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Case Report Open Access

An Unusual Case of Pyomyositis in a Neutropenic Patient with Acute Myelogenous Leukemia

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Abstract

Pyomyositis, a purulent infection of the skeletal muscle, is a rare condition that historically was seen in tropical climates in individuals with a recent history of muscular trauma. Recently, *Escherichia coli* pyomyositis has been recognized as a distinct clinical entity occurring with near exclusivity in the hematologic malignancy patient. *Mycobacterium tuberculosis* (TB) is a rare cause of pyomyositis in the United States and can arise in immunocompetent as well as immunocompromised hosts. Because of the relatively indolent presentation of this condition, a high degree of suspicion should be maintained when a patient in the appropriate population (Examples: neutropenic, on immunosuppressive drugs) presents with non-specific yet localized musculoskeletal pain. We report a unique case of pyomyositis due to *E. coli* and MTB arising in a patient with prolonged neutropenia secondary to refractory acute myelogenous leukemia (AML) and summarize the available literature on this rare disease.

Introduction

Pyomyositis is a purulent infection involving the skeletal muscle and the immediately surrounding soft tissues. Historically, the Gram-positive cocci, most notably *Staphylococcus aureus*, were considered the primary etiologic agents of the so-called "tropical pyomyositis" [1]. Recently, this disease has been described with increasing frequency in the hematologic malignancy patient, especially as these patients experience prolonged periods of neutropenia. In this vulnerable patient population, *E. coli*, a Gram-negative rod, seems to be the most common etiologic agent of pyomyositis [2,3]. Because the presentation of this serious condition can be relatively mild and non-specific, clinicians should maintain a high degree of suspicion for pyomyositis when at-risk patients present with signs and symptoms of soft-tissue infection or non-specific, localized musculoskeletal pain. We present a case of pyomyositis occurring in a patient with prolonged neutropenia secondary to refractory acute myelogenous leukemia (AML) and we summarize the available literature regarding pyomyositis.

Case Report

A 49-year-old Vietnamese female with a past medical history significant for *Mycobacterium tuberculosis* (TB) infection (diagnosed and treated in Vietnam as an adolescent), myelodysplastic syndrome (MDS) progressing to acute myelogenous leukemia (AML), and prolonged pancytopenia/neutropenia re-presented to our facility 18 days following discharge for an episode of sepsis due to *Pseudomonas aeruginosa*. She was discharged afebrile on ciprofloxacin 750 mg twice per day, voriconazole 200 mg twice per day, and acyclovir 800 mg twice per day as neutropenic prophylaxis. On presentation, she was febrile to 100.8°F and complained of bilateral frontal headache and profound fatigue. Of note, the patient spent 2 hours the night before presentation in a hot tub. Physical examination was unremarkable, apart from mild tenderness of the left calf with no associated skin changes. The patient was admitted for further work-up of neutropenic fever. At the time of admission, the suspected source of infection was sinusitis versus a urinary tract infection (UTI).

Over the next two days, the left lower extremity pain worsened in severity and urine cultures performed at admission grew *E. coli*. On hospital day 2, the patient received a magnetic resonance image (MRI) of the left lower extremity (LLE) (Figure 1). The MRI revealed a rim-enhancing intramuscular fluid collection within the left soleus muscle. There was increased T2 signal intensity and evidence of restricted diffusion by diffusion weighted imaging (DWI). Based on this finding, a presumptive diagnosis of muscle abscess with pyomyositis was made. The patient was continued on ciprofloxacin 750 mg twice per day, by mouth, and cefepime 1,000 mg per 6 hours intravenously (IV). On hospital day 4, drainage of the abscess and surrounding purulent fluid was made using a fine needle. Culture of the drained fluid revealed *E. coli* sensitive to piperacillin-tazobactam, which was started on hospital day 6 at a dose of 3,375 mg per 6 hours IV. She reported subjective improvement of the left calf pain with ambulation and was eventually discharged home on piperacillin-tazobactam continuous infusion (CI).

The patient presented to our facility again 40 days following discharge with a chief complaint of increased swelling and pain in the left lower extremity. A complete blood count (CBC) revealed persistent neutropenia (ANC<500 k/μL). Treatment with piperacillin-tazobactam was presumed to have failed and treatment with meropenem 1 gm per 8 hours IV was initiated. On the first hospital day, interventional radiology re-drained the soleus fluid collection under computed tomography (CT) guidance and left a Jackson-Pratt drain in place. Gram-stain and culture of the drained fluid again revealed abundant *E.*

coli. Of note, a sample of this fluid was inoculated onto a TB culture dish because of the patient's history of active TB infection in adolescence. The drain was removed after 7 days. The patient was discharged after 12 hospital days with a plan to continue meropenem 1 gm every 8 hours IV at home for 6 weeks.

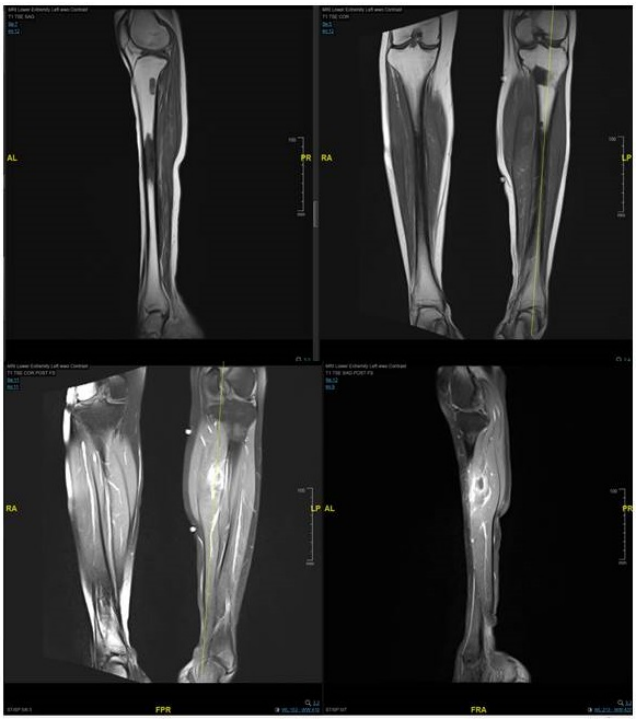

Figure 1: Magnetic Resonance Image of the left lower extremity; collection of fluid within the left soleus muscle. A: T1-weighted, anterior view. B: T1-weighted, left lateral view. C: T2 weighted anterior view. D: T2-weighted, left lateral view.

5 days later, the patient presented to the outpatient clinic for a scheduled follow-up visit. She was afebrile, but complained of subjective fevers, night sweats, bilateral rib cage pain with deep inspiration, and decreased appetite. She denied dyspnea and hemoptysis. Because of these complaints, she was admitted to the hospital. A CBC revealed an ANC of less than 1,500 k/μL and a CT scan of the thorax revealed multiple nodules in the apices of both lungs (Figure 2). By this time, the TB cultures from the previous hospitalization returned positive for an unspecified acid-fast bacillus (AFB). The treatment team relocated the patient to an airborne isolation room given the patient's distant history of TB (as an adolescent), apical pulmonary nodules, and now positive AFB culture. The patient continued to experience night sweats and experienced worsening pain of her LLE. The LLE was again drained and the fluid was sent for culture and AFB staining. The AFB stain of the aspirate was negative, but the cultures would return positive for TB less than a month later. An AFB sputum smear obtained on hospital day 5 was negative for AFB, but culture of this sputum would later grow TB. By hospital day 7, the original AFB aspirate culture was confirmed as TB and anti-TB therapy, consisting of rifampin, isoniazid (with vitamin B6), pyrazinamide, and ethambutol were initiated.

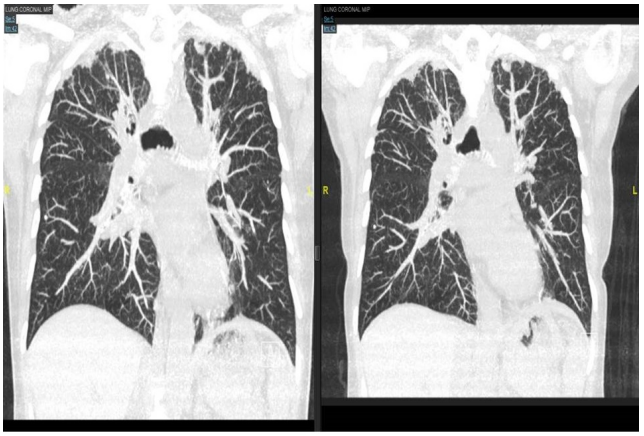

Figure 2: Computed tomography scan of thorax, coronal view; computed tomography (CT) scan of the thorax demonstrating increased apical nodularity over prior studies.

The patient remained febrile but experienced gradual resolution of her inspiratory chest pain. The pain in the LLE improved as well. However, on hospital day 19, 15 days after initiating anti-TB therapy, the TB isolate from the LLE aspirate was found to be resistant to isoniazid. Ciprofloxacin 400 mg per 8 hours IV was initiated in place of isoniazid. It should be noted that the patient by this point in her hospitalization had developed bacteremia with *Pseudomonas aeruginosa* and was experiencing a transaminitis secondary to chronic Hepatitis B virus infection. The bacteremia was treated successfully with cefepime and tobramycin. The chronic Hepatitis B virus infection was controlled with entecavir.

The patient was discharged after 51 hospital days well-appearing in guarded-yet-stable condition with instructions to follow-up with the county health administration for continued anti-TB therapy. The patient was also offered hospice care, given that her disseminated TB and persistent pancytopenia made her an inappropriate candidate for further chemotherapy for refractory AML. The patient refused hospice care and was discharged home, where she expired 47 days later.

Discussion

Pyomyositis progresses clinically in 3 stages as described in a classic article by Chiedozi [4]. The first stage involves inflammation of the affected muscles and their surrounding soft-tissues. Aspiration of the inflamed tissues at this stage will not yield frank pus. The second clinical stage arises between 2 and 3 weeks later, again with muscle pain that may be more severe, localized, and may closely mimic an abscess. In stage 3, patients appear clinically toxic with signs of Systemic Inflammatory Response Syndrome (SIRS) or frank sepsis.

Our patient's initial chief complaint was not musculoskeletal pain. The pain in her left calf was mentioned in passing and was found to become more severe during the hospital stay. The MRI proved efficacious in demonstrating the abscess and surrounding edematous tissue within the left soleus muscle (Figure 1). Aspiration using a fine needle improved the patient's pain and enabled culture and antimicrobial susceptibility testing. The recovery of extra-intestinal *E. coli* in this patient is not an unusual finding. Until recently, *E. coli* was the most common cause of bacteremia in neutropenic cancer patients

[5]. Over the course of the past decade, *S. aureus* has steadily overtaken *E. coli* as the most common cause of bacteremia in hematologic malignancy patients but, nevertheless, *E. coli* remains a major cause of nosocomial infection (including pneumonia, urinary tract infection, and bacteremia) and is responsible for some thousands of deaths each year [6-8].

Bacterial, or suppurative, myositis can be organized into 3 distinct categories based upon patient factors and bacterial etiology (Table 1). Cases of myositis that arise without pus formation are more likely to be viral in nature. While a plethora of viruses have been described as potential causes of non-suppurative myositis, the influenza virus is a notable cause of post-infection (i.e. convalescent phase) myositis, typically in children [9].

Type	Usual Etiology	Patient Context	Blood Cultures
Tropical	*S. aureus, Streptococcus spp.*	Tropical settings, usual history of muscle trauma	Usually Negative (>90 % of cases)
Tuberculous	TB, non-TB Mycobacteria	Prior exposure to TB followed by immunosuppressive drug therapy or immunocompetent	Variable
Neutropenic	Gram-negative, commonly *E. coli*	Hematologic malignancy, less commonly solid tumor	Often positive

Table 1: Comparison of the different forms of pyomyositis; TB: Tuberculosis.

E. coli has emerged as the most common Gram-negative cause of pyomyositis [2,3]. All 6 cases of *E. coli* pyomyositis reported by Vigil et al. occurred in patients receiving chemotherapy for a hematologic malignancy. More concerning is that 55% of the isolates recovered by Vigil et al. were found to be extended-spectrum β-lactamase (ESBL)-producing organisms. Approximately 1 year prior to that publication by Vigil et al. Chiu and Chang reported a case of pyomyositis caused by ESBL-producing *E. coli* (ESBLEC) in a patient with AML [10]. The patient described in that 2009 case report was treated successfully with surgical excision of the pyogenic focus and a 3-week course of meropenem.

Pyomyositis can also arise in patients undergoing treatment for solid-tumor malignancies [11,12]. Nakao et al. report a case of pyomyositis arising in a patient following chemotherapy for endometrial cancer. The causative organism in this case was *S. dysgalactiae equisimilis*, isolated from the bloodstream [11]. McRae and Sharma report a case of forearm pyomyositis, due to methicillin-resistant *S. aureus* (MRSA), arising in a patient undergoing chemotherapy for breast cancer [12]. It should be noted that cases of pyomyositis arising in the context of solid-tumor malignancy are much less common in the literature and that these two cases both report Gram-positive organisms. Takebayashi et al. report a unique case of pyomyositis arising in a patient with chronic myeloid leukemia (CML). Takebayashi reports that both blood and aspirated fluid cultures were negative, but that the patient demonstrated clinical improvement following initiation of linezolid [13]. The suspected organism in this unique case was MRSA, but no confirmatory cultures were obtained.

TB is also a well-described cause of pyomyositis. Unlike *E. coli*, TB has been identified as a cause of pyomyositis outside of the usual hematologic malignancy patient with prolonged neutropenia. Tuberculous pyomyositis has been seen in patients with autoimmune conditions taking immunosuppressive therapy [14-18]. Strikingly, tuberculous pyomyositis has also been described in immunocompetent individuals as well, diverging markedly from the patient population afflicted by *E. coli* pyomyositis [19-22]. From the reports available in the literature, it would also seem that tuberculous pyomyositis and *E. coli* pyomyositis favor different body sites. While *E. coli* pyomyositis clearly favors the lower extremity (with Sharma et al. reporting *E. coli* pyomyositis occurring at the hip and Vigil et al. reporting 5 out of 6 cases occurring in the lower extremity), pyomyositis caused by TB can arise in both the upper and lower extremities [2,3,14-18]. While this distinction is probably not sufficient to determine, clinically, the bacterial etiology of pyomyositis, it may guide the physician in ordering diagnositic studies on aspirated fluid (for instance, adding AFB stains on purulent fluid collected from the upper extremity or chest).

A final consideration in the differential diagnosis of myositis apart from the infectious causes that have been considered above is that of malignant myositis. While cases of malignancy mimicking infectious myositis are exceedingly rare, consideration must be given to myeloid sarcoma (also known as granulocytic sarcoma). Scheipl et al. have reported a case of myeloid sarcoma mimicking myositis of the lower extremity on T1 sequence MRI [23]. In cases where a neoplastic *vs.* infectious etiology of myositis is being considered, aspiration with subsequent cytologic and microbiologic analysis should yield a definitive diagnosis.

In summary, pyomyositis is a serious suppurative infection of the skeletal muscle and surrounding soft-tissues that often arises in the context of immunosuppression in hematologic malignancies or secondary to immunosuppressive medications for patients with autoimmune conditions. Ultimately, a high degree of suspicion must be maintained when neutropenic patients present with persistent, vague musculoskeletal pain. Imaging of the soft-tissues, followed by aspiration of the purulent focus, followed by antibiotics and frequent reassessment, is necessary to ensure resolution of this rare and persistent infection.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper. None of the authors are affiliated with, or have financial involvement in any organization or entity with direct financial involvement in the subject matter or materials of the research discussed in this manuscript. All authors have participated significantly in writing of this manuscript and approve of its content. There is no material which is under the copyright of another party or

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Permission

Permission to write this manuscript was granted by the patient as part of Moffitt Cancer Center's (Tampa, FL, USA) general waiver. No specific patient identifiers are disclosed in the finished manuscript. The authors certify that the below work is in compliance with the Health Insurance Portability and Accountability (HIPA) Act of the United States of America.

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