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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 phagocytophlium. 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

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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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Table 1. Results of Laboratory Investigations.

Laboratory investigation	Result	Reference range
Hemoglobin	13.1 g/dL	13.2-16.6 g/dL
Platelet count	101×10^9 L	$135\text{-}317 \times 10^9$ L
White blood cell count	7.5×10^9 L	$3.4\text{-}9.6 \times 10^9$ L
Neutrophils	2.28×10^9 L	$1.56\text{-}6.45 \times 10^9$ L
Lymphocytes	4.45×10^9 L	$0.95\text{-}3.07 \times 10^9$ L
Basophils	0.10×10^9 L	$0.01\text{-}0.08 \times 10^9$ 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 eauclairensis, 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

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. Burgdoferi*) and Babesiosis (*B. Mi*croti).[1] 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.[2] 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.[3] 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.[2] Peak tick activity is typically seen in

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 $\times$ 10^9 L
Neutrophils	3%	2% $\pm$ 4%
Lymphocytes	85%	60% $\pm$ 20%
Monocytes	12%	30% $\pm$ 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 1 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. Burgdoferi PCR	Negative	Negative
B. Mayonii PCR	Negative	Negative
B. garinni PCR	Negative	Negative
Lyme CNS infection IgG	Negative	Negative
B. miyamotoi PCR	Negative	Negative

May to June and September to October.[2] 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.[4] The peak monthly temperature was recorded on November 4, with a high of 73°F.[4] This contrasts to the average temperature of 32°F for November 2020.[4] Average humidity for the month was 76%, with peak 100% humidity recorded on November 7.[4] Given that *Ixodes* ticks are known to be sensitive to temperature and humidity[5], 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.[6] Accidental knife and bone shard cuts are common in the field dressing process.[7] This patient wore gloves to avoid exposure with bodily fluids during the field dressing process, consistent with current health recommendations.[8] 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.[9]

The clinical manifestations of anaplasmosis are non-specific constitutional symptoms with a rash being uncommon.[10] The patient reported headache, fever, myalgia, and arthralgias, which have a median incidence of 82%, 100%, 76%, and 56% respectively in patients with anaplasmosis.[11] Rare complications include heart and/or renal failure, respiratory distress, rhabdomyolysis, or sepsis.[10] One case study even noted the presence of cerebral infarction likely due to anaplasmosis induced platelet dysfunction.[12] 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.[11]

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

to be likely. Lyme disease was considered less likely given the absence of a rash. Given headache, neck stiffness and photophobia, meningitis was ruled out with a lumbar puncture. Bakken and Dumler[11] note that spinal fluid is usually negative, with only 5 cases (0.2%) of meningitis or encephalitis reported to the CDC in patients with anaplasmosis between 2000 and 2007.[13] Laboratory investigations were remarkable for thrombocytopenia and elevated liver transaminases which have been commonly reported in patients with Anaplasmosis, and are less likely to be seen in Lyme disease.[14,15] Interestingly, this patient had a normal white blood cell count with slight lymphocytosis, while most studies report leukopenia or lymphopenia associated with anaplasmosis.[1] A case series on ehrlichiosis found patients with a symptom duration of 5 days or greater were less likely to have lymphopenia.[16] This could explain the patient's lymphocytosis given his symptom duration of 2 weeks. However we found no study examining this association specifically in anaplasmosis patients.

Comprehensive serologic and PCR based testing for tick-borne illnesses should be performed as it was in this case. However, even at a facility with extensive laboratory capability, results often take 1 to 2 days or more. According to the Centers for Disease Control and Prevention, treatment for anaplasmosis should not be delayed while awaiting confirmatory laboratory results.[3] Given this patient's history of a known tick bite in a high risk area with awareness of unseasonably warm temperatures, empiric treatment was initiated and resulted in rapid clinical improvement.

Conclusion

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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