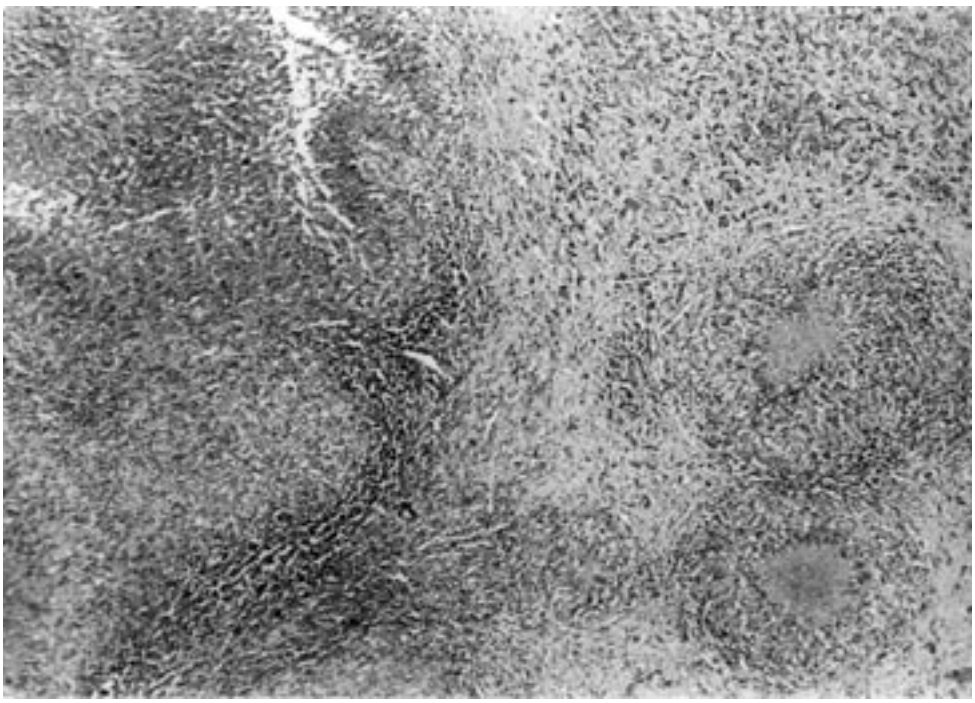

FIG. 2—*Liver section with a large stellate granuloma and many satellite granulomas (4×).*

right and 300 cc on the left). In addition there were 300 cc of serous ascites. Multiple white-tan soft lesions (3 mm in diameter) were present on the surfaces of the liver and spleen.

Microscopic Examination

Histological studies of the lung revealed noncaseating granulomatous lesions with a central core of macrophages and a peripheral Langerhans' giant cell (Fig. 1). Additional sections revealed no caseous necrosis or necrotizing granulomatous lesions. However, the liver exhibited a large central stellate granuloma with many satellite granulomas. These contained classical caseous necrosis, necrotic debris and palisading macrophages with Langerhans' giant cells (Fig. 2). The spleen also revealed similar granulomatous lesions. Special stains for fungal and acid fast organisms were negative in all three tissues. Warthin-Starry stains of the liver revealed pleomorphic rod shaped bacilli consistent with *Bartonella henselae.* The tonsils, thymus, and bone marrow revealed no granulomatous lesions. Multiple brain sections demonstrated mature lymphocytes in the subarachnoid spaces, generalized cerebral edema, and acute ischemic changes of the neurons (Fig. 3). In addition brain parenchyma revealed pleomorphic rod shaped bacilli consistent with *Bartonella henselae* (Fig. 4). Analysis of brain tissue using combined polymerase chain reaction (PCR) and radiolabeled Southern blot techniques for deoxyribonucleic acid (DNA) identified *Bartonella henselae bacteria* (Fig. 5).

Discussion

Clinically CSD is divided into typical and atypical types (4). This case belongs in the atypical group because the child was immunocompetent and because of the systemic and neurological manifestations, multiple organ involvement including multiple granulomatous lesions, encephalitis, and meningitis.

Encephalopathy due to cat scratch disease was first reported in 1952 (10). Other reports of CSD reviewed patients with neurologic complications, including encephalopathy (11). A large series of 76 patients with neurological complications was reported in 1991 (12). All of these patients recovered within one year, with the majority recovering within one to three months. A cluster of five children with acute encephalopathy associated with cat-scratch disease was reported from south Florida (13). More recently cat scratch disease encephalopathy was identified as a cause of status epilepticus in school-aged children (8). However, none of these series of cases has reported a death associated with the cat scratch encephalopathy. Although several cases have been reported as deaths in the literature they did not meet the diagnostic criteria for cat scratch disease (7).

Conclusions

At autopsy, this case had granulomatous lesions of the liver, spleen, and lungs. However, the cause for those lesions remained undetermined until one of us (J.E.J.) suggested using Warthin-Starry stains to check for cat scratch disease. Further investigation revealed that to be the cause of death. There are several lessons to be learned from this case, the first one of its kind documented in the literature.

Since there have never before been reported deaths from cat scratch disease, it is not one that the pathologist keeps in mind. Further, *Bartonella henselae* are fastidious slow growing bacteria which can take anywhere from one to six weeks to grow. Unless the forensic or general pathologist understands this cultures are destroyed and the cause of death can quite easily go undetermined. In this particular case, meningitis and encephalitis along with granulomatous lesions of the liver, spleen, and lungs were discovered. With this clinical picture, when the cause of death cannot be determined, consideration of cat scratch disease should be considered in

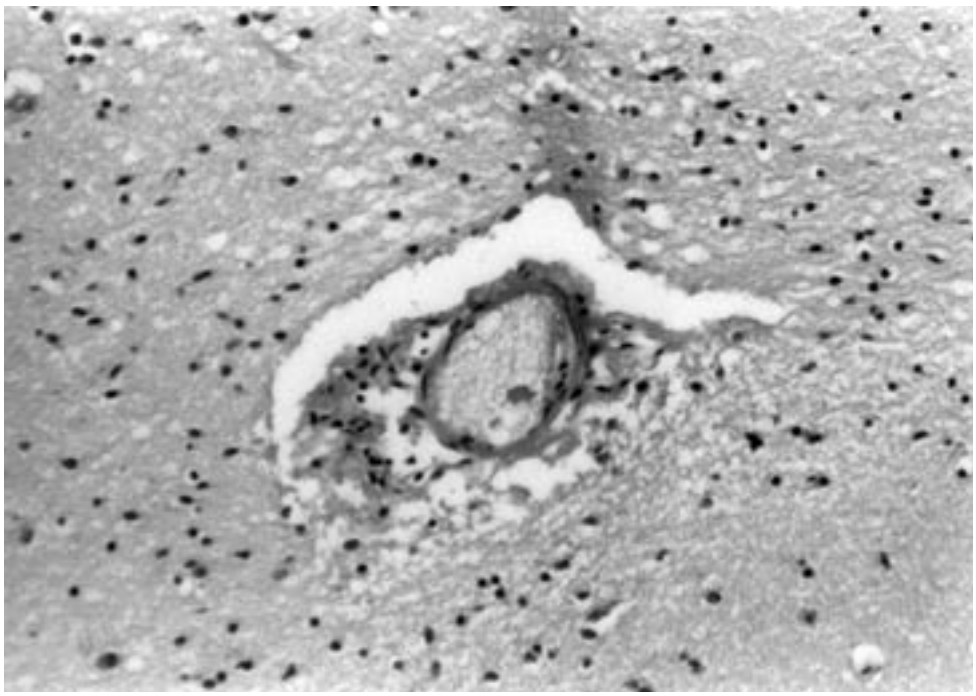

FIG. 3—*Brain section with perivascular mature lymphocytes and parenchymal edema (40×).*

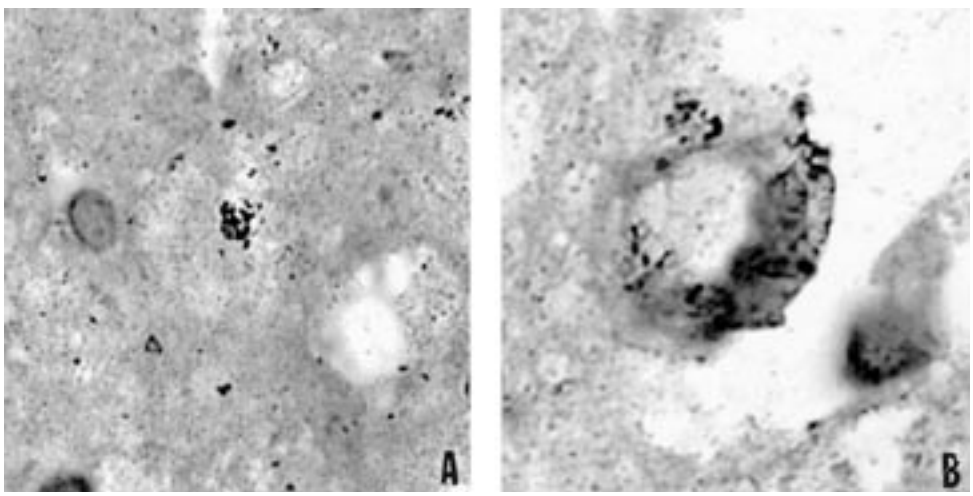

FIG. 4—*Silver deposition stain performed on brain parenchyma demonstrates filamentous organisms within parenchymal tissue (4A) and in the perivascular space (4B). Warthin-Starry stain, ×250 original magnification.*

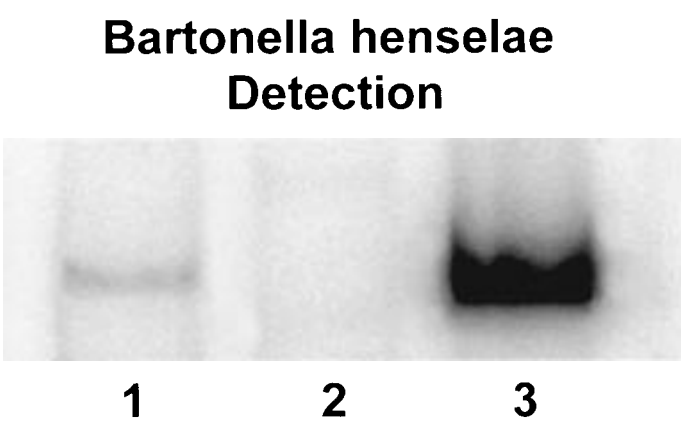

FIG. 5—*Electrophoresis:* Bartonella henselae. *Lane 1 = Patient Brain Tissue; Lane 2: Negative Control; Lane 3: Positive Control.*

the differential diagnosis. This case also reinforces the need to examine the living environment including pets and other animals that are part of the life of a case.

In summary, this is the first report of the death of a four-year-old child with meningitis, encephalitis, and granulomatous lesions of the spleen, liver, and lung as a result of *Barontella henselae,* who had no immunocompromising conditions. Because testing of those lesions with Warthin-Starry stains was suggested and confirmed with DNA studies, the cause of death, cat scratch disease was found.

Acknowledgments

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Additional information:
John E. Gerber, M.D.
Forensic Medical
850 R. S. Gass Blvd.
Nashville, TN 37216