A Case of Anaplasmosis during a Warm Minnesota Fall

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Abstract
A healthy 33 year old male presented in December with a 3 week history of fever and fatigue. He had been deer-hunting in northern Minnesota 1 month prior and had sustained a tick bite. Extensive laboratory investigations and a lumbar puncture were conducted. He was empirically with doxycycline and had rapid improvement in his symptoms. Subsequently, PCR and serologic testing returned positive for Anaplasma phagocytophilum. Anaplasmosis is a tick-borne illness caused by the bacterium Anaplasma phagocytophilum and is typically seen in the warmer months. This patient’s presentation in December was uncommon for a tick-borne illness in Minnesota. Regional weather records demonstrated unseasonably warm temperatures during the patient’s trip. Ixodes ticks are known to be sensitive to temperature and humidity, which likely contributed to increased tick activity, leading to disease transmission. This case highlights the importance for clinicians to be aware of local weather patterns and how this might influence seasonal disease presentations.

Keywords
tickborne illness, anaplasmosis, human granulocytic anaplasmosis, Anaplasma phagocytophilum, Ixodes

Case Presentation
A previously healthy 33 year old male presented in December to a rural southwestern Minnesota emergency department with a 3 week history of fevers and fatigue. In early November, the patient had been deer hunting near Leech Lake, Cass County, in Northern Minnesota. His trip was successful and he field dressed his deer wearing gloves for protection. Four days later, a tick of unknown type was noted on his lower back by his family and successfully removed. Two weeks after his trip, he started developing fevers and fatigue. Additionally, he reported arthralgias, myalgias, and a headache. He described his headache as frontal in location, sharp in nature, associated with photophobia and neck stiffness. He denied any rash. Given the nature of his symptoms and the concurrent COVID-19 pandemic, he sought outpatient COVID-19 PCR testing on 2 occasions, both of which were negative. When his fever, myalgias, and fatigue increased in severity, he presented to the emergency department for evaluation.

Physical Examination
Vital signs upon arrival were significant for fever of 41.1°C and tachycardia of 124 beats per minute. He was alert and oriented to person, place and time with a Glasgow Coma Scale of 15/15. Notable exam findings included an old tick bite present on his right flank with no surrounding erythema. Generalized stiffness was appreciated on neck range of motion testing. Photophobia was noted. Kernig’s and Brudzinski’s signs were negative. Cardiac, respiratory, abdominal, and neurological exams were unremarkable.

Investigations
A broad laboratory investigation workup was conducted which are outlined in Table 1. Notable findings included lymphocytosis, thrombocytopenia, hyponatremia, elevated aspartate aminotransferase, alanine aminotransferase, and C-reactive protein. Chest X-ray was negative for acute findings. Tick borne illness was the primary clinical concern, therefore, extensive antibody and PCR testing was ordered as shown in Table 1. With some concern for meningitis, a

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A lumbar puncture was performed, which was unremarkable (Table 2). COVID-19 PCR testing was also negative.

Clinical Course

In the rural emergency department, external cooling measures were initiated with ice packs and antipyretics. Given their concern for sepsis and febrile illness of unknown origin, he was fluid-resuscitated, given broad-spectrum IV antibiotics with Piperacillin-tazobactam, Vancomycin, and Levofloxacin, and subsequently transferred to our hospital for further management. Upon admission, ceftriaxone was initially administered to cover possible tick-borne illness with potential associated neurologic symptoms. When the lumbar puncture showed normal cerebrospinal fluid results (Table 2), his antibiotics were transitioned to doxycycline given our high clinical suspicion for tick-borne illness. After 24 hours of doxycycline therapy, the patient reported improvement in clinical symptoms, he became afebrile, and his heart rate normalized. He was discharged home on a 10-day course of oral doxycycline 100 mg twice daily with pending tickborne antibody testing. Two days after discharge, serologic and PCR testing for *Anaplasma Phagocytophilum* returned positive, which confirmed our clinical suspicion. At outpatient follow up with his primary care clinician, the patient reported complete resolution of his symptoms.

Discussion

Anaplasmosis, also known as human granulocytic anaplasmosis (HGA), is transmitted by the *Ixodes scapularis* deer tick, which is also responsible for transmitting Lyme Disease (*B. Burgdorferi*) and Babesiosis (*B. Microti*). Minnesota is home to 13 tick species, with the 3 most common being the blacklegged deer tick, the lone star tick and the American dog tick. With 4008 cases reported in the United States (US) in 2018, Anaplasmosis is endemic in the upper Midwestern and northeastern US, peaking in the summer months of June and July and is rarely seen in the winter. There are several intriguing aspects of this patient’s presentation in December that may contribute to increased tick activity leading to disease transmission at an unusual time.

The patient went deer hunting near Leech Lake in Cass County, Minnesota from November 6th to 8th, 2020. This area in north central Minnesota is known to be a high risk area for tick exposure. Peak tick activity is typically seen in

| Laboratory investigation                  | Result          | Reference range    |
|------------------------------------------|-----------------|--------------------|
| Hemoglobin                               | 13.1 g/dL       | 13.2-16.6 g/dL    |
| Platelet count                           | 101 × 10^9 L    | 135-317 × 10^9 L  |
| White blood cell count                   | 7.5 × 10^9 L    | 3.4-9.6 × 10^9 L  |
| Neutrophils                              | 2.28 × 10^9 L   | 1.56-6.45 × 10^9 L|
| Lymphocytes                              | 4.45 × 10^9 L   | 0.95-3.07 × 10^9 L|
| Basophils                                | 0.10 × 10^9 L   | 0.01-0.08 × 10^9 L|
| C reactive protein                       | 52.9 mg/L       | <=8.0 mg/L        |
| Lactate dehydrogenase (LD)               | 358 U/L         | 122-222 U/L       |
| Prothrombin time                         | 15.2 s          | 9.4-12.5 sec      |
| INR                                      | 1.3             | 0.9-1.1           |
| Aspartate aminotransferase (AST)         | 51 U/L          | 8-48 U/L          |
| Alanine aminotransferase (ALT)           | 145 U/L         | 7-55 U/L          |
| Lyme disease serology                    | Negative        | Negative           |
| Anaplasma phagocytophilum Ab, IgG        | 1:512 titer     | <1:64 titer       |
| Ehrlichia chaffeensis (HME) Ab, IgG      | <1:64 titer     | <1:64 titer       |
| Babesia microti IgG Ab                   | <1:64 titer     | <1:64 titer       |
| Anaplasma phagocytophilum, PCR           | Positive        | Negative           |
| Ehrlichia chaffeensis, PCR               | Negative        | Negative           |
| Ehrlichia ewingii/canis, PCR             | Negative        | Negative           |
| Ehrlichia muris eucauliensis, PCR        | Negative        | Negative           |
| HIV-1/-2 Ag and Ab screen, plasma        | Negative        | Negative           |
| Hepatitis B surface antigen              | Negative        | Negative           |
| Hepatitis B core IgM Ab                  | Negative        | Negative           |
| Hepatitis A IgM Ab, serum                | Negative        | Negative           |
| Hepatitis C virus Ab                     | Negative        | Negative           |
| Malaria/Babesia smear                    | Negative        | Negative           |
May to June and September to October. Upon review of local weather records in Cass County (Cass Lake weather station), temperatures were surprisingly warm that November weekend, with highs of 66°F, 61°F, and 70°F on November 6, 7, and 8 respectively. The peak monthly temperature was recorded on November 4, with a high of 73°F. This contrasts to the average temperature of 32°F for November 2020. Average humidity for the month was 76%, with peak 100% humidity recorded on November 7. Given that *Ixodes* ticks are known to be sensitive to temperature and humidity, this likely contributed to increased tick activity in the area. This highlights the importance for clinicians to be aware of local weather patterns and how this might influence seasonal disease presentations.

While the known history of a tick bite helped facilitate management, alternate methods of transmission for Anaplasmosis have been identified, such as through contact with blood of slaughtered deer. Accidental knife and bone shard cuts are common in the field dressing process. This patient wore gloves to avoid exposure with bodily fluids during the field dressing process, consistent with current health recommendations. Clinicians should be aware that deer blood exposure may be associated with tick-borne illnesses and elicit this information during history taking. Patients should be counseled to regularly check their skin for ticks and utilize adequate personal protection equipment (ie, gloves) to avoid direct contact with bodily fluids.

The clinical manifestations of anaplasmosis are non-specific constitutional symptoms with a rash being uncommon. The patient reported headache, fever, myalgia, and arthralgias, which have a median incidence of 82%, 100%, 76%, and 56% respectively in patients with anaplasmosis. Rare complications include heart and/or renal failure, respiratory distress, rhabdomyolysis, or sepsis. One case study even noted the presence of cerebral infarction likely due to anaplasmosis induced platelet dysfunction. No head CT or MR imaging was pursued in this case given the lack of focal neurologic deficits on exam. The patient developed symptoms approximately 9 days after likely tick bite exposure, which is consistent with studies reporting an average incubation period of 1 to 2 weeks.

Having a broad differential diagnosis is essential to guide investigation of suspected tick-borne illnesses. The patient’s symptoms of fever, fatigue and body aches were non-specific and could reflect several infectious disease processes. However, given our patient’s history of tick bite, tick borne illness from ehrlichiosis or anaplasmosis, although uncommon during this time of year, was thought

| Table 2. Results of Cerebrospinal Fluid Investigations. |
|--------------------------------------------------------|
| Cerebrospinal fluid investigation | Result | Reference range |
|----------------------------------|--------|-----------------|
| Appearance                       | Clear  | n/a             |
| Total nucleated cells            | 4      | 0-5/mcL         |
| Erythrocytes                     | 14     | 3.4-9.6 × 10^9/L |
| Neutrophils                      | 3%     | 2% ± 4%         |
| Lymphocytes                      | 85%    | 60% ± 20%       |
| Monocytes                        | 12%    | 30% ± 15%       |
| Protein                          | 42 mg/dL | 0-35 mg/dL |
| Glucose                          | 64     | n/a             |
| Escherichia Coli K1              | Negative | Negative      |
| Haemophilus influenzae           | Negative | Negative      |
| Listeria monocytogenes           | Negative | Negative      |
| Streptococcus agalactiae         | Negative | Negative      |
| Streptococcus pneumoniae         | Negative | Negative      |
| Cytomegalovirus                  | Negative | Negative      |
| Enterovirus                      | Negative | Negative      |
| Herpes simplex I and 2           | Negative | Negative      |
| Human herpes virus six           | Negative | Negative      |
| Human parechovirus               | Negative | Negative      |
| Cryptococcus neoformans          | Negative | Negative      |
| Bacterial culture                | No growth | n/a             |
| Gram stain                       | No organisms seen | n/a             |
| B. Burgdorferi PCR               | Negative | Negative      |
| B. Mayonii PCR                   | Negative | Negative      |
| B. garinii PCR                   | Negative | Negative      |
| Lyme CNS Infection IgG           | Negative | Negative      |
| B. miyamotoi PCR                 | Negative | Negative      |
Anaplasmosis is a tick-borne illness caused by the bacterium *Anaplasma phagocytophilum*. Although this condition is typically seen in the summer, the above case of Anaplasmosis in December in Minnesota was likely due to increased tick activity during a period of unseasonably warm temperatures. This case highlights the importance for primary care clinicians to be aware of local disease epidemiology and weather patterns, and how this might influence seasonal disease presentations. Having a broad differential diagnosis, in addition to a thorough history and examination, is important for prompt identification and appropriate management of tick-borne illnesses in patients who present with undifferentiated fever syndromes.

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