Fatal Rhabdomyolysis Caused by *Morganella morganii* in a Patient with Multiple Myeloma

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**Abstract**

A 64-year-old Japanese man with multiple myeloma was admitted to our institute due to fever and hypotension. He had received multiple courses of chemotherapy just before his febrile episode. Blood culturing detected *Morganella morganii*. At the time of the diagnosis, his laboratory findings revealed massive rhabdomyolysis with a significantly increased creatinine kinase level (CK; 3,582 U/L); 98.8% of which corresponded to the CK-MB isotype. We diagnosed the patient with sepsis caused by *M. morganii*, complicated with severe rhabdomyolysis. He died of multi-organ failure 2 days later. Clinicians should closely observe patients with possible systemic infection-associated rhabdomyolysis.

**Key words:** rhabdomyolysis, immunocompromised, *Morganella morganii*, gram-negative bacillus, multiple myeloma

(Intern Med 56: 369-371, 2017)  
(DOI: 10.2169/internalmedicine.56.7252)

**Introduction**

Bacterial infections affecting skeletal muscle can be categorized into several types. Pyomyositis affects the massive skeletal muscles and is most frequently caused by *Staphylococcus* bacteria (1). Pyomyositis generally presents as one or more localized necrotic lesions. Necrotizing fasciitis is a localized spread of infection that follows events such as trauma or surgery (2), and which is commonly affected by Group A *Streptococcus*.

Rhabdomyolysis is a completely different clinical entity from pyomyositis and necrotizing fasciitis. Rhabdomyolysis comprehensively affects the skeletal muscle and, like pyomyositis and necrotizing fasciitis, shows serum creatinine kinase elevation; however, rhabdomyolysis occurs as a systemic disease and is not associated with the focal manifestation of abscesses (3). Rhabdomyolysis is sometimes complicated by a systemic infection (3). The pathogenesis of infectious rhabdomyolysis is thought to be associated with the systemic or local metabolic changes related to a systemic or local infection (4); however, the mechanisms underlying its pathogenesis have not been established. In addition, gram-negative bacillus rhabdomyolysis is rare, and its microbiological pathology remains to be elucidated.

**Case Report**

We diagnosed the patient, a 64-year-old Japanese man with multiple myeloma, with bacteremia caused by *Morganella morganii*. He was admitted to our institute due to septic shock at the sudden onset of a febrile episode. He had lumargia due to an old L1-2 compression fracture. His vital signs at admission were as follows: blood pressure, 82/60 mmHg; heart rate, 78/min; body temperature, 39.1°C; respiration rate, 20/min; and SpO2, 95% (room air). A physical examination revealed no clear focus of infection. He did not complain of muscular pain throughout his clinical course. The laboratory findings at the time of his diagnosis showed massive myolysis and a significantly elevated level of creatinine kinase (CK; 3,582 U/L); thereafter, an isotype analysis of the patient’s CK confirmed that the elevated CK was derived from the patient’s skeletal muscle (98.8%).

The status of the patient’s multiple myeloma, which had been diagnosed 5 years earlier, was stage IIIA, IgG λ type. He had undergone treatment with a variety of chemotherapies: melphalan (MP; 12 mg/day for 4 days + prednisolone 60 mg/day for 6 days, repeated triweekly), VAD (vincristine...
Discussion

Infectious rhabdomyolysis is caused by various pathogens including viruses, bacteria and fungi (3). The clinical entity of infectious rhabdomyolysis was established in 1982 (5), and a review (3) identified the predisposing risk factors for rhabdomyolysis: alcohol ingestion, compression injury, and generalized seizures. Regardless of the pathogen that causes infectious rhabdomyolysis, the underlying mechanism of the disease is metabolic. The most frequent differential diagnosis is necrotizing fasciitis, which occurs when the infection spreads into the deep fascial layers (2). Necrotizing fasciitis is generally caused by infection, and the initial entry site is sometimes trivial. In contrast, rhabdomyolysis is caused by the following two critical conditions: (1) physical distress (for example, distress due to or involving excessive exercise, seizure, muscle compression, hyperthermia, or hypothermia); and (2) systemic metabolic disorders (for example disorders due to hypoxia, acidemia, drug abuse, infection, or inflammation). Thus, rhabdomyolysis is a systemic illness. The localization of a soft-tissue infection can be distinguished by systemic imaging, especially by sensitive MRI (6). In the reported cases of rhabdomyolysis, the local radiological findings are faint. In the present case, CT imaging could not detect necrotizing rhabdomyolysis.

Our evaluation of the present case raised an important question: what is the microbiological mechanism underlying the development of rhabdomyolysis accompanied by systemic infection (3, 7)? Bacterial rhabdomyolysis and fungal rhabdomyolysis usually develop in immunocompromised hosts. Viral myositis induces diffuse myolysis, resulting not
only in rhabdomyolysis but also myocarditis. In addition, bacillus-associated myolysis can cause rhabdomyolysis. Thus, rhabdomyolysis is relatively common among patients with miscellaneous bacterial infections including, but not limited to, *Legionella* (4), *Pneumococcal* (8), and *Salmonella* (7). We underscore that patients these types of infectious rhabdomyolysis share the following common findings: 1) the patients were immunocompromised due to malignancy or a severe wound; 2) precedent or concomitant acute renal failure were observed in the patient’s clinical course; and 3) metabolic abnormalities such as dehydration or acidemia due to single/multi-organ failure existed as the underlying pathogenesis. Thus, ischemia or hypoxia caused by systemic infection are considered to be involved in the mechanism underlying the development of rhabdomyolysis. *M. morganii* is rarely pathogenic in humans, but it sometimes develops into an opportunistic infection in a compromised host. Although there are no reported cases of infectious rhabdomyolysis caused by *M. morganii*, Arranz-Caso et al. published the first anecdotal case of pyomyositis caused by *M. morganii* (9). The authors noted that gram-negative bacterial pyomyositis can occur in an immunocompromised case followed by enteric organism translocation. Our case differs from this case of pyomyositis caused by *M. morganii*. Gram-negative bacterial infection does not favor pyomyositis, which is usually raised by gram-positive bacteria. Our case suggests that infectious rhabdomyolysis may be underdiagnosed as a comorbidity of gram-negative bacterial infections, even if the causative organism is an opportunistic pathogen such as *M. morganii*.

Regarding myolysis/rhabdomyolysis complicated with a systemic bacterial infection and the accumulation of muscle damage is associated with both bacteremic and non-bacteremic mechanisms (7, 10). The bacteremic mechanism involves direct bacterial invasion and a direct endotoxin effect. The non-bacteremic mechanism includes alterations of systemic metabolism (i.e., hypoxia, acidosis) and an intracellular metabolism in situ (e.g., disturbances of glycolysis and oxidation in muscle cells) (7). The non-bacteremic mechanism of rhabdomyolysis accompanied by systemic infection is similar, regardless of the pathogen that is involved (3, 7). The common mechanisms underlying muscle damage arise from a combination of hypoxia, dehydration, and acidemia in the tissue (4).

In general, rhabdomyolysis develops during the course of systemic infection in up to 5% of bacterial and viral cases (7). Rhabdomyolysis is a specific term describing the excess leakage of enzymes derived from muscular tissue, which can result in multi-organ failure. In our patient, the apparent infection focus was not identified by repeated systemic CT. This negative finding caused a delay in our differentiation of the cause of the patient’s rhabdomyolysis. We treated the patient with meropenem, to which the causative pathogen, *M. morganii*, is sensitive; however, an adequate antimicrobial therapy cannot always rescue a patient from advanced multiple-organ deterioration. Rhabdomyolysis should thus be recognized as a more aggressive clinical situation than local myositis, and one that requires intensive care. Furthermore, non-specific myolysis/rhabdomyolysis can occur due to any pathogen (7); thus, it may be underdiagnosed during the infection. Myalgia and scant laboratory signs of myolysis/rhabdomyolysis (usually appearing as liver damage in laboratory data) can be misdiagnosed in patients with the overlapping leakage of transaminases due to various etiologies. Clinicians should keep in mind that abnormal liver function test results may be linked to a muscular problem.

Clinicians should be aware of the possibility of systemic infection-associated myolysis/rhabdomyolysis and closely observe immunocompromised patients. This is the first report of lethal rhabdomyolysis caused by *M. morganii* as a complication in a non-HIV patient.

The authors state that they have no Conflict of Interest (COI).

**Short description:** Fatal rhabdomyolysis caused by *M. morganii* can occur in a multiple myeloma patient without HIV. (94/100 characters)

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