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An Unusual Case of Transient Psychosis from *Ehrlichia* Infection

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The incidence of *Ehrlichia* infection has been increasing since it was first discovered in 1986. *Ehrlichia* is transmitted by ticks and is endemic to many areas of the United States. Patients with symptoms of *Ehrlichia* may present to their primary care provider or an emergency department. The authors describe the case of a 50-year-old woman who was initially diagnosed with transient ischemic attack in the emergency department after experiencing facial and unilateral extremity weakness. Imaging studies were persistently negative for brain abnormality. She followed up with her primary physician with persistent symptoms, which began to include hallucinations. She was diagnosed with *Ehrlichia* infection through laboratory studies. This patient was treated with doxycycline therapy for three weeks and has not had a recurrence of symptoms. The diagnosis of ehrlichiosis needs to be considered in the differential for patients with neurologic and/or psychiatric symptoms, especially in areas of the country where tick-borne illnesses are endemic.

Ehrlichiosis has been increasing in incidence in the United States since its discovery in 1986. Nearly 600 cases of ehrlichiosis were reported to the Centers for Disease Control and Prevention (CDC) in 2006, the last year for which the CDC has published data. In 2001-2002, ehrlichiosis incidence was highest in persons 50 to 59 years of age.[1]

Case presentation

Chief complaint: A 50-year-old female, D.L., presented to a primary care office as a new patient for evaluation to follow-up several hospital visits.

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History of present illness: Within the past two months, the patient had visited the local emergency department (ED) five times with complaints of facial numbness in addition to slurred speech, unilateral upper extremity weakness, paresthesia, and headaches that lasted several hours at a time.

At each ED visit, the patient was examined for stroke. Testing included neurological examinations, laboratory studies, and imaging. Each work-up failed to reveal any significant cerebrovascular disease.

Over the course of her five visits, several computed tomography and magnetic resonance imaging scans of her brain were done and did not reveal any pathology.

The patient was discharged each time with the diagnosis of a transient ischemic attack and was prescribed aspirin, simvastatin, and lisinopril.

Three days before her initial office visit, D.L. had a new and alarming symptom. While getting ready for bed, she thought she heard witches casting spells and pit-bulls barking outside her house. This was a very frightening experi-

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ence for her. Her husband, who was present at the time, reported that she frantically called all of her pets inside and examined all the locks on all the doors. Although the experience was disturbing, given her frustration with the ED, the patient decided not to visit the hospital.

Past medical/surgical history: D.L.'s history was only significant for recently diagnosed transient ischemic attacks.

Past psychiatric history: D.L. had no prior psychiatric symptoms or disease.

Medications: Metoprolol, lisinopril/hydrochlorothiazide, simvastatin, and aspirin.

Social history: D.L. denied using tobacco, daily alcohol, or recreational drugs. She is employed as a laboratory technician.

Family history: Significant family history included hypertension and coronary artery disease in her parents.

Physical examination: Vital signs (blood pressure 120/80 mm Hg, temperature 98.1°F, respirations 16/min, pulse 82 bpm) were within normal limits. D.L. was a well-appearing, overweight female. A thorough physical examination, with attention to neurologic examination, failed to reveal any asymmetries. Cranial nerve functions including pupil dilation, visual fields, fundi, and extra-ocular movements were normal. There were no abnormalities of facial, palatal, or lingual musculature, and speech was natural. The motor examination revealed normal tone and strength throughout. Sensory examination was symmetric to pin and temperature. Deep tendon reflexes were symmetric and toes were downgoing. Gait and Romberg testing were unremarkable. Cardiac examination failed to reveal a murmur. No rash was detected. Respiratory and abdominal examinations revealed no abnormalities. Psychiatric examination demonstrated a well-groomed woman oriented to person, place, and time with no abnormalities.

Differential diagnosis: At that point, the differential diagnosis included transient ischemic attack, tick-borne illness, heavy metal poisoning, neurosyphilis, cytomegalovirus, and new-onset psychiatric disorder.

Work-up: The patient was given a prescription for laboratory studies and told to return to the office to review the results. Blood tests included complete blood count/differential, complete metabolic panel, heavy metal screen, thyroid-stimulating hormone, rapid plasma reagin, B_{12}/folate, HIV, antinuclear antibody, Ehrlichia IgM/IgG, *Babesia* IgM/IgG, and Lyme titer.

Results: Lab results demonstrated a positive Ehrlichia IgG titer of 1:512 and IgM titer of 1:80 (normal values are $<$1:64 and $<$1:20, respectively). All other testing showed results within normal limits.

Treatment: When D.L. returned to the office, she was advised of her abnormal laboratory results. A three-week course of doxycycline 100 mg twice daily was prescribed and she was referred to an Infectious Disease specialist.

Follow-up: D.L. was seen back in the office several days after completing antibiotic therapy and again approximately two months after diagnosis. Having completed her course of treatment, the patient has not had recurrent neurologic or psychiatric symptoms.

Discussion

Ehrlichiosis consists of two separate tick-borne illnesses: human monocytic ehrlichiosis (HME) and human granulocytic anaplasmosis (HGA). HME is caused by *Ehrlichia chaffeensis* and is usually found in the mid-Atlantic, southeast, and south central United States. It is transmitted by the Lone star tick (*Amblyomma americanum*) and its reservoir is the white-tailed deer. A second cause of HME is *Ehrlichia ewingii*, which shares a vector and reservoir with *E. chaffeensis*. Cases of *E. ewingii* have been documented in Florida and Missouri. HGA is caused by *Anaplasma phagocytophilum*, is transmitted by the deer tick (*Ixodes* spp.), and has reservoirs in many animals including the white-footed mouse, white-tailed deer, raccoons, skunks, and chipmunks. Documented cases of HGA are found from coast to coast.[2,3] It should be noted that D.L. lives in a heavily wooded area in Southern New Jersey, where there is an abundance of each of these vectors.

Patients typically present with symptoms after an incubation period of approximately nine days. The syndrome most commonly starts with the sudden development of fever, chills, headache, nausea, fatigue, malaise, and myalgia. The patient may also develop diarrhea, abdominal pain, arthralgia, confusion, and cough. Rash occurs more commonly in children and involves the trunk but spares the hands. A rash is even less common in HGA.[3-5] Of these presenting symptoms, this patient only had a headache. She may have had other symptoms earlier, considered them to be insignificant, and neglected to mention them.

Mortality rates in *E. chaffeensis* and *A. phagocytophilum* are approximately 3% and 1%, respectively. Complications of infection include acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), hemorrhage, acute renal failure, or meningitis. Central nervous system manifestations are rare but can include mental status changes, meningitis-like symptoms, cranial nerve palsies, plexopathies, seizures, hyperreflexia, ataxia, optic neuritis, and demyelinating disorders. Chronic infection can result in memory and cognitive impairments, headache, and neuropathy. Should these occur, a practitioner should con-

Table 1 Diagnostic criteria for *Ehrlichia* infection

Patient must have:
Fever
One of the following:
• headache
• myalgia
• anemia
• leukopenia
• thrombocytopenia
• transaminitis
One of the following:
• IgG antibody 4x normal in 2 samples by IFA assay taken 2–4 weeks apart
• identification of DNA by polymerase chain reaction
• *Ehrlichia/Anaplasma* grown in culture
• Antigen present in biopsy sample

sider the possibility of an immunosuppressed patient. Central nervous system (CNS) infections are more common with *E. chaffeensis* than *A. phagocytophilum.*[3,5] D.L. had a preponderance of CNS symptoms, including facial and extremity weakness and hallucinations, and therefore may have been more likely to have been infected with *E. chaffeensis*. The exact identity of the organism remains unknown, however.

The differential diagnosis of ehrlichiosis includes: meningitis, encephalitis, Lyme disease, Rocky Mountain spotted fever, babesiosis, Colorado tick fever, brucellosis, Q fever, leptospirosis, typhus, and thrombotic thrombocytopenia purpura.[4] To make the diagnosis, the CDC promulgates a system that uses both symptom (i.e., subjective) and laboratory (i.e., objective) criteria (Table 1). The patient must have a documented fever with at least one of the following: headache, myalgia, anemia, leukopenia, thrombocytopenia, or transaminitis. In addition, one of the following three must be demonstrated: an increase in the IgG-specific antibody by at least four times normal by immunofluorescent assay twice, on samples taken two to four weeks apart; identification of DNA by means of polymerase chain reaction; finding of *Ehrlichia/Anaplasma* grown in culture; or presentation of the antigen in biopsy.[3] It is unknown whether this patient had fever during her initial illness, but she did have headache. A single IgG titer was obtained, which was four times higher than the normal value, but a second was not completed. Instead, the patient was sent to see an infectious disease specialist at that time, who confirmed the diagnosis of *Ehrlichia* infection.

Although ehrlichiosis itself is a relatively uncommon diagnosis, this case was even more interesting because of the patient's history of hallucinations. Literature on the subject of hallucinations in ehrlichiosis is rare. A Medline search was performed from 1950 to present using the terms "ehrlichiosis," "Ehrlichia," "hallucinations," "psychosis," and "psychiatry" and then limited to "English language" and "humans." The results of each of these individual searches were combined in various ways; however, no articles were returned. After this, a Google Scholar search was performed, which did yield three articles. Of these, only two had any epidemiologic data regarding hallucinations.

Olano et al. studied 41 patients with laboratory-confirmed acute HME and reviewed their symptomatology. Of the 41 patients, four had documented hallucinations, giving a prevalence of nearly 10%.[6] Ratnasamy et al. listed the symptoms of 21 patients with ehrlichiosis. One patient was reported as having hallucinations, and nine had confusion, disorientation, and delirium.[7] Everett et al. followed 30 patients with "suspected human ehrlichiosis." Of these 30 patients, six developed mental status changes. According to the authors, mental status changes were mainly confusion or hallucinations or both, but they did not specify how many of the six had hallucinations.[8]

The treatment for ehrlichiosis is doxycycline for both adults and children. The dose is 4 mg/kg/day every 12 hours to a maximum dose of 200 mg daily.[9] Other treatment agents include chloramphenicol, azithromycin, fluoroquinolones, and rifampin; however, these have yet to be effectively evaluated in appropriate studies. Treatment is for at least seven days and/or for at least three days after fever subsides. It should be understood that some symptoms (malaise, headache, and weakness) may continue for weeks.[3]

D.L. was treated with three weeks of doxycycline, 100 mg twice a day, per the recommendation of her infectious disease specialist, with complete resolution of her symptoms. In the five months between her symptoms and submission of this manuscript, she has remained symptom free.

Conclusion

Ehrlichiosis is a tick-borne illness that can present with a number of different complaints. Recognizing this illness as a potential cause may save many patients lengthy and expensive ED visits. Blood testing is readily available and treatment is simple and effective with oral doxycycline in most cases. Primary care physicians, especially those in areas endemic for tick-borne illnesses should keep ehrlichiosis in their differential diagnosis in patients with neurologic and/or psychiatric symptoms.

References

1. Centers for Disease Control and Prevention: Ehrlichiosis statistics. Available at: http://www.cdc.gov/ehrlichiosis/.
2. Thomas R, Dumler JS, Carlyon JA: Current management of human granulocytic anaplasmosis, human monocytic ehrlichiosis and *Ehrlichia ewingii* ehrlichiosis. Exp Rev Antiinfect Ther 7:709-722, 2009
3. Picker LK; Committee on Infectious Diseases, American Academy of Pediatrics: Red Book®: 2009 Report of the Committee on Infectious Diseases, 28th ed. Chicago, IL: American Academy of Pediatrics, 2009
4. Hongo I, Bloch K: Ehrlichia infection of the central nervous system. Curr Treatment Options Neurol 8:179-184, 2006

5. Dumler JS: Anaplasma and *Ehrlichia* infection. Ann N Y Acad Sci 1063:361-373, 2006
6. Olano J, Hogrefe W, Seaton B, et al: Clinical manifestations, epidemiology, and laboratory diagnosis of human monocytotropic ehrlichiosis in a commercial laboratory setting. Clin Diagn Lab Immunol 10:891-896, 2003
7. Ratnasamy N, Everett ED, Roland W, et al: Central nervous system manifestations of human ehrlichiosis. Clin Infect Dis 23:314-319, 1996
8. Everett ED, Evans K, Henry RB, et al: Human ehrlichiosis in adults after tick exposure: diagnosis using polymerase chain reaction. Ann Intern Med 120:730-735, 1994
9. Centers for Disease Control and Prevention: Traveler's health–yellow book. Available at: http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-5/rickettsial-and-related-infections.aspx. Accessed August 29, 2011.