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Bacterial Pyomyositis Associated with Human Immunodeficiency Virus: Diagnosis, Management, and Review of the Recent Literature

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Abstract

Purpose of review We present a case and provide a review of all the confirmed cases of pyomyositis in human immunodeficiency virus (HIV)-positive patients in the literature after the last published case series, from September 16, 2004 to February 1, 2019. The goal of this review is to examine recent trends in causative organisms, diagnostic modalities, and duration of therapy for patients with HIV and pyomyositis in the antiretroviral therapy (ART) era.
Recent findings Pyomyositis affects predominately the lower extremities and can have extra-muscular manifestations. Magnetic resonance imaging is the gold standard for diagnosis but computed topography may be sufficient. Without appropriate clinical suspicion, pyomyositis can be misdiagnosed.
Summary HIV remains an important risk factor to develop pyomyositis. While magnetic resonance imaging is the preferred diagnostic imaging modality, computed tomography may also be sufficient. Treatment is non-standardized and consists of surgical source control coupled with systemic intravenous and oral antibiotics of variable duration.

Introduction

Sir William Osler described the first case of pyomyositis in the English literature in 1892. He defined pyomyositis as "diffuse purulent infiltration of the muscle" [1]. Early accounts of the disease process are predominantly reported from the tropical regions, which led to the term "tropical pyomyositis" or "*myositis tropicans*" to describe the clinical entity [2]. Tropical pyomyositis presents in young and healthy adults with *Staphylococcus aureus* and *Streptococcus* spp. implicated as the most common causative organisms [3]. In more recent literature, pyomyositis is reported in temperate climates and typically affects immunocompromised individuals including those with human immunodeficiency virus (HIV) [4]. We describe a unique case of methicillin-resistant *Staphylococcus aureus* (MRSA) pyomyositis in a patient with uncontrolled HIV and provide a review of the recent literature to examine diagnostic trends and management in the antiretroviral therapy (ART) era.

Case report

A 34-year-old male with a history of treated primary syphilis, untreated hepatitis C virus, uncontrolled HIV infection with CD4 of 126 and viral load of 600,000 copies/mL, and a history of non-adherence to medications and clinic visits presented to the emergency department with a 2-week history of constant, progressive, and bilateral thigh pain that was more intense on the left. He described the pain as constant and severe that worsened on weight bearing with no relieving factors. The patient also reported associated swelling and redness of the involved skin on his bilateral thighs along with weakness of the corresponding muscle groups. He experienced subjective fevers and chills for 1 week and denied pain in any other muscles or joints as well as preceding history of trauma. The patient was non-adherent to ART for several years prior to admission but took atovaquone for *Pneumocystis jiroveci* pneumonia prophylaxis due to development of hives on trimethoprim/sulfamethoxazole. His social history was notable for brief incarceration. No recent travel outside of the USA was reported. The patient denied intravenous drug use. Two days prior to presentation, a referring hospital evaluation resulted in the presumed diagnosis of atovaquone-associated myalgias.

On physical exam, the patient had an elevated temperature of 39.5° C with tachycardia of 100 beats per minute, tachypnea of 33 breaths per minute, and saturating 100% on room air. Blood pressure was 116/88 mmHg. He did not appear to be in overt distress. There was palpable anterior cervical and bilateral inguinal lymphadenopathy. Examination of the extremities revealed bilateral swelling of the thighs, left greater than right, with tenderness on palpation and mild erythema on the left. There were no associated ecchymoses, vesicles, or bullae. No joint swelling was appreciated. Cardiovascular, pulmonary, and abdominal exams were unremarkable.

Abnormal laboratory values are noted in Table 1. Bacterial and fungal blood cultures were negative. Magnetic resonance imaging (MRI) showed findings consistent with multiloculated abscesses involving the anterior compartments of bilateral thighs (Fig. 1).

The patient was initiated on broad-spectrum antibiotics of intravenous vancomycin and piperacillin-tazobactam on admission. He underwent incision and drainage of bilateral thigh abscesses with purulent material noted from the

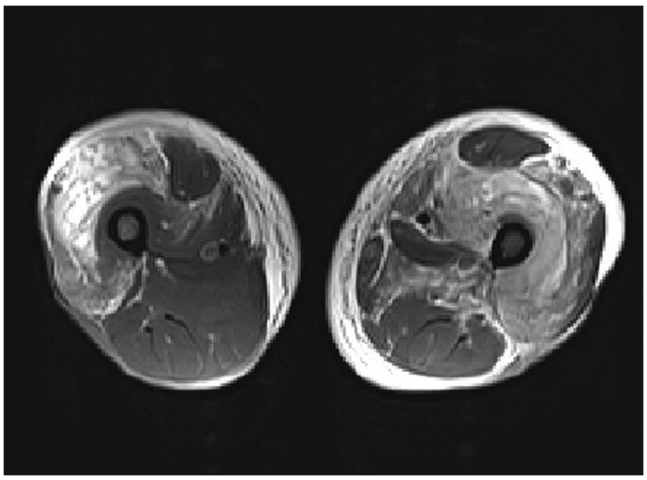

Fig. 1. Magnetic resonance imaging of bilateral lower extremities with findings of multiloculated abscesses involving the anterior compartments of the bilateral thighs consistent with the diagnosis of pyomyositis.

right thigh and growth of MRSA on cultures. Fungal cultures were negative. Antimicrobial therapy was subsequently narrowed to intravenous vancomycin alone. However, he developed renal insufficiency that required transition to daptomycin at 6 mg/kg/day. The patient completed 4 weeks of intravenous antibiotics with significant clinical improvement on hospital follow-up visits. He continues to do well 4 months later.

Discussion

Evidence review

Two review articles on pyomyositis are published in the last 40 years, most recently in 2004.

Christin and Sarosi provided two case reports and a review of the literature from 1972 to 1992. They described 100 cases of pyomyositis in North America,

Table 1. Abnormal laboratory values

	Patient's value (reference range)
Sodium	131 mmol/L (135–145 mEq/L)
Potassium	5.4 mmol/L (3.6–5.1 mmol/L)
Blood urea nitrogen	57 mg/dL (8–23 mg/dL)
Creatinine	1.57 mg/dL (0.60–1.20 mg/dL)
White blood cell count	4.4×10e9/L (3.7–9.7×10e9/L)
Hemoglobin	7.7 g/dL (13.3–17.2 g/dL)
Creatinine kinase (peak)	756 units/L (40–350 units/L)

Table 2. Reported cases of pyomyositis in human immunodeficiency virus-positive patients after 2004

Year	Author	Age/sex	Culture	Clinical	Extra-muscular involvement	CD4	ART
2004	Lawn	45/F	*Mycobacterium avium*	Chronic unilateral LE pain that acutely worsened 2 weeks after starting ART	Cutaneous abscesses	84→101	Yes
2004	Buckland	34/M	*Staphylococcus aureus*	Fever, low back pain, bilateral LE swelling, and pain with UE involvement	Lumbar osteomyelitis and discitis	350	Yes
2004	Marquez	NC	NC	NC	–	NC	NC
2007	Garcia-Luchez	32/F	*Streptococcus pneumoniae*	NC	–	NC	NC
2007	Garcia-Luchez	40/F	*Streptococcus pneumoniae*	NC	–	NC	NC
2009	Chen	42/M	*Mycobacterium tuberculosis*	Chronic intermittent LE pain that acutely worsened 1 week after ART	–	102→225	Yes
2010	Yassin	50/M	*Streptococcus anginosus*	2 weeks of fevers, chills, unilateral LE pain	Brain abscesses (co-infection)	250	Yes
2013	Kole	NC	NC	NC	–	NC	NC
2013	Kole	NC	NC	NC	–	NC	NC
2018	Present	34/M	Methicillin-resistant *Staphylococcus aureus*	2 weeks of fevers, chills, and progressive bilateral LE pain	–	21	No

Year	Trauma	Imaging	Surgical	Therapy	Duration of therapy	Outcome
2004	No	MRI	Yes	Quadruple drug regimen →Rifabutin, clarithromycin, ethambutol	NC	δ
2004	Yes	MRI	Yes	Cefuroxime and erythromycin→flucloxacillin IV→flucloxacillin and gentamicin→flucloxacillin PO	8 weeks IV then 4 months of PO	δ
2004	NC	NC	NC	NC	NC	NC
2007	NC	NC	Yes	NC	NC	δ
2007	NC	NC	Yes	NC	NC	δ
2009	NC	CT	Yes	Quadruple drug regimen and steroids	NC	δ
2010	NC	MRI	Yes	Ampicillin and amoxicillin clavulanate→pyrimethamine* and clindamycin*	15 months	δ
2013	NC	NC	NC	NC	NC	NC
2013	NC	NC	NC	NC	NC	NC
2018	No	MRI	Yes	Vancomycin and piperacillin-tazobactam→daptomycin	4 weeks	δ

ART antiretroviral therapy, *δ* resolved, *NC* no comment, *F* female, *M* male, □ indicates a change, *LE* lower extremity, *MRI* magnetic resonance imaging, *IV* intravenous, *PO* by mouth
*Treatment also for possible CNS toxoplasmosis

21 of whom had HIV. In the series, pyomyositis affected the right and left side equally, with a predilection for large muscle groups, particularly the quadriceps femoris. *Staphylococcus aureus* accounted for 70% of the infections with *Streptococcus* spp. being the second most implicated pathogen at 16% of the infections [2].

Crum et al. compared cases of 84 HIV-positive individuals and 247 HIV-negative individuals. Their ages ranged from 7 weeks to 66 years old. Ninety-two percent of the HIV-positive persons had acquired immunodeficiency syndrome (AIDS). *Staphylococcus aureus* (70%) was the predominant pathogen and only one methicillin-resistant species that was treated with vancomycin. The average duration of treatment was 4 weeks, which included 2 weeks of intravenous therapy followed by 2 to 3 weeks of oral antibiotics [5].

A literature search was conducted using the PubMed database to identify case reports of pyomyositis in HIV-positive patients published between September 2004 and February 2019. The date of September 2004 was selected to capture cases after the most recently published case series. Our search used the matrix ("pyomyositis"[MeSH Terms] OR "pyomyositis" [All Fields]) AND ("hiv"[MeSH Terms] OR "hiv"[All Fields] OR ("human"[All Fields] AND "immunodeficiency"[All Fields] AND "virus"[All Fields]) OR "human immunodeficiency virus"[All Fields]). We restricted case reports to adult (aged ≥ 18 years) human data reported in the English language. A total of 9 cases met our search criteria and are summarized in Table 2, along with our case.

Epidemiology

Approximately 330 cases of pyomyositis are reported in the USA [6]. The first case of pyomyositis in an HIV-positive patient was described in 1987 [7]. Ten additional cases of pyomyositis in HIV-positive adults have been described in the literature since 2004 [8–13, present case]. The decrease in incidence of case reports could be due to a decline in the incidence of pyomyositis secondary to increased ART and/or decreased reporting of the condition in the literature.

Pyomyositis has a male predominance [4] that occurred in 4/10 cases [8, 11, 12, 14, present case] though 3/10 cases did not specify the sex of the patient [9, 13]. Acquired immune deficiency syndrome (AIDS) is a risk factor [15]. Five cases had CD4 counts reported [8, 11, 12, 14, present case] and only two patients had a CD4 count greater than 200/mm^3 [11, 14] with one of these patients undergoing immune reconstitution inflammatory syndrome (IRIS) [11]. Half of the patients were on ART but compliance was not described [8, 11, 13, 14]. Of note, two cases of pyomyositis were associated with IRIS after initiating ART [8, 11]. In addition to HIV, comorbid conditions such as diabetes, sickle cell disease, and intravenous drug use were found to be associated with approximately half of pyomyositis cases [16].

Staphylococcus aureus compromise approximately 70% of all reported cases in North America [6, 17]. Two cases [14, present case] report *Staphylococcus aureus* as the causative organism. Methicillin-sensitive *Staphylococcus aureus* causes the majority of infections [6] but an increasing number of MRSA positive pyomyositis are being reported [16, 18, present case]. *Streptococcus pneumonia*

[10] accounted for two cases while *Streptococcus anginosus* accounted for one [12]. Interestingly, in the two cases of pyomyositis associated with IRIS, *Mycobacterium tuberculosis* and *Mycobacterium avium*, were the causative organisms [8, 11].

Pathogenesis

The pathogenesis of pyomyositis is not completely understood. Skeletal muscles are intrinsically resistant to infection; hence, infections associated with them are rare [17]. Theoretically, intramuscular hematomas form and serve as a nidus for infection [17]. Transient bacteremia subsequently seeds the hematomas and results in infection. Hence, etiology of pyomyositis appears to be hematogenous [18]. Interestingly, in temperate zones, only 22–42% of patients have positive blood cultures [19]. Prior trauma is a reported risk factor of pyomyositis [2, 5, 6]. However, in our review, only one case reported prior trauma [14].

Clinical presentation

Pyomyositis occurs in three clinical stages. The first stage is the invasive stage and is variable from an acute to chronic presentation on our review. During this stage, the presenting complaints are somewhat vague [17]. The pain is mild, intermittent, and localized to the presenting muscle group. Previously, this stage was described to last from 12 h to 1 year with an average of 24 days. In our review, only the two cases associated with IRIS and *Mycobacterium* spp. reported pain that lasted longer than 1 month [8, 11].

The second stage is the purulent stage [16], a collection of pus forms at the site of pain. The purulent stage will progress to the late, septic stage if left untreated.

All the patients in our review were febrile. About half of the cases reported the location of pyomyositis. All reported locations involved the lower extremities [8, 11, 12, 14, present case]. One case had an upper extremity involved in addition to the lower extremity [14]. The majority of presentations that reported laterality were unilateral [8, 11, 12]. Two cases, including the one described here, reported bilateral involvement [14]. Other individual cases reported extramuscular involvement including brain abscesses (likely a co-infection) [12], cutaneous abscesses [8], and discitis/osteomyelitis [14] which reflect the similar pathogenesis of metastatic infectious seeding.

The clinical presentation of pyomyositis with a swollen, erythematous and painful lower extremity mimics other diagnoses, especially if a patient is afebrile. A previous case described an initial venous duplex that was falsely positive for deep venous occlusion likely due to edema causing an occlusion of flow [2].

Diagnosis

Typically, the diagnosis of pyomyositis is made through radiological studies. Supporting laboratory findings include a low or normal leucocyte count in immunocompromised hosts [5, present case] and mild elevations in *creatinine kinase* (CK), even in cases with associated myonecrosis [20].

The Infectious Diseases Society of America (IDSA) recommends diagnosing pyomyositis with MRI [21]. Magnetic resonance imaging has a higher sensitivity in detecting the multiple small fluid collections that the disease can produce;

therefore, it is preferred over computed tomography (CT) [18, 22]. Computed tomography and ultrasound are useful imaging modalities in the event MRI is unavailable [21]. Ultrasound may have limitations to detect abnormalities in deeper soft tissue infections [22]. Cultures of the blood and abscess material should be obtained [21] and utilized in identifying the causative organism.

Blood cultures are less likely to be positive in the HIV population with pyomyositis compared with non-HIV-infected persons [6]. Half of the cases reported imaging modalities [6, 8, 12, 14, present case] to aide in the diagnosis. Four used MRI [8, 12, 14, present case] while one utilized contrast CT [6].

Treatment

Pyomyositis should be initially managed with intravenous antibiotics and early fluid collection drainage [21]. Selection of antibiotics initially includes vancomycin to cover the most common causative organism of *Staphylococcus* species [21]. For immunocompromised patients, including those with HIV, initial coverage should also include antibiotics that cover enteric gram-negative organisms [21, 23]. Antibiotic therapy can be narrowed once a causative organism is identified on culture data. It is clinically logical to repeat imaging to assess for persistent fluid collections if patient shows evidence of persistent infection. If there is clinical improvement, antibiotic therapy can be transitioned from intravenous to systemic oral antibiotics to complete 2–3 weeks course of therapy [21].

Of the 10 case reports since 2004, 7 commented on surgical management. They underwent surgical incision and drainage of the infected site identified [8, 10–12, 14, present case]. Only 5 of the 10 cases commented on antibiotic management of the pyomyositis infections [8, 11, 12, 14, present case]. One case identified *Mycobacterium tuberculosis* (TB) as the causative organism [11] and another isolated *Mycobacterium avium* [8] both of which were treated with quadruple antibiotic therapy (Table 2). However, the duration of this therapy was not described. Two additional cases utilized a penicillin class antibiotic with gentamicin [14] and the other with intravenous clindamycin and pyrimethamine for possible coinfection CNS toxoplasmosis [12]; the duration of initial treatment was 6 weeks and 2–4 weeks respectively followed by an oral antibiotic duration of 4 months and 1 year. The present case was treated with vancomycin and piperacillin-tazobactam initially and was transitioned to vancomycin and then daptomycin when cultures returned positive for MRSA to compete a total 4-week course of antibiotics.

Conclusions

Pyomyositis is an uncommon condition occurring in temperate zones and is characterized by acutely worsening extremity swelling, pain, and fever in primarily the large muscles of the lower extremities. Pyomyositis is frequently diagnosed as myalgias, deep vein thrombosis [2], and cellulitis. Diagnosis by MRI is recommended [21] since it is the most sensitive but CT scan would be appropriate if MRI is not available. Regardless of diagnostic modality, surgical drainage or aspiration in addition to systemic antibiotics is imperative for treatment especially to target therapy to offending pathogen. Choice and duration of antibiotic therapy is not well defined by prospective studies; however,

intravenous and oral antibiotic combinations ranging from 4 weeks to 15 months were reported with longer durations in cases with extramuscular involvement. Although pyomyositis is an uncommon condition, HIV-positive individuals particularly those with lower CD4 counts are at an increased risk for developing this skeletal muscle infection and it remains an important diagnostic consideration even in the ART era.

Compliance with Ethical Standards

Conflict of Interest

Dr. Laura Pedersen declares that she has no conflict of interest.
Dr. Kathryn Hess declares that she has no conflict of interest.
Dr. Sangeeta Sastry declares that she has no conflict of interest.
Dr. Gonzalo Bearman declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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