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CASE REPORT
Cardiovascular imaging

Case report: human granulocytic anaplasmosis causes acute myopericarditis with atrial fibrillation

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Background Tick-borne illness are becoming increasingly common, in a spreading geographic area. Lyme disease is a well-known cause of cardiovascular disease, but anaplasmosis has previously had relatively little reported association with conduction and myocardial disease.

Case Summary A 65-year-old man with fever and malaise was admitted to the intensive care unit in shock. Electrocardiogram showed new atrial fibrillation and conduction abnormalities. Transthoracic echocardiogram demonstrated normal left ventricular ejection fraction but significant right ventricle dysfunction. Cardiac magnetic resonance imaging findings were consistent with myopericarditis. Workup revealed human granulocytic anaplasmosis without Lyme. He recovered with doxycycline.

Conclusion To our knowledge, this is one of the first reported cases of anaplasmosis causing electrical conduction and myocardial disease with haemodynamic instability in an isolated infection. Treatment with appropriate antibiotics and supportive care allowed the patient to recover to his functional baseline within a month from being discharged from the hospital. Recognition of anaplasmosis in the absence of Lyme disease as a potential cause of electrical and myocardial disease is important in the context of increasing anaplasmosis incidence across the United States.

Keywords Human granulocytic anaplasmosis • HGA • myopericarditis • myocarditis • pericarditis • case report • tick-borne diseases

ESC Curriculum 6.5 Cardiomyopathy • 6.7 Right heart dysfunction • 7.1 Haemodynamic instability • 2.3 Cardiac magnetic resonance

Learning points

(1) To recognize anaplasmosis in the differential diagnosis for myopericarditis
(2) To recognize the importance of treating for anaplasmosis in endemic regions in the appropriate clinical context

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Introduction

Incidence of human granulocytic anaplasmosis (HGA) is rising in the United States, with more than three-fold increase over several years of tracking cases.[1] The geographic range of the ixodes scapularis tick, the vector carrying the causative agent, anaplasma phagocytophilum, is also growing.[1] We present the case of a patient who presented to the emergency department (ED) and was found to be in mixed shock requiring intensive care unit admission (ICU). He was found to have an isolated HGA infection, and cardiac workup showed evidence of myopericarditis as well as conduction system disease. Recognizing that HGA infection can, in the absence of concomitant Lyme infection, be causative of such severe acute illness is important as the incidence of infection rises.

Timeline

1 week prior to presentation:	• Patient developed fevers and malaise. • Chest x-ray and COVID swab performed.
Hospital Day 0:	• Patient presented to ambulatory respiratory care unit for further evaluation. • Referred to emergency department. • Found to be in shock.
Hospital Day 1:	• Admitted to medical intensive care unit. • Cardiac biomarkers peak. • Able to be fully weaned from vasopressor support. • Transferred to cardiac intensive care unit.
Hospital Day 3:	• Transferred out of cardiac intensive care unit to general cardiology service.
Hospital Day 4:	• Coronary angiogram without evidence of obstructive coronary artery disease.
Hospital Day 5:	• Cardiac magenetic resonance imaging demonstrating myopericarditis.
Hospital Day 6:	• Anaplasma polymerase chain reaction testing shows acute infection. Discharged with doxycycline.
Follow-up 2 weeks:	• Followed up with infectious disease, stopped antibiotics. • Repeat cardiac magnetic resonance imaging.
Follow-up 4 weeks:	• Followed up with heart failure. • Patient back to baseline functional status. • Electrocardiogram and ambulatory rhythm monitoring showing sinus rhythm without recurrence of atrial fibrillation.

Case summary

The patient is a 65-year-old male with a history of hypertension and depression who developed fever and malaise in July 2020. Initial outpatient evaluation included a chest x-ray that was unremarkable, nasopharyngeal swab negative for COVID-19, and electrocardiogram (ECG) showed sinus rhythm with an incomplete right bundle branch block and left anterior fascicular block. The fevers and malaise persisted for one week, prompting evaluation in our ambulatory respiratory care unit. He had dental work done the day prior to onset of symptoms. He was ill-appearing and referred to the ED. Vital signs in the ED were temperature 97.7 Fahrenheit, heart rate 63 beats per minute, blood pressure 74/44 mm of mercury, respiratory rate 20 breaths per minute, and oxygen saturation 99% on room air. Examination was notable for crackles at the right lung base and a II out of VI holosystolic murmur at the cardiac apex. Laboratory findings were notable for AST 89 IU/L (normal 0–40), ALT 103 IU/L (normal 0–40), proBNP of 16 093 pg/mL (normal 0–229), Troponin-T of 0.79 ng/mL (normal 0–0.0.1), CRP > 300 mg/L (normal 0–5.0), creatinine 2.6 mg/dL from a baseline of 1.1 the week prior (normal 0.5–1.2), and lactate 3.4 mmol/L (normal 0.5–2.0). ECG showed atrial fibrillation, non-specific intraventricular conduction delay, and minimal ST elevation in the lateral leads (*Figure 1*).

Past medical history includes hypertension, treated with amlodipine and losartan, and depression, treated with lamotrigine. He resides in a southeastern suburb of Boston, in a home surrounded by wooded areas. He reported being outdoors regularly for kayaking trips in the few months prior to presentation.

The initial differential diagnosis included severe COVID-19, community-acquired pneumonia with septic shock, bacteremia/endocarditis secondary to recent dental work, a tick-borne illness, pulmonary embolism, and myocarditis. Concern was lower for acute coronary syndrome.

In the ED the patient had a beside echocardiogram showing preserved left ventricular ejection fraction (LVEF), tricuspid regurgitation, and no evidence of pericardial effusion. A broad infectious workup with blood and urine cultures and Lyme and anaplasma serologies was sent from the ED. Blood cultures grew gram-positive cocci that ultimately grew out to multiple species of coagulase-negative staphylococcus, likely contaminants. A CT angiogram was negative for pulmonary embolism. Urine antigens were tested and negative for streptococcus pneumonia and legionella. A formal transthoracic echocardiogram performed after patient was stabilized off pressors showed LVEF 54%, dilated right ventricle (RV) with basal diameter 4.6 cm, with moderate-to-severe RV systolic dysfunction and tricuspid annular plane systolic excursion (TAPSE) 1.3 cm, leftward interventricular septal shift in systole and diastole consistent with RV pressure and volume overload, mild to moderate tricuspid regurgitation, no significant left-sided valvular disease, and no pericardial effusion (see Supplementary material online, *Videos S1 and S2*). Coronary angiography demonstrated no significant obstructive epicardial coronary artery disease. Cardiac magnetic resonance (CMR) imaging obtained on hospital day five showed a mildly dilated RV with normal free wall motion, small circumferential pericardial effusion, pericardium with normal thickness but diffuse late gadolinium enhancement, and sub-epicardial late gadolinium enhancement in the basal and mid-lateral left ventricular walls with native global T1 of 1270 ± 67 ms (*Figure 2* and *3*; see Supplementary material online, *Video S3*). Lyme IgG serology was positive, with western blot negative for three of three different IgM bands, and positive for only one of 10 different IgG bands, consistent with a negative test for acute Lyme infection. PCR for babesia was negative. Anaplasma serologies were positive for IgM and negative for IgG, and subsequent PCR detected anaplasma phagocytophilum DNA.

He was admitted from the ED to the medical ICU in circulatory shock. He was administered IV fluids, vasopressors and empiric antibiotics, including vancomycin, ceftriaxone, and doxycycline. He developed new onset atrial fibrillation and was started on an infusion of unfractionated heparin (dosing via PTT-guided protocol). Over the next eight hours fever abated, blood pressure stabilized, vasopressors were weaned, and renal function improved. His cardiac biomarkers peaked 12 h after ICU admission, with peak troponin-T 1.24 and CK-MB 57, which then trended down. He had coronary angiography which excluded obstructive coronary artery disease. CMR imaging revealed findings consistent with myopericarditis. Broad spectrum antibiotics were initially continued with vancomycin (dosed to renal function), ceftriaxone

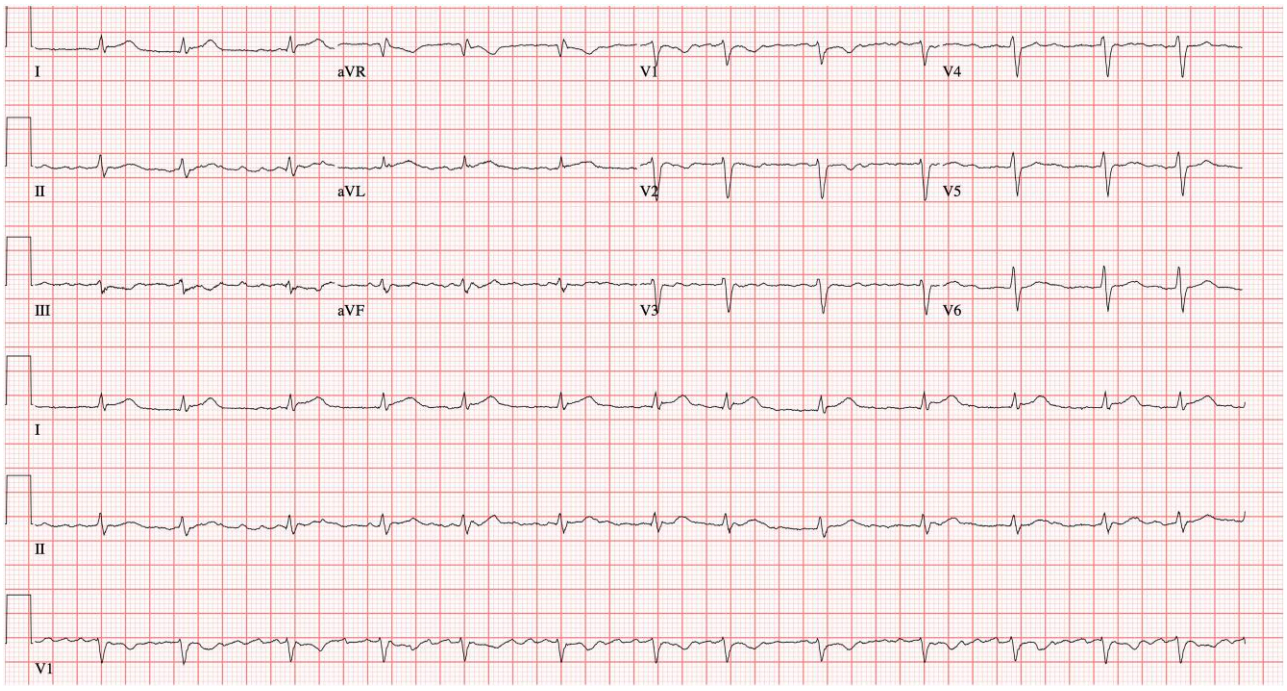

Figure 1 ECG obtained in emergency room on initial presentation. ECG demonstrates atrial fibrillation, non-specific intraventricular conduction delay, and minimal ST elevation in the lateral leads.

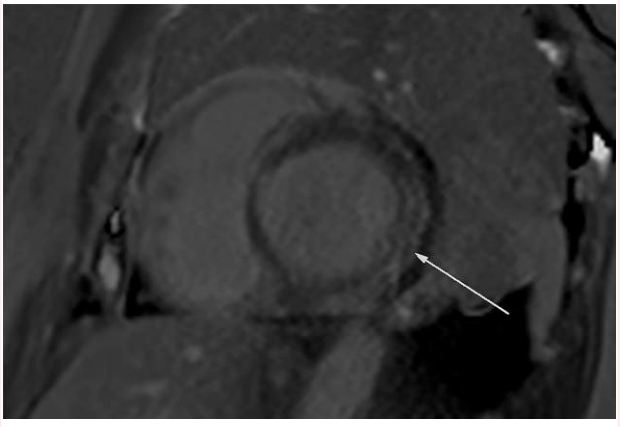

Figure 2 Cardiac MRI, hospital Day 5. LGE (*Figure 3*) and T_1 (*Figure 4*) imaging demonstrates sub-epicardial late gadolinium enhancement in the basal and mid-lateral left ventricular walls with native global T_1 of 1270 ± 67 ms.

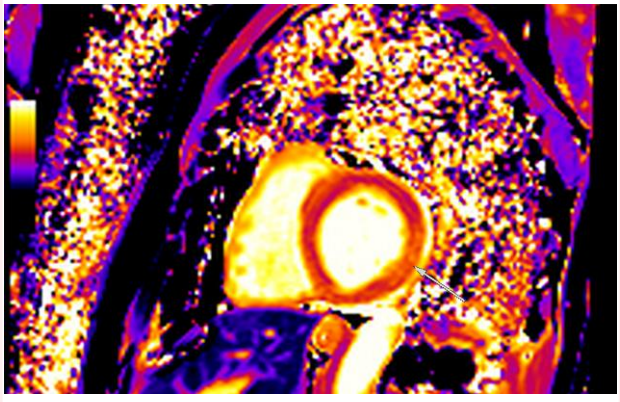

Figure 3 Cardiac MRI, hospital Day 5. LGE (*Figure 3*) and T_1 (*Figure 4*) imaging demonstrates sub-epicardial late gadolinium enhancement in the basal and mid-lateral left ventricular walls with native global T_1 of 1270 ± 67 ms.

(2 grams every 24 h), and doxycycline (100 mg every 12 h), and then narrowed to doxycycline once anaplasma serology and PCR returned positive and other sources of infection had been excluded. Anticoagulation was transitioned from unfractionated heparin to apixaban (5 mg twice daily). He was discharged home on hospital day six to complete a 14-day course of doxycycline, with an ambulatory loop recorder to screen for recurrent atrial fibrillation.

Two weeks after discharge, the patient followed up with infectious disease and reported feeling well with no recurrent fevers. Doxycycline was stopped. He followed up in the Heart Failure Cardiology clinic 1 month after discharge and reported feeling well with no fevers, dyspnoea, or chest pain. His physical examination was unremarkable. ECG showed normal sinus rhythm with no conduction abnormalities. A 14-day loop recorder revealed predominantly sinus rhythm with

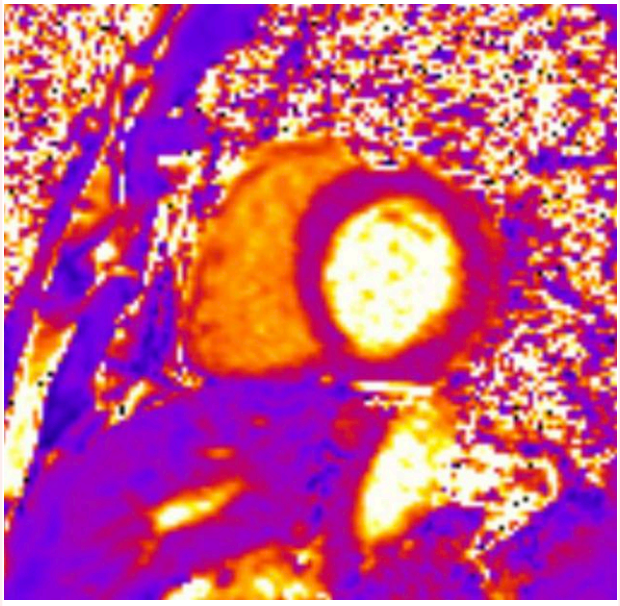

Figure 4 Cardiac MRI, post-discharge 2 week follow-up. T_2 imaging demonstrates normal relative regional signal intensity suggesting resolution of oedema/inflammation.

no recurrent atrial fibrillation and no episodes of high-grade heart block. A repeat CMR showed LVEF of 59%, normal RV size and systolic function, resolution of the pericardial effusion, and normal T_2 signal intensity (*Figure 4*).

Discussion

Aetiologies of myocarditis include infection, immune related, or toxin mediated. Viral causes are the most important cause in North America and Europe.[2] Other infectious aetiologies include bacterial, spirochetal, fungal, protozoal, parasitic, and rickettsial. In endemic areas, tick-borne illnesses, especially borrelia burgdorferi, are well-known culprits.

Our patient presented with mixed shock due to vasodilation, hypovolaemia, and RV dysfunction. He was found to have myopericarditis, with workup revealing isolated anaplasma phagocytophilum infection. He stabilized with fluids and a brief course of vasopressors, while receiving treatment with broad antibiotics, which were narrowed to doxycycline after diagnosis of HGA.

In our patient HGA was the sole identifiable culprit. This is an uncommon finding; isolated HGA myocarditis or myopericarditis has been reported only once previously.[3] Human monocytic ehrlichiosis is also an uncommon culprit, and when it does cause myocarditis, it is almost always in immunocompromised individuals.[4]

This case adds further evidence that myopericarditis and serious haemodynamic compromise are potential severe complications of HGA infection, without the need for a concomitant Lyme infection. Given the rising number of cases seen in a broader geographic distribution, we emphasize the importance of testing for anaplasma phagocytophilum in such presentations, and continuation of doxycycline until HGA has been ruled out, even if Lyme testing returns negative.

Unique to this case is the finding of moderate-to-severe RV dysfunction. Previously, ehrlichial infections have been linked with left ventricle dilation and dysfunction exclusively.[5] The RV dysfunction markedly improved between the time of the echocardiogram, performed within 48 h of his presentation, and the first CMR, performed five days later, suggesting an acute and reversible injury.

Additionally, conduction and rhythm abnormalities presented concurrent with the deterioration in clinical status of our patient. Conduction and rhythm abnormalities are frequently associated with Lyme disease but have not been previously reported with HGA.[6] This case highlights that conduction and rhythm disturbance can be a feature of myocarditis in the setting of isolated HGA infection.

Conclusions

We demonstrate that anaplasma phagocytophilum infection, in the absence of any concomitant Lyme disease, can cause acute myopericarditis, and that HGA myopericarditis can present with electrical disturbances including atrial fibrillation and conduction system disease. This case highlights the importance of including HGA in the differential diagnosis and initial workup of patients presenting with a clinical syndrome consistent with myopericarditis, and continuing doxycycline until both Lyme and HGA have been ruled out, especially in endemic regions during the late spring through early fall. While HGA is an uncommon cause of myopericarditis, it represents a very treatable cause where initiation of appropriate early antibiotic therapy may help reduce illness duration and severity and mitigate myocardial injury.

Lead author biography

Alexander Levy is a resident physician in internal medicine at Beth Israel Deaconess Medical Center. He is applying to cardiology fellowship in the current application cycle. His interests include cardiac critical care and medical education.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Patient Consent: Consent was obtained verbally and in writing with the patient whose case is presented above and in the supplemental materials, in accordance with COPE guidelines.

Conflict of interest: None declared.

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