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Case report

Severe rhabdomyolysis as a rare complication of human granulocytic anaplasmosis

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ABSTRACT

Human granulocytic anaplasmosis (HGA) is a tick-borne illness caused by infection with *Anaplasma phagocytophilum*. Although rare, rhabdomyolysis and acute renal failure are potential complications of HGA. We present the case of an 86-year-old male who exhibited severe myopathy, rhabdomyolysis, and acute renal failure necessitating hemodialysis. Treatment with doxycycline resulted in partial renal function improvement, allowing discontinuation of dialysis after 8 weeks. This case underscores the importance of considering rhabdomyolysis as a manifestation of HGA, particularly in individuals residing in or traveling to endemic areas.

Introduction

Human Granulocytic Anaplasmosis (HGA) is a tick-borne zoonotic disease caused by the Rickettsial microorganism *Anaplasma phagocytophilum* [1]. It is transmitted via Ixodes tick bites and is endemic to regions including the Northeastern, Northcentral, and West Coast of the United States, as well as parts of Europe, and Asia such as China and Korea. HGA typically manifests as an acute febrile illness with symptoms including fever, chills, headache, myalgia, arthralgia, and gastrointestinal symptoms, resembling viral etiologies. The incubation period ranges from 5 to 21 days following an infected tick bite [2]. Laboratory assessments commonly reveal leukopenia, thrombocytopenia, and elevated hepatic transaminase levels. Rhabdomyolysis, though infrequent, represents a clinically significant complication of HGA. Herein, we discuss a case of rhabdomyolysis in a patient with confirmed HGA in an endemic area, ultimately requiring hemodialysis.

Case

This case report involves an 86-year-old Caucasian male who presented to the emergency department (ED) with acute onset profound generalized weakness, slurred speech, and a three-day history of progressive functional decline, including multiple falls at home resulting in head injuries. The patient also reported experiencing loose stools on the morning of presentation. A coworker visited him and noticed the patient's deteriorating condition and accompanied him to the hospital. Past medical history included essential hypertension, hyperlipidemia, benign prostatic hyperplasia, prediabetes, and chronic kidney disease (CKD) stage IIIb. Home medications included amlodipine, valsartan, finasteride, and simvastatin. The patient, who works as a landscaper, had possible exposure to ticks and denied significant tobacco or alcohol use.

Upon ED arrival, vital signs were recorded as follows: blood pressure of 157/70 mmHg, respiratory rate of 20/minute, heart rate of 81/minute and oxygen saturation of 100 % on room air. Physical examination revealed the patient reclined in bed with visible rigors and superficial abrasions on the forehead and bilateral knees. Cardiovascular examination revealed a regular rate and rhythm without murmurs. Pulmonary auscultation revealed equal air entry bilaterally with clear lung sounds. Abdominal examination indicated a soft, non-tender abdomen with normoactive bowel sounds. The neurological examination revealed dysarthria and generalized motor weakness; however, no other focal deficits were found. Dermatologic inspection identified a small, crusted scab over the left lateral hip, suggestive of an insect bite. Initial laboratory findings included a white blood cell (WBC) count of 6.1, hemoglobin (Hgb) level of 14.4, platelet count of 78,000, potassium level of 5.0, lactic acid level of 4.4, calcium level of 8.1, albumin level of 3.9, aspartate transaminase (AST) level of 2992, alanine transaminase (ALT) level of 267, creatine kinase (CK) levels exceeding 20,000 (detection limit), creatinine level of 4.63, estimated glomerular filtration rate (eGFR) of 12, and blood urea nitrogen (BUN) level of 62. The patient had a baseline 6 months ago showing WBC of 6.5, Hgb of 13.9, platelet 204,000, creatinine 1.55, eGFR 44, and BUN of 23. Peripheral blood smear revealed neutrophils with cytoplasmic inclusions, as well as some

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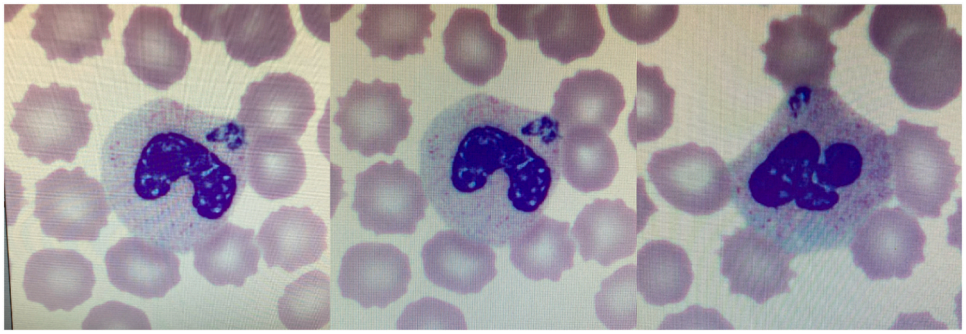

Fig. 1. Peripheral smear shows morulae of *A. phagocytophilum* within infected neutrophils.

neutrophils exhibiting cytoplasmic vacuoles, toxic granulations, and Dohle bodies (Fig. 1). Imaging studies, including non-contrast head computed tomography (CT) and head and neck CT angiogram (CTA), were unremarkable for acute intracranial pathology. Abdominal ultrasound that revealed mild right hydronephrosis and possibly left hydronephrosis, in conjunction with multiple renal calculi. Electrocardiography (EKG) demonstrated sinus rhythm with a ventricular rate of 75 beats per minute.

Given the clinical presentation, laboratory findings, and history of potential tick exposure, the patient was empirically administered doxycycline in the ED and admitted for further management. CT and CTA were negative and neurological symptoms resolved in 24 h, obviating the need for MRI. Statin therapy was discontinued due to rhabdomyolysis. During hospitalization, the patient received intravenous fluids for the acute kidney injury (AKI) secondary to rhabdomyolysis but showed no renal function improvement. Nephrology consultation prompted initiation of hemodialysis on hospital day two, resulting in gradual CK level reduction to under 20,000 by hospital day six. A positive Anaplasma PCR detected the *A. phagocytophilum* gene confirmed HGA, and doxycycline 100 mg twice daily was continued for 10 days. Lyme and *Ehrlichia chaffeensis* PCR and antibody were negative.

The patient was discharged with scheduled nephrology follow-up for hemodialysis. With appropriate treatment for Anaplasmosis and continuation of dialysis, the patient experienced partial renal function improvement, leading to dialysis discontinuation after weight weeks. Regular nephrology follow-up continues.

Discussion

Upon successful transmission, *A. phagocytophilum* invades neutrophils and develops into morulae. It also causes cytokine release that leads to tissue injury, while resembling other associated disease such as hemophagocytic lymphohistiocytosis (HLH) [3]. HGA is usually a self-limiting disease. HGA typically resolves spontaneously, with 5 to 10 % of healthy individuals exhibiting elevated antibody titers from past exposure [4]. Severe cases may progress to meningoencephalitis, acute respiratory distress syndrome, and sepsis.

Myopathy and Rhabdomyolysis are rare presentations of HGA [5–9]. Myopathy is damage to one or more muscles, resulting in weakness, myalgia, and rhabdomyolysis. AKI due to rhabdomyolysis presents in 13 to 50 % of all cases [10]. Creatinine kinase level does not always correlate with the occurrence of rhabdomyolysis, while other factors, including sepsis, intravascular volume depletion, acidosis, and vasoconstriction increase the risk [11]. Rhabdomyolysis pathogenesis in HGA remains unclear. One of the proposed mechanisms is cytokine-induced skeletal muscle damage due to macrophage activation from anaplasmosis [12]. Statin therapy may contribute to rhabdomyolysis and concurrent use of statin with anaplasmosis-associated rhabdomyolysis was reported [9]. Despite the lack of testing for HMG-CoA reductase antibody, our patient was restarted on his home statin regimen upon discharge without recurrence of rhabdomyolysis during outpatient follow-up, making statin-induced myopathy and rhabdomyolysis extremely unlikely, as the recurrence rate of reinitiating a statin on confirmed statin-associated muscle-related adverse effects (MAE) patients is 100 % in a case series comprising of 354 patients [13].

Up to 15 % of patients have AKI [3], which can progress to acute renal failure (ARF) either due to severe rhabdomyolysis or direct effects of HGA [14]. Literature review reveals a few cases of HGA-associated acute renal failure requiring hemodialysis, with varying underlying mechanisms. Two cases described ARF requiring dialysis and steroid therapy due to anaplasmosis-associated membranoproliferative glomerulonephritis (MPGN) [15,16]. One case presented with ARF secondary to acute tubular necrosis resulting from anaplasmosis-induced hemophagocytic lymphohistiocytosis (HLH) [17]. Our patient did not undergo renal biopsy due to thrombocytopenia and did not require escalated care during hospitalization, being discharged in a stable condition to complete 10 days of doxycycline without no steroid administration, rendering these differential diagnoses less likely. Pre-renal cause of AKI due to his diarrhea is unlikely the primary etiology given his worsening renal function despite aggressive fluid administration. Hemodialysis was continued for 8 weeks with an incomplete recovery of renal function to chronic kidney disease (CKD) stage IV. Considering the overall clinical presentation, our patient most likely experienced acute-on-chronic renal failure secondary to acute tubular necrosis (ATN) in the context of rhabdomyolysis.

While central nervous system (CNS) involvement in anaplasmosis is rare, cases have been documented, presenting with symptoms such as lingering aphasia and subarachnoid hemorrhage [18]. While MRI and CSF analysis may reveal nonspecific findings, treatment approaches remain consistent. Our case initially presented with slurred speech suggestive of CNS involvement; however, symptoms completely resolved within 1–2 days with hydration and doxycycline. Coupled with a negative brain CT, the likelihood of anaplasmosis with CNS involvement is diminished.

Diagnosis of anaplasmosis is prompted by hallmark findings including leukopenia, thrombocytopenia, anemia, and elevated transaminases on complete blood count (CBC) and comprehensive metabolic panel (CMP) usually obtained in the ED. Peripheral blood smears may be performed by hematology laboratories in endemic areas to identify granulocytic morulae in infected neutrophils, although with low sensitivity. Serology plays a role in diagnosis, demonstrating higher sensitivity 2–4 weeks after disease onset, while acute-phase diagnosis relies on PCR testing from blood samples. Empirical doxycycline treatment is initiated pending confirmatory PCR testing [19]. Routine blood cultures cannot detect *A. phagocytophilum*. Treatment regimen and duration are adjusted based on potential co-infection with other tick-borne diseases such as Lyme disease, babesiosis, and Powassan disease.

In conclusion, we present a case of anaplasmosis associated with rhabdomyolysis complicated with acute renal failure requiring hemodialysis. Rhabdomyolysis should be considered as a presentation of HGA, especially in endemic areas.

Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions

All authors reviewed the clinical records, wrote the article and critically revised the manuscript for intellectual content. All authors read and approved the final version of the article.

CRediT authorship contribution statement

Ocheita Daniel: Writing – original draft. **Mohammed Saleh:** Conceptualization, Writing – original draft. **Prarthana Desai:** Writing – original draft, Writing – review & editing. **Chun-Yu Peng:** Software, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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