Histoplasmosis Myocarditis in an Immunocompetent Host After a Recreational Mud Run

Briana L. Scott, MD, a Jennifer I. Sherwin, MD, a,b Kyle J. Rehder, MD, a,b Michael J. Campbell, MD, a,c Caroline P. Ozment, MD a,b

Abstract

Mud runs are an increasingly popular recreational fitness activity across the United States, combining a running race through an obstacle course with submersion in mud. Recent reports estimate 4 million people have participated in these types of events over the last 5 years. We describe an atypical case of myocarditis and multiorgan failure from disseminated histoplasmosis in a previously healthy pediatric patient, likely acquired during participation in a mud run. Although cases of histoplasmosis-associated endocarditis and pericarditis have been reported in the literature, cases of histoplasmosis myocarditis are rare.

Histoplasmosis is typically a mild pulmonary infection acquired by inhalation of Histoplasma capsulata spores that reside in soil with heavy bird or bat dropping contamination.1 These dimorphic fungi are endemic to the central and eastern United States, particularly around the Ohio and Mississippi River valleys. Severe disseminated, multiorgan diseases can be seen in immunocompromised patients, and cases of endocarditis and pericarditis have been well described.1,2 We report an extremely rare case of myocarditis secondary to disseminated histoplasmosis in an immunocompetent, previously healthy pediatric patient, presenting with acute multiorgan failure shortly after participating in a mud run.

A 16-year-old, previously healthy girl presented to an outside hospital with malaise, fever, vomiting, and diarrhea. She rapidly progressed to multiorgan failure, including cardiac dysfunction, acute respiratory distress syndrome, and renal failure (Fig 1). An initial echocardiogram revealed mild to moderately depressed left ventricular systolic function with wall motion abnormalities and mild mitral regurgitation. Because of progressive and refractory respiratory and renal failure, she required support with veno-venous extracorporeal membrane oxygenation (ECMO) and continuous renal replacement therapy. During this time, she developed worsening cardiac function with hypotension, elevated cardiac enzymes, and episodic ventricular tachycardia requiring inotropic support as well as antiarrhythmic therapy with lidocaine and amiodarone. She improved with these therapies over the next 14 days and was decannulated from ECMO, removed from continuous renal replacement therapy, weaned to minimal ventilator settings, and weaned off all vasopressors. She still required amiodarone for ventricular tachycardia. Several days later, she suffered a second cardiorespiratory decompensation and was transferred to our quaternary care center for further evaluation and management. On arrival to our institution, she required reintiation of veno-venous ECMO, inotropic support, and continued antiarrhythmic therapy for...
ventricular tachycardia. At this time, an echocardiogram demonstrated moderate tricuspid and severe mitral regurgitation, abnormal left ventricular diastolic function, and global decreased left ventricular systolic function. The etiology of her illness had not yet been identified, and an extensive rheumatologic and infectious workup, including a bronchial alveolar lavage, was initially unrevealing. Given her acute cardiac dysfunction, she was treated for presumed viral myocarditis with intravenous steroids and immunoglobulin. She also received empirical vancomycin, meropenem, and fluconazole for broad bacterial and fungal coverage.

On day 8 of her second ECMO run, the results of a urine *H capsulata* antigen test returned positive, and antifungal therapy with amphotericin B was initiated. Shortly thereafter, inotropic support was rapidly weaned, although she continued to have intermittent ectopy, primarily nonsustained ventricular tachycardia. Her pulmonary disease improved, and she was successfully decannulated for the second time on day 14. Although biopsy currently remains the gold standard for a diagnosis of myocarditis, the risk of further irritating her already proarrhythmic myocardial tissue was felt to outweigh the benefit, and thus noninvasive imaging was pursued instead. Cardiac MRI (CMRI), obtained 5 days after ECMO decannulation, revealed moderate to severely reduced left ventricular systolic function, severe mitral regurgitation, and nearly transmural midmyocardial hyperenhancement in the septum and inferior wall, consistent with myocarditis (Fig 2). Twelve days after starting amphotericin B, the results of repeat urine *H capsulata* antigen tests were negative. She was transitioned to oral antiarrhythmic drugs and continued a slow steroid taper for myocarditis. After a 2-month hospital stay during which she received 6 weeks’ worth of intravenous amphotericin B, she was discharged from the hospital on oral posaconazole to complete a total of 12 months of therapy for disseminated histoplasmosis. She also left the hospital wearing a LifeVest, with plans to monitor her cardiac function before further permanent interventions. The LifeVest is an external personal monitor and defibrillator most often used as a bridge to implantable cardioverter defibrillator placement. She later underwent implantable cardioverter defibrillator placement because of persistent left ventricular systolic dysfunction with ventricular tachycardia. During the hospitalization, she also had an immunologic workup that was unremarkable.

Further research into the patient’s history revealed that she had participated in a mud run in western North Carolina ~4 weeks before becoming ill. After a thorough review of the patient’s epidemiologic risk factors for infection with histoplasmosis and discussion with our infectious disease team, it was suspected that this immunocompetent patient inhaled a heavy inoculum of *H capsulata* during the mud run, resulting in disseminated disease characterized by myocarditis and multiorgan failure. No other known reports of illness surfaced surrounding the same mud run. Despite the low prevalence of histoplasmosis in North Carolina, local infectious disease physicians suggest a possible endemic area in the western part of the state.

Myocarditis has been defined by the World Health Organization as an inflammatory disease of the heart muscle, diagnosed by established histologic, immunologic, and immunohistological criteria. In previous postmortem literature, researchers describe the incidence of myocarditis in the general population as 0.15% to 0.6%, and the researchers for more recent studies suggest that 4% to 7.5% of sudden cardiac deaths in adolescents are attributable to myocarditis. Additionally, the prevalence of pediatric cases in emergency departments has been reported via retrospective review to be 0.5 cases per 10,000 visits. The true incidence of myocarditis likely remains largely unknown given the wide range of clinical presentations. Myocarditis presents along a broad clinical spectrum, from minimal symptoms such as resting tachycardia, diaphoresis, malaise,
and/or anorexia, to severe heart failure and sudden cardiac death. Biopsy remains the gold standard for diagnosis, although with significant limitations, because myocarditis affects the myocardium in a sporadic manner, and a negative biopsy result may not exclude disease. CMRI has become a valuable noninvasive diagnostic tool for myocarditis, and there are now widely accepted myocarditis protocols. This modality provides a detailed assessment of the tissue markers of myocarditis: edema, inflammation, and fibrosis. Criteria have been developed by the International Consensus Group on Cardiovascular Magnetic Resonance to standardize the diagnosis of myocarditis by using CMRI. The guidelines report the ultimate balance of diagnostic sensitivity and specificity for acute myocarditis with the presence of 2 or more of the following criteria: myocardial edema (T2 short TI inversion recovery), hyperemia and/or capillary leak (early enhancement), or myocardial fibrosis (late gadolinium enhancement).

Numerous etiologies of myocarditis have been described in the literature, including viruses, bacteria, fungi, toxins, and autoimmune diseases. The most common viral etiologies in developed countries are enterovirus, adenovirus, parvovirus B19, human herpes virus 6, Epstein-Barr virus, and cytomegalovirus. Myocarditis secondary to H capsulata has rarely been reported. A review of the literature reveals just a single case report from 1961 involving 2 siblings, ages 5 and 9, with histoplasmosis myocarditis and pericarditis. The severity of symptoms related to H capsulata infections is related to the individual host immune response, as well as the inoculum size.

Most cases are self-limited and either asymptomatic or present with vague, nonspecific symptoms such as fever, headache, cough, and malaise. Patients with disseminated disease usually have a high fungal burden, lending to rapid diagnosis with antigen detection. Urine antigen detection sensitivity for disseminated disease is estimated at 80% to 90%. The majority of pediatric disseminated histoplasmosis cases are seen in immunocompromised patients, namely infants given the immaturity of their immune system, children with rheumatologic conditions, or transplant recipients taking immunosuppressive therapy. Disseminated histoplasmosis is rare in immunocompetent children.

Well-known cardiac complications in immunocompromised adults include endocarditis and pericarditis; however, myocarditis has seldom been reported in the literature. Providers should be aware of the rare but real possibility of disseminated fungal disease with corresponding cardiac dysfunction in immunocompetent patients. Additionally, this case supports the need for increased provider awareness surrounding potential health hazards associated with popular recreational activities such as mud runs.

**ACKNOWLEDGMENTS**

We thank the multidisciplinary care team, including pediatric critical care and infectious disease physicians, pediatric residents, nurses, respiratory therapists, ECMO specialists, and physical, speech, and occupational therapists. We acknowledge the perseverance of this patient and her family and admire their courage.

**ABBREVIATIONS**

CMRI: cardiac MRI
ECMO: extracorporeal membrane oxygenation

**REFERENCES**

10. Weinberg QA, Kleiman MB, Grosfeld JL, Weber TR, Wheat LJ. Unusual manifestations of histoplasmosis...


Histoplasmosis Myocarditis in an Immunocompetent Host After a Recreational Mud Run
Briana L. Scott, Jennifer I. Sherwin, Kyle J. Rehder, Michael J. Campbell and Caroline P. Ozment
*Pediatrics* 2018;141;S462
DOI: 10.1542/peds.2017-1074

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>including high resolution figures, can be found at: <a href="http://pediatrics.aappublications.org/content/141/Supplement_5/S462">http://pediatrics.aappublications.org/content/141/Supplement_5/S462</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>References</td>
<td>This article cites 16 articles, 9 of which you can access for free at: <a href="http://pediatrics.aappublications.org/content/141/Supplement_5/S462">http://pediatrics.aappublications.org/content/141/Supplement_5/S462</a> #BIBL</td>
</tr>
<tr>
<td>Subspecialty Collections</td>
<td>This article, along with others on similar topics, appears in the following collection(s): Infectious Disease <a href="http://www.aappublications.org/cgi/collection/infectious_diseases_sub">http://www.aappublications.org/cgi/collection/infectious_diseases_sub</a> Cardiology <a href="http://www.aappublications.org/cgi/collection/cardiology_sub">http://www.aappublications.org/cgi/collection/cardiology_sub</a></td>
</tr>
<tr>
<td>Permissions &amp; Licensing</td>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="http://www.aappublications.org/site/misc/Permissions.xhtml">http://www.aappublications.org/site/misc/Permissions.xhtml</a></td>
</tr>
<tr>
<td>Reprints</td>
<td>Information about ordering reprints can be found online: <a href="http://www.aappublications.org/site/misc/reprints.xhtml">http://www.aappublications.org/site/misc/reprints.xhtml</a></td>
</tr>
</tbody>
</table>
Histoplasmosis Myocarditis in an Immunocompetent Host After a Recreational Mud Run
Briana L. Scott, Jennifer I. Sherwin, Kyle J. Rehder, Michael J. Campbell and Caroline P. Ozment
*Pediatrics* 2018;141:S462
DOI: 10.1542/peds.2017-1074

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/141/Supplement_5/S462