Anaplasmosis Presenting as Septic Shock of Unknown Origin

AbdelMaseeh, Tony MD[1]; Cadiz, Ian MD[1]; Arabnia, Alireza MD[1]; Dempsey, William MD[1]; Grant, Michelle MD[2]; Dhaubhadel, Pragya MD[3]; Mogaka, Edwin MD/PhD[1]

1. The Wright Center for Graduate Medical Education, Scranton, PA
2. Geisinger Diagnostic Medicine Institute
3. Geisinger Community Medical Center, Scranton, PA

Abstract

Human ehrlichiosis and anaplasmosis represent acute febrile tick-borne illnesses manifesting with varied symptoms, ranging from mild febrile episodes to severe multi-organ dysfunction. This case report highlights a 77-year-old Caucasian female residing in Northeast Pennsylvania, who initially sought medical attention for confusion and abdominal pain during the summer. She was initially diagnosed with a urinary tract infection and commenced on cefdinir. Subsequently, her condition deteriorated, necessitating hospitalization.

Laboratory investigations revealed elevated transaminases, acute kidney injury, troponemia, and thrombocytopenia. Despite initial interventions, including intravenous fluids, the patient progressed to acute respiratory failure, requiring positive pressure ventilation. Consequently, she was transferred to a tertiary care facility. Notably, a peripheral blood smear exhibited neutrophilic intracytoplasmic inclusions.

Empiric therapy with intravenous doxycycline, enteral azithromycin, and atovaquone via nasogastric tube was initiated, resulting in rapid clinical improvement. Peripheral blood PCR confirmed the diagnosis of anaplasmosis, ruling out babesiosis. Consequently, azithromycin and atovaquone were discontinued, and the patient completed a 10-day course of doxycycline. This case underscores the critical importance of promptly diagnosing tick-borne infections in individuals with nonspecific symptoms, particularly in geographically endemic regions.

Key words: *Tickborne, Transaminitis, Intracytoplasmic inclusions*

Introduction

The rise in human infections attributable to ehrlichiosis and anaplasmosis has become more pronounced, coinciding with the expansion of animal reservoirs and tick vectors in regions densely populated by humans. This case report delineates an instance of anaplasmosis, wherein the clinical presentation mimicked sepsis and manifested as multiorgan failure involving myocarditis, renal failure, respiratory failure, and encephalopathy. Vigilant management, incorporating broad-spectrum antimicrobial coverage with doxycycline, azithromycin, and atovaquone, yielded prompt and substantial clinical amelioration. This case underscores the escalating relevance of these tick-borne illnesses and emphasizes the efficacy of comprehensive therapeutic strategies in mitigating their clinical impact.

Case

A 77-year-old Caucasian female residing in Northeast Pennsylvania presented to her primary care physician in June with a three-day history of urinary frequency, urgency, chills, generalized body aches, anorexia, intermittent disorientation, altered balance, and fever that commenced on the day of presentation. Her medical history was notable for hypertension, type 2 diabetes mellitus, osteoarthritis, restless legs syndrome, and anxiety.

During the clinic visit, vital signs indicated a fever (102.5˚F) and tachycardia (119 beats per minute), while the rest were unremarkable. Clinic labs revealed transaminitis (AST 222 U/L, ALT 144 U/L, ALP 182 U/L), acute kidney injury (BUN 20, Cr 1.1, eGFR 53 ml/min), hyponatremia (Na 132 mmol/L), and thrombocytopenia (platelets 99 K/uL). Urinalysis showed 4+ ketones, 3+ protein, and 1+ leukocyte esterase. Blood culture and viral panel were negative, and the patient was initiated on Cefdinir 300 mg bid.

Two days later, the patient's son brought her to a local hospital due to worsening confusion, vague abdominal pain, and nausea. A head CT scan was negative, but labs indicated worsening transaminitis, direct hyperbilirubinemia, escalating AKI, hyponatremia, and thrombocytopenia. Following a fluid bolus, she developed pulmonary edema, leading to acute hypoxic respiratory failure. Broad-spectrum antibiotics, stress steroids, and furosemide were administered. Due to worsening condition, she was transferred to a higher-level care facility, where a pending peripheral blood smear revealed neutrophilic intracytoplasmic inclusions suggestive of anaplasmosis.

Upon transfer, vital signs indicated hypotension, tachycardia, tachypnea, and a GCS of 8. Labs showed metabolic acidosis and elevated lactate. Chest X-ray revealed pulmonary edema and left basilar opacity. Infectious disease department-initiated empiric treatment with IV doxycycline, enteral azithromycin, and atovaquone. The patient was admitted to the ICU, and hematology was consulted for elevated LDH and thrombocytopenia. Peripheral smear ruled out intravascular hemolysis. After

24 hours, peripheral blood PCR confirmed *Anaplasma phagocytophilum*. Azithromycin and atovaquone were discontinued, and doxycycline were continued.

During the hospital stay, cardiology and nephrology monitored the patient for acute systolic heart failure and stage 3 Acute Kidney Injury (AKI). Aspirin and beta blockers were initiated, diuretics administered for fluid overload, and lisinopril withheld due to kidney injury. Troponins trended down, and NT-Pro BNP remained elevated. On discharge, the patient was started on carvedilol, and lisinopril was restarted. Nine months later, a repeat TTE showed recovery of EF to 36%.

Discussion

The inaugural documentation of human anaplasmosis dates back to 1986, delineating a patient's clinical presentation marked by fever, hypotension, confusion, acute renal failure, coagulopathy, and gastrointestinal hemorrhage (1). Both anaplasmosis and ehrlichiosis are zoonotic tick-borne diseases caused by obligate intracellular gram-negative bacteria. Human granulocytic anaplasmosis (HGA) and human monocytic ehrlichiosis (HME) denote the white cell line involvement in each infection (2). Symptoms are typically nonspecific, encompassing myalgia, tendon pain, soft tissue tenderness, right upper quadrant pain, slumped posture, hepatomegaly, diaphoresis, muscle spasms, elevated liver enzymes (intrahepatic pattern), and, notably, a diminished white cell count (3,4).

A presumptive diagnosis of HME/HGA may be established in patients exhibiting a compatible systemic febrile illness with pertinent epidemiologic exposures and an absence of a clear alternative explanation. For instance, outdoor exposure in an endemic area during spring or summer, coupled with a febrile illness and isolated leukopenia and/or thrombocytopenia, provides substantial circumstantial evidence for anaplasmosis. The diagnosis should not be dismissed even in those with a history of HGA or HME, given that prior infection may not confer enduring immunity, as evidenced by cases with recurring episodes spaced years apart (5).

Recognizing the potential for swift progression to serious illness, the Centers for Disease Control and Prevention (CDC) advocates for initiating antimicrobial treatment promptly upon clinical suspicion, even before laboratory confirmation (6). When HME or HGA is suspected, blood samples should be subjected to polymerase chain reaction (PCR), serology, and peripheral blood smear examination. In endemic regions for both HME and HGA, separate PCR and serologic tests should be conducted for each organism.

PCR, widely employed, offers acute diagnostic results, though a positive result confirms infection, while a negative result does not definitively rule out disease. Although serology can provide a definitive diagnosis, its utility in the acute setting is limited. If PCR yields negative results with continued suspicion, a second serologic test should be administered two to four weeks later, with a fourfold rise in antibody titers between acute and convalescent tests confirming the diagnosis. Microscopic examination of a blood smear, though less sensitive than PCR, is highly specific and can offer rapid results. Buffy coat examination, while enhancing sensitivity, is labor-intensive and infrequently performed (6).

Hospitalization is required in over 50 percent of reported cases (7). The broad differential diagnosis for HME and HGA encompasses infectious and noninfectious etiologies. Coinfection with other tick-borne infections should also be considered. The clinical presentation aids in narrowing the differential diagnosis:

1. Individuals with severe sepsis or septic shock – Resembling severe HME and HGA infections, broad-spectrum antimicrobial therapy should be initiated until a definitive microbiologic diagnosis is established for bacterial infections such as bacteremia, acute cholangitis, community-acquired pneumonia, urosepsis, and meningoencephalitis.
2. Individuals with fever plus leukopenia, thrombocytopenia, and/or abnormal aminotransferases – Lab findings akin to HME and HGA may also be attributed to mononucleosis-like illnesses caused by Epstein-Barr virus, cytomegalovirus, and acute HIV. Other viral infections with similar syndromes include hepatitis A, B, and C.
3. Other arthropod infections – Consideration should be given to Rocky Mountain spotted fever (RMSF) and babesiosis, which may share symptoms and lab findings with HME and HGA.
4. Noninfectious illnesses – Conditions such as thrombotic thrombocytopenic purpura (TTP), hemolytic-uremic syndrome (HUS), *Hemophagocytic lymphohistiocytosis* (HLH), hematologic malignancy, and drug reactions (e.g., to trimethoprim-sulfamethoxazole and chemotherapeutic agents) may mimic the clinical presentation of HME and HGA.

In our patient, the initial indication of anaplasmosis was the discovery of neutrophilic intracytoplasmic inclusions in the peripheral smear conducted at the first facility, later confirmed by a positive PCR for *Anaplasma phagocytophilum* in the second facility. Empiric treatment with vancomycin and piperacillin/tazobactam failed to yield clinical improvement, and it was only after the initiation of doxycycline that the patient exhibited improvement, resolving the associated multisystem organ impairment.

Conclusion

Human granulocytic anaplasmosis (HGA) and human monocytic ehrlichiosis (HME) represent tick-borne maladies characterized by predominantly nonspecific symptoms. Severe cases may precipitate multiorgan system failure, rendering diagnosis challenging owing to the lack of distinct clinical manifestations. Sustaining a heightened clinical suspicion, particularly in endemic regions and during the spring and summer seasons, proves pivotal for expeditious diagnosis and intervention. The primary therapeutic modality remains doxycycline, supported by peripheral smear findings and a positive polymerase chain reaction (PCR). Failure to institute timely treatment may culminate in the progression of HGA/HME to multisystem organ failure, ultimately resulting in mortality.

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