MRSA-pyomyositis in a Patient with Acute Myelogenous Leukemia after Intensive Chemotherapy

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Abstract. *Background: A case of methicillin-resistant Staphylococcus aureus (MRSA)-pyomyositis in association with acute myelogenous leukemia (AML) is reported. MRSA-sepsis developed in a 51-year-old Japanese man with AML, during the neutropenic period after high-dose 1-β-D-arabinofuranosylcytosine (Ara-C). Although the MRSA-sepsis initially improved with arbekacin sulfate (ABK) administration, a high fever recurred with left thigh pain despite recovery of the neutrophil count after ABK was stopped. A computed tomographic (CT) scan showed a low-density area in the left quadriceps femoris muscle, which led to a diagnosis of pyomyositis. MRSA was cultured from the abscess aspirates. The fever and thigh pain disappeared after administration of ABK and minocycline hydrochloride (MINO), and the abscess completely disappeared with the oral administration of levofloxacin (LVFX) for about 3 months. Conclusion: If an immunocompromised patient complains of fever and muscle pain after intensive chemotherapy, MRSA-pyomyositis should be considered.*

Pyomyositis is an infection of the large skeletal muscles characterized by single or multiple intramuscular abscess formation and typically occurs in tropical regions (1). Since the 1980s, pyomyositis has also been reported in non-tropical regions as an opportunistic infection occurring in immunocompromised patients, including those with human immunodeficiency virus (HIV) infection, diabetes mellitus, hematological malignancies and recipients of corticosteroid or anticancer drugs (2-9). Both in tropical and non-tropical regions, the most common cause is *Staphylococcus aureus* (1-9) and the clinical symptoms include high fever with muscle pain. A case of methicillin-resistant *S. aureus* (MRSA)-pyomyositis occurring in a patient with acute myelogenous leukemia (AML) after high-dose 1-β-D-arabinofuranosylcytosine (Ara-C) as post-remission chemotherapy is reported.

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Case Report

A 51-year-old Japanese man was referred to our hospital with petechia. His peripheral blood cell count at admission showed: hemoglobin 11.1 g/dl, white blood cells 16,200/mm^3 with 54% blasts and platelet count 15,000/mm^3. The bone marrow was hypercellular and contained 64% myeloblasts, 6% promyelocytes and 5% myelocytes. Bone marrow cell karyotyping revealed 46, XY, der (18;21)(q10;q10), +21 of 10/20 and 46, XY of 10/20 in metaphases; therefore, he was diagnosed with AML (French-American-British Group (FAB) classification subtype M2, World Health Organization (WHO) classification AML with maturation). Antibodies to HIV were negative. He achieved complete remission with one course of mitoxantrone, behenoyl Ara-C, etoposide plus 6-mercaptopurine and then received five courses of post-remission chemotherapy, including one course of high-dose Ara-C (3,600 mg, every 12 hours for 5 days). During the period of bone marrow suppression due to the subsequent chemotherapy, there was marked neutropenia with repeated episodes of severe infection, such as MRSA-lymphangitis and grade 4 febrile neutropenia according to the WHO criteria (10). Accordingly, he received 50% reduced high-dose Ara-C (1,800 mg, every 12 hours for 5 days) as a sixth course of post-remission chemotherapy. In spite of the administration of filgrastim, neutropenia after chemotherapy was also marked: the neutrophil count remained below 100/mm^3 for ten days and febrile neutropenia subsequently developed on day 15 (day 1 defined as the day of beginning of the 50% reduced high-dose Ara-C) (Figure 1). C-reactive protein (CRP) was markedly elevated (30.7 mg/dl), but lactic acid dehydrogenase (LDH) and creatine kinase (CK) were normal. Intravenous antibiotic therapy with 2.0 g/day

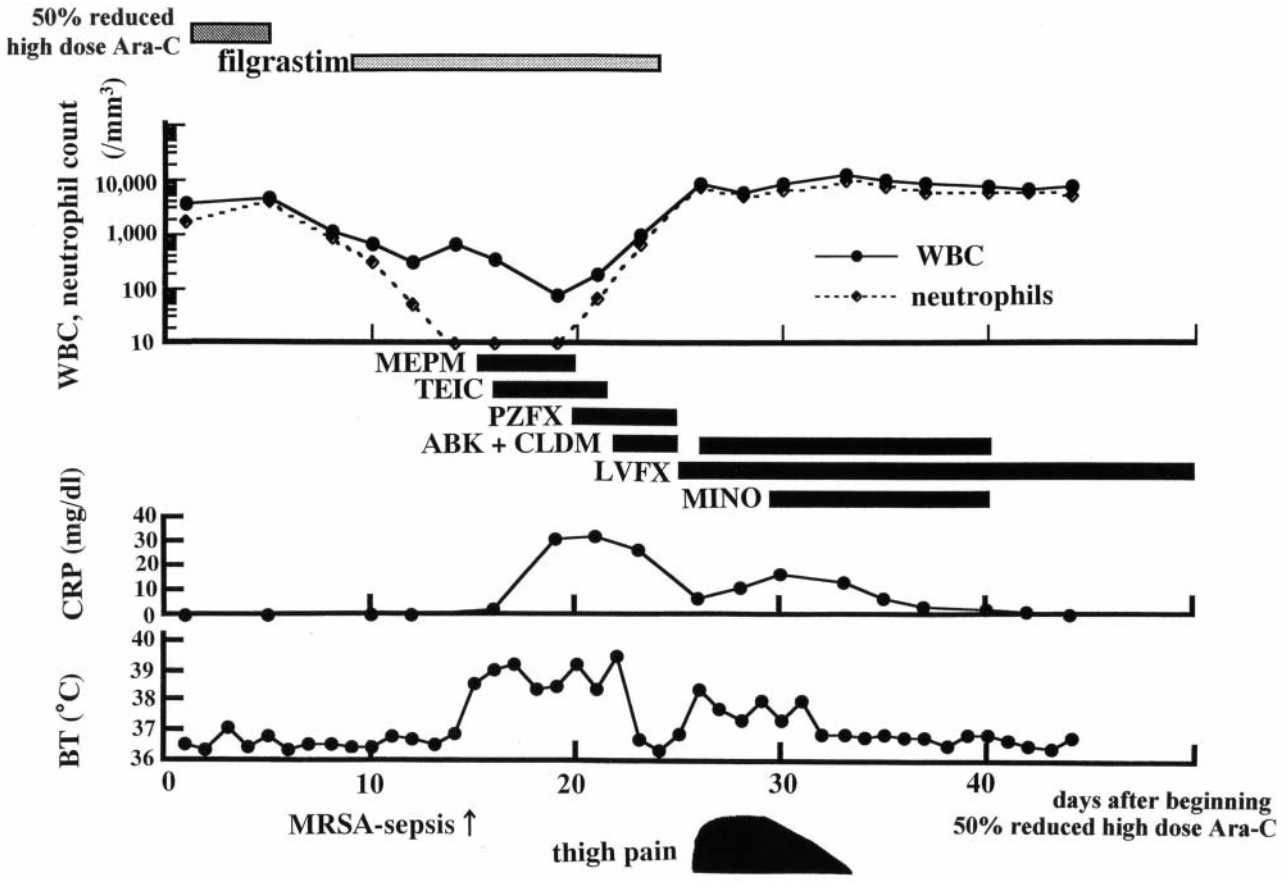

Figure 1. *Clinical course. MEPM, Meropenem trihydrate; TEIC, teicoplanin; PZFX, pazufloxacin mesilate; ABK, arbekacin sulfate; CLDM, clindamycin; LVFX, levofloxacin; MINO, minocycline hydrochloride; WBC, white blood cells; CRP, C-reactive protein; BT, body temperature.*

meropenem trihydrate (MEPM) was started immediately. Since MRSA was detected by blood culture, 400 mg/day teicoplanin (TEIC) was used in combination with MEPM from day 16, but the fever persisted. Therefore, MEPM was replaced by 1.0 g/day pazufloxacin mesilate (PZFX) on day 20, and TEIC was replaced by 200 mg/day arbekacin sulfate (ABK) and 1.2 g/day clindamycin (CLDM) on day 22. The fever disappeared on day 23. On day 25, intravenous antibiotic therapy was stopped and 400 mg/day levofloxacin (LVFX) by oral administration was started. Fever recurred with left thigh pain on day 26 despite recovery of the neutrophil count (8,200/mm^3). His left thigh was slightly warm, but not erythematous or swollen. The CRP was markedly elevated again (16.5 mg/dl), but LDH and CK were normal. No bacteria were detected by blood culture. A computed tomographic (CT) scan on day 27 showed a low-density area in the left quadriceps femoris muscle (Figure 2-A), which led to a diagnosis of pyomyositis. Percutaneous needle aspiration of the abscess was performed and MRSA was cultured from the aspirate. ABK and CLDM were restarted on day 26 and 200 mg/day minocycline hydrochloride (MINO) was added on day 29. Ga scintigraphy on day 34 revealed abnormal uptake in the left thigh (Figure 2-B) and T2-weighted magnetic resonance imaging (MRI) on day 39 showed high signal intensity areas 2 cm and 4 cm in diameter in the left vastus medialis muscle and left vastus lateralis muscle, respectively (Figure 2-C), which were compatible with a diagnosis of pyomyositis (11). Since the fever and left thigh pain completely disappeared on day 34, the administration of ABK, CLDM and MINO was stopped on day 39. Only LVFX was continued for about 3 months, and the abscess completely disappeared without surgical drainage. Pyomyositis did not recur during the neutropenic period despite subsequent chemotherapy.

Discussion

The pathogenesis of pyomyositis occurring as an opportunistic infection is obscure. Though many patients had a history of previous trauma or injections into the muscles (1, 2, 4, 5, 7),

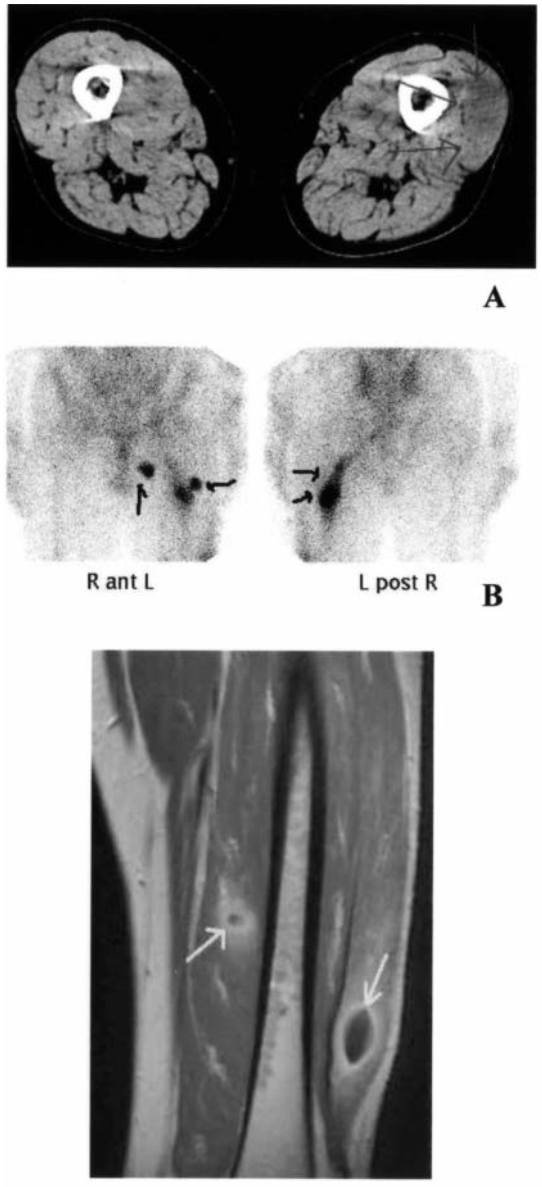

Figure 2. *Computed tomography, Ga scintigraphy and magnetic resonance image of the left thigh. A: Computed tomographic scan on day 27 showing a low-density area in the left quadriceps femoris muscle (arrows). B: Ga scintigraphy on day 34 revealing abnormal uptake in the left thigh (arrows). C: T2-weighted magnetic resonance imaging on day 39 showing high signal intensity areas 2 cm and 4 cm in diameter in the left vastus medialis muscle and vastus lateralis muscle, respectively (arrows).*

the present patient had no history of recent trauma or injections into the muscles. He did not have HIV infection or diabetes mellitus. He had not received corticosteroids when MRSA sepsis or pyomyositis occurred. A catheter was not used at the onset of pyomyositis. In this patient, colonization of MRSA in the pharynx had previously been noted. The resistance patterns of MRSA detected from the pharynx, blood culture and abscess aspirates were the same, suggesting that they might be the same MRSA strain. During the neutropenic period after 50% reduced high-dose Ara-C, the colonized MRSA in the pharynx or the other sites might have caused bacteremia, and spread intravascularly to the left quadriceps femoris muscle and developed pyomyositis. ABK and MINO have been reported to pass easily into muscle tissue or abscesses (12), which may be one reason why ABK and MINO were effective for the treatment of the MRSA-pyomyositis in this patient.

No pyomyositis was observed in 542 patients who developed infections during remission-induction chemotherapy for AML based on the Japan Adult Leukemia Study Group AML-87 and AML-89 protocols (13), but infections of unknown origin occurred in 41.1% of patients. Recently, pyomyositis has been reported as a complication of chemotherapy for acute leukemia (4, 5, 7, 8). High-dose Ara-C is effective for post-remission chemotherapy for AML (14), especially for the core-binding factor-type AML (15). On the other hand, there was a clear-cut relationship between hematological toxicity and the Ara-C dose schedule (14). As chemotherapy becomes more intensive, it seems that the risk of opportunistic infections, including pyomyositis, increases.

Pyomyositis is a rapidly progressive infection and the mortality rate is not low (1, 2, 4, 7, 8). Early treatment is the key to a better prognosis; therefore, in immunocompromised patients who complain of muscle pain, pyomyositis should be considered and CT and MRI studies should be actively performed. Since the most common cause is *S. aureus* (1-9), and since the majority of *S. aureus* detected in hospitals is MRSA, empiric anti-MRSA therapy should be performed.

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