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A Rare Case of Bartonella Encephalitis With Hemiplegia

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Abstract

The authors describe a 12-year-old girl with an atypical presentation of *Bartonella* encephalitis. She presented with fever and altered mental status and developed flaccid paralysis of her left upper extremity a day later. An electroencephalogram showed slowing over her right hemisphere. She had mild leukocytosis and bandemia, but her imaging and cerebrospinal studies were unrevealing. After five days, her symptoms resolved and she was discharged home on doxycycline due to suspicion for *Bartonella* encephalitis. The patient admitted to playing with a kitten two months prior, but she lacked the classic regional lymphadenopathy. *Bartonella* titers were sent during her hospitalization and returned positive after her discharge. Cat scratch disease neurologic manifestations are uncommon, with hemiplegia being exceedingly rare. This case illustrates that focal neurologic signs may develop during cat scratch disease infection and suggests that cat scratch disease encephalitis should be considered during evaluation of a pediatric patient with acute flaccid paralysis.

Keywords

EEG, electroencephalogram, pediatric, adolescents, encephalitis, Todd paralysis, infectious disease, cat scratch disease, epidemiology

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In the United States, there are an estimated 22000 cases per year of cat scratch disease (CSD), with over 2000 cases requiring hospital admission.[1] Cat scratch disease is caused by *Bartonella henselae* and most often presents with fever and regional lymphadenopathy.[1] Over 90% of patients recall contact with a cat prior to illness.[1] It is primarily a pediatric disease: One study reported 84% of cases occurred in patients younger than 18 years.[2] The higher incidence in the younger population may be attributed to children having an immature immune system or children playing with cats more frequently than adults do. Neurological manifestations occur in up to 7% of patients and on average appear within 2 weeks after fever and lymphadenopathy onset.[1,2] The authors present a case of cat scratch disease encephalitis with acute flaccid paralysis of the left arm alongside a electroencephalogram (EEG) correlate of right hemispheric slowing.

Case Presentation

A 12-year-old girl presented to the emergency department in the early morning after her parent found her hiding under and hitting herself against her bed while jerking and crying. This pediatric patient with acute onset of altered mental status and possible seizure had a recorded temperature of 103.1°F and a Glasgow Coma Scale of 12. She opened her eyes to voice, she had confused speech, and she localized to pain in all extremities. She had no known prior episodes and her family history was negative for seizures, although she had a personal history of anxiety treated with sertraline. A rapid antigen detection test for group A streptococcus was positive, but she had no sore throat or tonsillar erythema on examination, indicating carrier status. A complete blood count demonstrated mild leukocytosis

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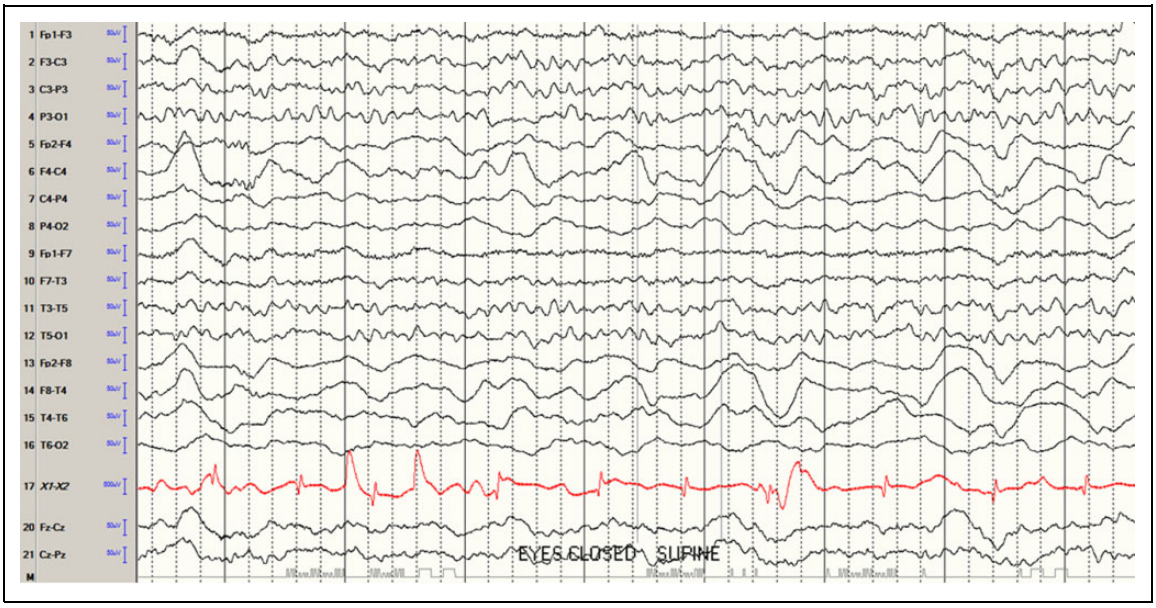

Figure 1. Electroencephalogram showing slowing over right hemisphere consistent with a widespread functional disturbance in that hemisphere.

(white blood cells, 14.6/μL) and bandemia (18%). Urine drug screen, complete metabolic panel, cerebrospinal fluid (CSF) cell counts, urinalysis, and head computed tomography scan were all within normal limits. The patient's initial presentation of altered mental status with a high fever and abnormal peripheral white blood cell count prompted treatment with vancomycin, ceftriaxone, and acyclovir due to a concern for infectious encephalitis. Despite the normal CSF, infectious encephalitis was still in the differential diagnosis. The patient's presentation raised clinical suspicion for an encephalitis and some studies demonstrate normocellular CSF can occur in encephalitis, although more rarely.[3] She was started on levetiracetam for seizure prophylaxis due to concern that her initial presentation may have represented a postictal state after an unwitnessed seizure, particularly since herpes simplex virus encephalitis was in the differential diagnosis.

The morning after admission, she was found to have left upper extremity flaccid paralysis that improved after two days. She also experienced urinary incontinence overnight. Magnetic resonance imaging (MRI) with and without contrast of the brain and magnetic resonance angiography of the head showed no abnormalities except for mild paranasal sinus inflammation. A routine EEG showed slowing over her right hemisphere consistent with a widespread functional disturbance in that hemisphere (Figure 1). With these EEG and head imaging findings, the patient's paralysis was attributed to a Todd paralysis phenomenon. Her urinary incontinence was attributed to subclinical seizures versus encephalopathy.

Blood, urine, and CSF cultures were sent and returned no growth. Herpes simplex virus polymerase chain reaction (PCR) and varicella virus PCR were both negative in the CSF. The treatment team discontinued her vancomycin, ceftriaxone, and acyclovir on day three of hospitalization. West Nile virus immunoglobulin M and Epstein-Barr virus PCR were negative. Serum *Mycoplasma pneumoniae* antibodies demonstrated elevated immunoglobulin M at 1861 U/mL, but PCR was negative. Serum anti-streptolysin (ASO) titers were elevated at 675 IU/mL, and anti-DNAse B antibodies were high at 583 U/mL. Serum arbovirus panel was sent and resulted negative. Serum *Bartonella* titers were sent as well.

The patient improved clinically with return of her left arm function on the fifth day of hospitalization. Infectious disease team was consulted, and they interviewed the family with targeted questions to look for unusual exposures to more uncommon infectious agents. The team learned through their questions that the patient had played with a friend's kitten two months prior to admission. Empiric treatment with doxycycline was initiated due to suspected *Bartonella* encephalitis. The patient was discharged on doxycycline 100 mg twice daily and completed a total 14-day course. *Bartonella* titers came back after time of discharge at 1:2560. At her follow-up appointment one week later, the patient had made a complete recovery. She stayed on levetiracetam for six months and then was weaned off the medication, as she was seizure-free at the six-month follow-up.

Discussion

Bartonella henselae bacteria can be transmitted from a cat scratch or bite, from cat saliva that contacts broken skin or mucosal surfaces, or from a cat or dog with fleas.[4] Although our patient recalled playing with a kitten, her presentation did not include any enlarged and erythematous lymph nodes as is typical for this disease.[4]

The patient's elevated anti-DNAse B antibodies and elevated ASO titers are indicative of past infection with group A streptococcus.[5] In addition, all treatment teams felt that

pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections was an unlikely diagnosis, as the patient did not exhibit features of tic disorder or obsessive compulsive disorder associated with the syndrome.[6]

The patient's positive *Mycoplasma pneumoniae* immunoglobulin M must be considered in combination with the patient's negative *Mycoplasma pneumoniae* PCR: this combination of results is not necessarily diagnostic of acute infection.[7-10] The Infectious Disease Society of America recommends PCR as the diagnostic test of choice due to high specificity.[11] One small study suggests that serologic tests do not distinguish *Mycoplasma pneumoniae* disease status from carrier status.[12] A larger study looking at neurologic manifestations of *Mycoplasma pneumoniae* noted 2 distinct disease patterns: one characterized by high immunoglobulin M and frequent respiratory symptoms and the other with neither trait.[13] Our patient did not fit either clinical picture in that larger study.[13] Nevertheless, a coinfection picture cannot be completely ruled out in our patient.

Diagnosis of *Bartonella henselae* infection is also challenging due to several factors. The length of time from obtaining serum for testing to receiving the test result is over one week in our hospital's laboratory. Specificity and sensitivity of IgG titers have been studied with varying results.[14-17] For high titers like our patient's, one study suggests that there is a 100% sensitivity and a 98.5% specificity for cat scratch disease.[17] Generally, a titer result of greater than 1:256 is suggestive of acute infection.[14–17] High titers alongside encephalopathy support the diagnosis of *Bartonella* encephalitis.

The infectious disease team chose doxycycline monotherapy rather than adding rifampin due to concerns about the family's compliance with taking antibiotics as well as levetiracetam when discharged from the hospital. Doxycycline with rifampin is the preferred regimen for cat scratch disease–associated neurologic disease.[18]

Focal neurologic signs are common when considering all etiologies of pediatric infectious encephalitis.[19] In one large study from Toronto, 60% of pediatric encephalitis cases presented with focal seizures and 50% had other focal neurologic signs.[19] Of the patients with cat scratch disease who have neurological manifestations, encephalopathy, status epilepticus, convulsions, retinitis, cerebral vasculitis, and transverse myelitis are all documented presentations.[20-24] Encephalopathy is the most common neurologic manifestation of cat scratch disease, and it can present several weeks after initial exposure to a cat.[2,25]

One case report from Brazil describes a child who had cat scratch disease–associated left hemiplegia and a right frontoparietal lesion on head imaging.[26] Another case report from Peru describes a child who had temporary right hemiparesis after cat scratch disease–associated status epilepticus, suggestive of Todd paralysis.[27] There have also been at least two case reports of cat scratch disease–associated vasculitis as etiology for stroke and resultant hemiparesis.[2] One retrospective review found 20 cases of cat scratch disease–related vertebral osteomyelitis, and within that case series, there is one patient who had severe transient paresis.[28] These case reports suggest that the flaccid paralysis from cat scratch disease encephalitis could be due to a direct infection of the right hemisphere, a postictal Todd paralysis, or spinal cord involvement. However, the mechanism by which Bartonella causes CNS disease is currently not well understood. One unfortunate case describes a patient who died from cat scratch disease–associated encephalitis and microglial nodules were found on his brain biopsy at autopsy.[29] Further study on this mechanism through animal models may assist with developing treatment approaches that shorten duration of symptoms.

In our patient, focal arm paralysis with confusion and incontinence was found the morning after the patient had been admitted, on morning rounds. Since she went the night without these changes being noted on examination, our working hypothesis was that she had an unwitnessed seizure during the night. Whether she had a focal motor seizure (resulting in Todd paralysis) followed by secondary generalization (resulting in confusion and incontinence postictally) is difficult to ascertain. She may also have had two separate seizures during the night, 1 focal motor, and 1 with secondary generalization.

As illustrated in the worldwide cases discussed above, an important differential the team considered was direct infection of the contralateral hemisphere. The MRI obtained did not have evidence of direct infection on postcontrast sequences. Another differential considered was spinal cord involvement due to the urinary incontinence. Magnetic resonance imaging of the spine was not obtained during her hospitalization. On repeated physical examinations during the hospital stay, she did not develop increased tone or hyperreflexia in her left upper extremity, as would be expected for spinal cord lesions (upper motor neuron findings after early lower motor neuron findings), and her incontinence also resolved. The patient also had no personal or family history of classic migraine or hemiplegic migraine, the latter of which is a diagnostic possibility in children with acute flaccid paralysis.

Conclusion

To our knowledge, our patient's case is the second reported case of cat scratch disease associated with focal weakness. The report of her disease adds to the literature, demonstrating that focal neurologic signs on examination, including acute flaccid paralysis, may indicate cat scratch disease encephalopathy. Given the right clinical history, this disease should be considered, even without the classic regional lymphadenopathy. Our case also illustrates that in cases of fever and focal paralysis, if initial imaging is negative, EEG can provide valuable diagnostic assistance and help to guide medical management.

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Author contributions

LR, KR, CM and AB contributed to conception and design. All authors drafted the manuscript and gave final approval. All authors

agree to be accountable for all aspects of the work in ensuring that questions relating to the accuracy.

Declaration of Conflicting Interests

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Ethical Approval

The patient's information has been anonymized according to ICMJE guidelines.

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