

# Splenomegaly, Non-Traumatic Splenic Rupture, and Pancytopenia in Patient with Human Granulocytic Anaplasmosis

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## ABSTRACT

**BACKGROUND:** Splenic rupture is a well-described complication of babesiosis but is rarely associated with anaplasmosis.

**CASE PRESENTATION:** We report a case of a 37-year-old man with no significant past medical history who presented with malaise, myalgias, arthralgias and severe left upper quadrant pain. He was found to have splenic rupture secondary to infection by *Anaplasma phagocytophilum*. He reported a single tick bite the week prior to onset of his symptoms. On presentation, he was found to have left upper quadrant abdominal tenderness, pancytopenia, and splenomegaly with evidence of splenic rupture and hemoperitoneum on contrasted computed tomography. Blood smear did not demonstrate intraerythrocytic parasites or morulae. His hemoperitoneum was treated conservatively and he was empirically treated for babesiosis. Diagnosis was confirmed by a positive serum PCR for *Anaplasma phagocytophilum*.

**CONCLUSIONS:** This case study adds to the small number of prior case reports and provides evidence for anaplasmosis-associated splenic rupture.

**KEYWORDS:** splenic rupture, splenomegaly, anaplasmosis

## BACKGROUND

Anaplasmosis is a tick-borne disease caused by *Anaplasma phagocytophilum* and was first identified in 1994.<sup>1</sup> Typically occurring in summer months, anaplasmosis has an incidence of 6.3 cases per million,<sup>2</sup> and is predominately reported in New England and the upper Midwest.<sup>3</sup> Vermont, Maine, Rhode Island, Minnesota, Massachusetts, Wisconsin, New Hampshire, and New York report 90% of all cases,<sup>3</sup> with incidence ranging from 6.5 per million in Massachusetts to 32.1 per million in Rhode Island from 2000 to 2007.<sup>4</sup> *Anaplasma* is primarily transmitted by the *Ixodes scapularis* tick, which is also competent vector for *Borrelia burgdorferi sensu lato* (infectious agent of Lyme disease), *Babesia microti*, *Borrelia miyamotoi*, and *Ehrlichia chaffeensis*.<sup>5</sup> Coinfection with *Babesia* and *Anaplasma* have been reported at a rate of 7% in New York<sup>6</sup> and 5.3% in the Wisconsin and Minnesota.<sup>7</sup>

In the literature, splenic rupture is a well-known complication of babesiosis.<sup>8</sup> However, to date there has been only two case reports of non-traumatic splenic rupture in the setting of anaplasmosis. Those cases ultimately resulted in splenectomy<sup>9</sup> and death.<sup>10</sup> This case study adds to the limited body of literature of non-traumatic splenic rupture in anaplasmosis, unique in a relatively mild hospital course and absence of long-term sequelae of splenic rupture.

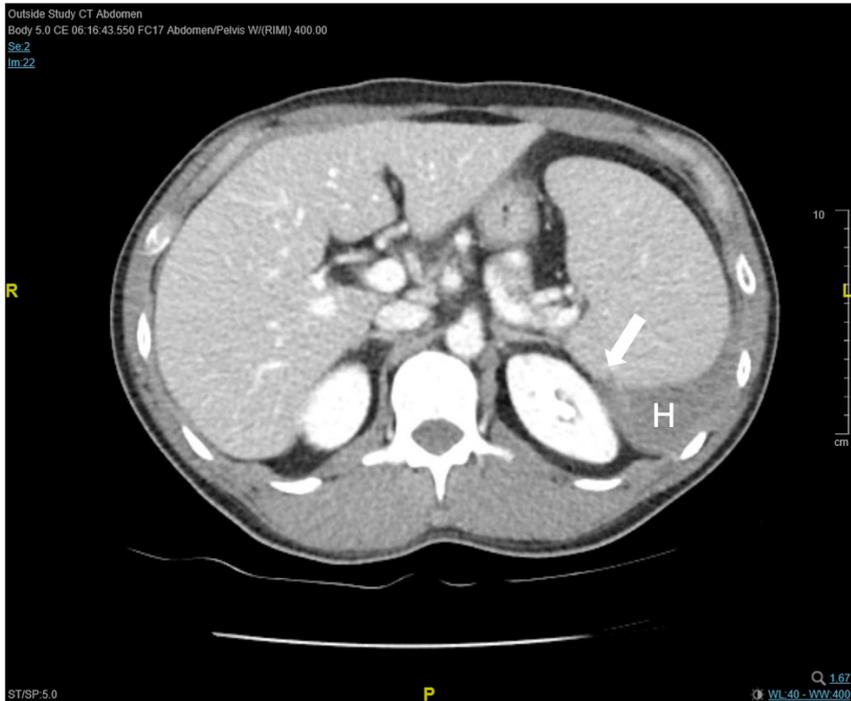
## CASE PRESENTATION

A 37-year-old man with no significant past medical history presented with severe left upper quadrant pain. He worked outdoors as a stonemason's aide and reported a single tick bite one week prior to presentation. About five days after the tick bite, he developed fatigue, myalgias, arthralgias, and malaise. Two days later, he developed acute onset of left upper quadrant abdominal pain radiating to the ipsilateral shoulder. The pain increased over the following 12 hours until he could not find a position of comfort, prompting him to seek medical care. He also reported a new retroorbital headache, but denied fever, rash, or neurologic changes.

He initially presented to the emergency department with a heart rate of 101, blood pressure of 107/79, respiratory rate of 16, and temperature of 97.9°F. On admission, his laboratory studies were notable for aspartate transferase of 24 IU/L, alanine transferase of 13 IU/L, white blood cell count of  $1.5 \times 10^9/L$  (87% neutrophils and 7% lymphocytes), hemoglobin of 10.3 g/dL (baseline 15.4 g/dL), and platelet count of  $56 \times 10^9/L$ . Blood smear did not demonstrate intraerythrocytic parasites or morulae. On contrasted CT, he was found to have moderate hemoperitoneum, splenomegaly to 15.4 cm, and hypodense focus in the periphery of the posterior spleen, which could represent a site of splenic rupture. He remained hemodynamically stable and his hemoperitoneum was treated conservatively.

Based on findings of anemia, leukopenia, thrombocytopenia, and splenic rupture with recent tick exposure in a highly endemic area, he was started on empiric treatment with azithromycin and atovaquone for concern of babesiosis. Additional workup included negative Lyme serology, Rickettsial serology including Rocky Mountain Spotted Fever and Rickettsia typhi, Epstein - Barr virus serology, Cytomegalovirus serology and PCR, Parvovirus serology, Hepatitis B serology,

**Figure 1.** CT Abdomen Pelvis with contrast of the patient on admission demonstrating splenic rupture (arrow) and hemoperitoneum (H).



and Hepatitis C serology. His white cell count and platelet count improved over the next two days, with resolution of lymphopenia, and his hemoglobin remained stable. His abdominal pain and malaise improved rapidly.

Prior to discharge, serum PCR testing was positive for *Anaplasma phagocytophilum* and had not yet resulted for *Babesia microti*. He was discharged on doxycycline for treatment of anaplasmosis and empiric azithromycin and atovaquone for presumed babesiosis coinfection. His serum PCR later resulted as negative for *Babesia microti*. He was evaluated in the outpatient infectious disease clinic a week after discharge and reported complete resolution of his symptoms. He completed a ten-day course of doxycycline as well as azithromycin and atovaquone.

## DISCUSSION AND CONCLUSION

The initial presentation of anaplasmosis is often non-specific and overlaps with other tick-borne diseases, with symptoms including fever, chills, malaise, nausea, vomiting, arthralgias, headache.<sup>11</sup> Symptoms usually develop five to fourteen days after tick bite. To date, the only two case reports of non-traumatic splenic rupture in the setting of *Anaplasma* infection resulted in splenectomy<sup>9</sup> and death.<sup>10</sup> This patient presented with a constellation of non-specific symptoms as well as splenic rupture.

Laboratory values findings in anaplasmosis include elevated transaminases, thrombocytopenia, leukopenia, and mild

anemia.<sup>12</sup> A previous study found low platelets or low WBC in 81.3% of patients with anaplasmosis, with 49.3% with both low platelets and low WBC. Decreased hemoglobin was found to be statistically significant only in women, not men.<sup>13</sup> The majority of patients initially present with lymphopenia and a minority of patients initially present with neutropenia.<sup>13,14</sup> Neutropenia is more common in patients that had a longer duration of symptoms, typically greater than 4 days.<sup>14</sup> This patient presented with neutropenia, thrombocytopenia, and normal LFTs. The significant drop in hemoglobin could be explained by the hemoperitoneum more so than anaplasmosis.

Diagnosis of anaplasmosis and babesiosis are primarily determined by clinical presentation in compatible season and geography, peripheral blood smear, and/or serum PCR. For *Anaplasma*, morulae in granulocytes can be seen on blood smear or buffy coat.<sup>12</sup> Buffy coat and DNA PCR have a sensitivity of 77–80%. Serologic testing requires both acute and convalescent titers, as acute titers are not sufficiently sensitive.<sup>15</sup> Microscopic detection of *Anaplasma* lacks sensitivity compared to PCR.<sup>14</sup> In New York, patients with known anaplasmosis had positive PCR at a rate of 75.9% and microscopic detection at a rate of 60.7%.<sup>13</sup> In babesiosis, the *Babesia* parasites can be identified on Giemsa- or Wright-stained thin or thick blood smears, where thin smear analysis adds information about degree of parasitemia. DNA PCR is more sensitive than blood smears, with a high sensitivity and specificity with little cross-reactivity with similar pathogens.<sup>15,16</sup> However, it can remain positive weeks to months after parasitemia is no longer found on blood smear. IgM/IgG antibody serologic testing by indirect immunofluorescent assay can be performed, however seropositivity does not necessarily indicate active infection and may not immediately become positive in an active infection.<sup>15</sup> Blood smear and PCR are the primary modes of confirming the diagnosis for both anaplasmosis and babesiosis.

This case study presents the diagnostic challenge of non-traumatic splenic rupture with normal LFTs, leukopenia, and thrombocytopenia. Splenic rupture is a known complication of babesiosis particularly in patients that present like this one. A case series from the same endemic area found splenic rupture in babesiosis at a rate of 1%, and was notable for being found in younger, healthier males with lower degrees of parasitemia.<sup>17</sup> Anaplasmosis has been shown to be responsible for non-traumatic splenic rupture in only two reported cases of sicker patients. In this case, splenic rupture

and hemoperitoneum were the presenting symptoms of anaplasmosis, however the normal LFTs and low hemoglobin raise the question of an occult co-infection with *Babesia microti*. Serum PCR testing confirmed the presence of *Anaplasma* and absence of *Babesia*. Direct testing for potential coinfections is warranted in endemic areas for *Babesia* and *Anaplasma* in atypical presentations such as non-traumatic splenic rupture.

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