Pseudomonas aeruginosa Pyomyositis in a Child With Acute Lymphoblastic Leukemia: A Case Report and Review of Literature

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Background: We report the case of an 11-year-old girl with a recent diagnosis of common B-cell acute lymphoblastic leukemia who presented with *Pseudomonas aeruginosa* pyomyositis of the left lower limb during severe neutropenia associated with the induction phase of chemotherapy.

Observations: Presenting signs included fever, leg pain, and refusal to walk. Popliteal knee ultrasonography was unremarkable, whereas magnetic resonance imaging showed 2 intramuscular fluid collections requiring surgically drainage.

Conclusion: A review of medical literature showed that pyomyositis is an infrequent complication in children with hematological malignancies, and most cases are due to *Staphylococcus aureus*, whereas *Pseudomonas aeruginosa* appears to be rarely involved.

Key Words: *Pseudomonas aeruginosa*, pyomyositis, leukemia, children, pediatric population

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Pyomyositis is a suppurative infection of skeletal muscle usually owing to hematogenous spread of bacteria. Once considered mostly a disease of tropical climates, it has been increasingly reported also in temperate areas, where it often occurs in patients with a history of trauma or underlying predisposing conditions, including immunodeficiency, immunosuppression, injective drug use, vascular devices, or concurrent infections.[1–3] It has been seldom reported in children with hematological malignancies, in whom it can nevertheless result in significant morbidity and delay of therapies. Most cases are due to Gram-positive cocci, mainly *Staphylococcus aureus*,[4] whereas cases of *Pseudomonas aeruginosa* pyomyositis or other gram-negative species are unusual.

MATERIALS AND METHODS

Case Report

An 11-year-old girl with a recent diagnosis of common B-cell acute lymphoblastic leukemia (ALL) was admitted to the Hematology-Oncology Unit because of fever and neutropenia. Blood tests at ALL diagnosis showed neutropenia and thrombocytopenia (white blood cells, 6090/μL; neutrophils, 620/μL; lymphocytes, 1880/μL; hemoglobin, 9.7 g/dL; and platelets, 62,000/μL). Two weeks before, she had begun the induction phase of chemotherapy according to the Associazione Italiana di Ematologia e Oncologia Pediatrica ALL 2017 observational protocol. In particular, she had received the first 2 courses of vincristine and daunorubicin plus PEG-asparaginase and daily oral therapy with prednisone, as indicated as standard therapy for all patients with B-cell ALL according to the protocol. Prophylaxis with amoxicillin-potassium clavulanate (50 mg/kg/d of amoxicillin) had been started the previous week for severe neutropenia. In the 3 days preceding admission, she had complained of intermittent, subfebrile, temperatures without other symptoms. At admission, she presented with fever and severe pain in the left calf. Pain was exacerbated by calf pressure and by active and passive flexion-extension movements of the leg, which was maintained in a semiflexed antalgic position, with refusal to walk and bear weight. Physical examination was otherwise unremarkable; in particular, there were no signs of infection in the limb (eg, soft tissue swelling or redness), and the knee joint was normal in appearance. Blood tests at admission showed severe leukopenia (200/mcL) and neutropenia (50/mcL), thrombocytopenia (14,000/mcL), and a marked increase of acute-phase reactants (C-reactive protein, 62.8 mg/L and procalcitonin, 4.88 ng/mL). Empiric antibiotic treatment was started with ceftazidime and amikacin, as per local guidelines for febrile neutropenia. Popliteal and knee ultrasonography were unremarkable and did not show local signs of edema or abnormal echogenicity of muscles, joint, or tendons, with normal vascular blood flow, with no signs of venous thrombosis. Blood cultures grew multisensitive *Pseudomonas aeruginosa*; therefore, antibiotic therapy was not changed. Fever and pain gradually improved, and she was sent home after 8 days with oral therapy with ciprofloxacin. In the following days, however, leg pain and mild fever persisted; therefore, a leg magnetic resonance imaging (MRI) was performed, which showed 2 intramuscular fluid collections, one in the lower part of the vastus lateralis muscle, measuring 35×15 mm, and the second in the proximal portion of the external gastrocnemius muscle, measuring 38×18 mm (Fig. 1). Both presented a pseudocapsule, which enhanced after gadolinium contrast and were surrounded by coarse areas of muscular edema. Bone and periosteum were not involved. Intravenous antibiotic therapy with ciprofloxacin and ceftazidime was therefore restarted, and the collections were surgically drained. Cultures from the drained material grew *Pseudomonas*

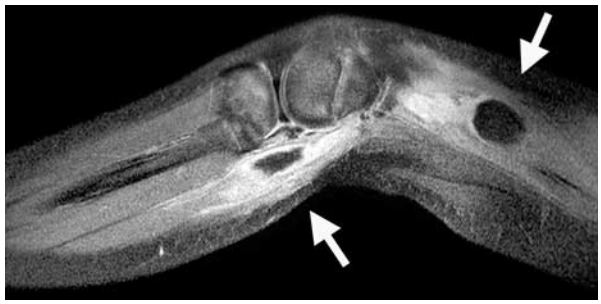

FIGURE 1. Magnetic resonance imaging of the left lower limb, showing 2 fluid collections above and under the knee (arrows), with surrounding tissue edema.

aeruginosa. Subsequent clinical course was uneventful, yet several months of rehabilitation therapy were required to regain normal lower limb functionality.

Systematic Review of Literature

Although pediatric cases represent ~35% of cases of pyomyositis reported in literature,[5,6] its occurrence in children with hematological malignancies appears to be infrequent, despite the presence of known risk factors in these patients, such as immunosuppression and indwelling vascular catheters. We therefore reviewed medical literature focusing on children affected by leukemia. We performed a systematic literature search from inception to April 21, 2020 using PubMed database and the following queries: "leukemia AND (pyomyositis OR myositis OR "muscle abscess" OR "muscular abscess")" and "leukemia AND children AND (pyomyositis OR myositis OR "muscle abscess" OR "muscular abscess" OR abscess)." We selected only articles in English describing pediatric patients (age 0 to 18 y) with infectious pyomyositis and with an underlying hematological neoplasm such as leukemia or lymphoma.

RESULTS

We found 11 articles that were deemed to be relevant for the review. A total of 14 cases of pyomyositis in children affected by hematological malignancy were reported (Table 1). In most cases, local muscular pain was the main reported symptom (11/14),[7–15] whereas fever was not always present. A minority of patients presented a tense palpable mass or multiple nodular lesions (3/14)[10,11,16]; redness and skin warmth in the area were reported only in 2 cases.[9,13] The majority of children (10/14) were affected by ALL. Most patients developed pyomyositis during most therapy-intense phases of chemotherapy (7 during induction and 2 during reinduction phases). Notably, pyomyositis was the first presentation sign of hematological malignancy in 2 patients: 1 was subsequently diagnosed having ALL,[13] and the other chronic myeloid leukemia.[14] In most cases (9/14), MRI was performed as the first radiologic examination to detect the muscular infection.[8,11–17] When ultrasound was chosen as the first radiologic examination (2/14), it resulted diagnostic, showing an abscess,[7,10] yet it is unclear if it would have been similarly diagnostic in the earlier, non-suppurative phases of the infection. Evolution in muscular abscess occurred in most patients (10/14) during the course of infection, despite intravenous antibiotic therapy, and was followed by drainage.[7–10,13–17] Methicillin-sensitive *S. aureus* was the most common causative agent, isolated in cultures in 9/14 patients, whereas only 1 patient grew a Gram-negative species (*Escherichia coli*) and 1 patient had a fungus isolated from cultures (*Acremonium* spp.).

DISCUSSION

Pyomyositis is an uncommon cause of fever in children, and may present with nonspecific signs and symptoms, especially in immunocompromised patients, in whom local inflammatory changes may be subtle. Our patient had no local signs of infection at physical examination, apart from pain. This may be owing to the reduced suppurative inflammatory response in neutropenic patients, which may

TABLE 1. Reports of Pediatric Patients With Pyomyositis Associated With Hematological Malignancies

References	Underlying Malignancy	Chemotherapy	Cultured Microorganism, Either From Drainage or Blood
Kao et al[7]	Acute lymphoblastic leukemia	Induction phase of chemotherapy	*Staphylococcus aureus* methicillin-sensitive
Montazeri et al[8]	Acute lymphoblastic leukemia	Induction phase of chemotherapy	*Staphylococcus aureus* and oxacillin-sensitive
Blatt et al[9]	Acute lymphoblastic leukemia	Induction phase of chemotherapy	*Staphylococcus aureus* oxacillin-sensitive
Corden and Morgan[10]	Acute lymphoblastic leukemia	Induction phase of chemotherapy	*Staphylococcus aureus*
Corden and Morgan[10]	Acute lymphoblastic leukemia	Induction phase of chemotherapy	*Staphylococcus aureus* oxacillin-sensitive
Domínguez-Pinilla et al[11]	Promyelocitic leukemia	Induction phase of chemotherapy	*Staphylococcus aureus*
Al-Sayyed et al[12]	Acute lymphoblastic leukemia	Reinduction phase of chemotherapy	*Escherichia coli*
Blatt et al[9]	Acute lymphoblastic leukemia	Reinduction phase of chemotherapy	*Staphylococcus aureus* oxacillin-sensitive
Traina et al[13]	Acute lymphoblastic leukemia	No chemotherapy	*Staphylococcus aureus* methicillin-sensitive
Chen et al[14]	Chronic myeloid leukemia	No chemotherapy	Negative
Yu et al[15]	Acute lymphoblastic leukemia	Not specified	*Staphylococcus aureus*
Yu et al[15]	Large B-cell lymphoma	Not specified	Negative

therefore hinder the diagnosis. Notably, ultrasonography was also normal; therefore, a high index of suspicion may be required. MRI has been reported to have a higher sensitivity in the early stages of disease, when it can detect mild edema before colliquative changes occur.[2–4]

Despite *P. aeruginosa* being a frequent etiological agent of febrile neutropenia infection in children with leukemia, in whom it can cause sepsis and severe infections, including perineal cellulitis, ecthyma gangrenosum, and pneumonia,[18] the occurrence of *P. aeruginosa* pyomyositis has never been reported in this population. At pyomyositis onset, our patient presented severe neutropenia (neutrophils 40/μL) and oral mucositis, but she had no neutropenic colitis or other potential risk factors that could explain *Pseudomonas* as the causal agent.

More generally, pseudomonal pyomyositis is a rare entity, both in adults with underlying hematological comorbidities such as multiple myeloma,[19] or in children with other underlying conditions.[20] Although the occurrence of pyomyositis and or other musculoskeletal infections warrants empiric antibiotic therapy covering *S. aureus*, the most frequently involved microorganism in patients with pyomyositis (representing around 75% of positive cultures),[21,22] our case underscores the importance of considering also *P. aeruginosa*, and more generally, Gram-negative bacteria such as *E. coli* (which has been described as the most frequently isolated Gram-negative germ in this group of patients) in neutropenic children with localized musculoskeletal infections, thus adopting a wide-spectrum antibiotic choice covering these agents pending definitive culture results. In case of no improvement or appearance of muscular abscess by imaging, an invasive procedure for drainage is mandatory, either with open surgery or a percutaneous ultrasonography-guided procedure.[2]

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