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Etiology, Characteristics, and Outcomes of Community-Onset Pyomyositis in Korea: A Multicenter Study

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ABSTRACT

Background: Pyomyositis (PM) is a serious soft tissue infection and despite its clinical importance, previous studies have not been able to fully determine the clinical characteristics and microbial epidemiology of PM in Korea, which we therefore aimed to investigate.
Materials and Methods: We retrospectively identified 140 adult patients diagnosed with PM from 13 general hospitals between January 2012 and December 2015. We analyzed the clinical and microbial characteristics of community-onset PM and compared them with community-acquired (CA) and healthcare-associated (HCA) PM.
Results: One hundred eleven organisms were isolated from 96 (68.6%) patients with PM. *Staphylococcus aureus* (38 patients) was the most common pathogen, followed by streptococci (24 patients), and enteric Gram-negative organisms (27 patients). Methicillin-resistant *S. aureus* (MRSA) was identified in four (2.9%) patients and in-hospital mortality reached 8.6% (12/140). Enterococci isolates were identified in the HCA PM subgroup only The proportion of MRSA isolates was not comparable between CA and HCA PM subgroups. In the 83 patients with PM infected by monomicrobial pathogens, isolates of Gram-negative organisms were more commonly found in HCA PM subgroup than in CA PM subgroup (47.6% [10/21] of patients with HCA PM *vs.* 20.7% [12/58] of patients with CA PM; $P = 0.01$).
Conclusion: Gram-positive cocci such as *S. aureus* and streptococci were dominant etiologies in community-onset PM, whereas MRSA appears to an uncommon causative organism of PM

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Conflict of Interest
SHC is an editorial board member of Infect Chemother; however, he did not involve in the peer reviewer selection, evaluation, and decision process of this article. Otherwise, no potential conflicts of interest relevant to this article was reported.

Author Contributions
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in Korea. Enteric Gram-negative organisms should also be considered as major etiologies, especially in HCA PM patient population in Korea.

Keywords: Pyomyositis; Community; Etiology

INTRODUCTION

Pyomyositis (PM) is a serious soft tissue infection that is usually accompanied by abscess formation [1]. Pyomyostis is dangerous for patients because it requires long-term treatment with antibiotics and repeated surgical interventions [2]. Despite its clinical importance, previous research has been unable to fully determine the clinical characteristics and microbial epidemiology of PM in Korea. In previous studies conducted across the United States, Gram-positive cocci, such as streptococci, and *Staphylococcus aureus*, were major pathogens of PM [3, 4], and the rate of resistance to methicillin was high [5]. In the guideline published by the Infectious Diseases Society of America, vancomycin is recommended for initial empirical therapy [6]. However, because microbial epidemiology can vary by region, universal application of this guideline may not be appropriate. To establish a unique treatment strategy appropriate for managing PM in Korea, it is necessary to collect and collate our own data on PM in Korea. For these reasons, we conducted a multicenter study to identify the clinical and microbial characteristics of PM in Korea.

MATERIALS AND METHODS

1. Study design and definitions

Between January 2012 and December 2015, we retrospectively reviewed the medical records of adult patients (>18 years) who had been diagnosed by use of the Korean Standard Classification Disease and Cause of Death codes (M6000 – M6009, M7100 – M7109, and M6500 – M6509) relevant with PM across thirteen teaching hospitals in Korea. A PM diagnosis was confirmed in cases of abscess formation or inflammation in skeletal muscle without fascia involvement in imaging or surgical findings [6]. Patients who did not have compatible findings with PM were excluded from the analysis. PM that had been contracted outside of the hospital, rather than during patient stay, was a prerequestite for elibility for data usage. Informed consent was waived by the Institutional Review Board of Soonchunhyang University Bucheon Hospital, given that this work was a non-interventional, retrospective study and did not involve work on extra clinical specimens (IRB No 2017-01-001).

We categorized cases into healthcare-associated infection (HCA), if any one of the following conditions were satisfied:

(1) Previous admission within 3 months for 2 or more days prior to the episode
(2) Previous intravenous antibiotics, chemotherapy, or nursing care at home within 1 month prior to the episode
(3) Previous hemodialysis within 1 month prior to the episode
(4) Residence in a nursing facility [7]

All other patients were categorized as having a community-acquired (CA) infection.

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2. Clinical characteristics

We compiled the data on demographics (age and sex), site of infection, and underlying diseases (diabetes mellitus, liver cirrhosis, end-stage renal disease, alcoholism, solid tumor, hematologic malignancy, and immunocompromised state).

We also compiled data on intensive care unit (ICU) admissions and septic shock [8] as the severity indices and on laboratory findings, such as white blood cells, platelets, creatinine, and C-reactive protein. We also investigated surgical intervention as a treatment modality and in-hospital mortality as an outcome indicator.

3. Microbial characteristics

Cultures grown from from blood, pus, and intra-surgical specimens were analyzed and the results reviewed. Microorganism identification was conducted using standard methods at each hospital, in which the quality control of microbial tests had passed the evaluation of the accredited institutions. Susceptibility testing was performed using the microdilution method, and results were interpreted according to the National Committee for Clinical Laboratory Standards guidelines [9].

4. Statistical analysis

Statistical analysis was performed using SPSS version 26.0 (SPSS, Chicago, IL, USA). We used a chi-square test or Fisher's exact test for comparison of categorical variables, and the Mann-Whitney *U* test to analyze continuous variables. All tests were two-tailed, and differences were considered significant at $P<0.05$.

RESULTS

1. Clinical characteristics

A total of 140 patients with PM were enrolled during the study period. With the exception of 16 (11.4%) patients whose intraoperative findings were indicative of PM, magnetic resonance imaging and computerized tomography were conducted in 80 (57.1%) and 75 (53.6%) patients, respectively. We then categorized 38 (27.1) patients into the HCA infection group; the median number of enrolled patients at each hospital was 8 (range 2 - 31 patients). The clinical characteristics and laboratory findings of patients with PM are shown in **Table 1**. The most common underlying disease was diabetes mellitus (n = 47, 33%), while lower extremity involvement (n = 76, 54%) was most prevalent. Seventy-three (52.1%) patients with PM received surgical intervention and in-hospital mortality occurred in 12 patients (8.6%). Severity indices, such as ICU admission (83.3% [10/12] of patients with in-hospital mortality *vs.* 18.8% [24/128] of patients without in-hospital mortality; $P<0.01$), and septic shock shock (58.3% [7/12] of patients with in-hospital mortality *vs.* 7.8% [10/128] of patients without in-hospital mortality; $P<0.001$) were associated with in-hospital mortality in the univariate analysis.

2. Microbial etiologies

Microbial etiologies of PM are shown in **Table 2**. We isolated a total of 111 organisms from 96 (68.6%) patients, and found polymicrobial infections in 12 of these 96 (12.5%) patients. We did microbial tests in 131 (93.6%) patients: 118 for blood culture, 66 for intraoperative specimens, and 55 for aspiration or biopsy. The positive rates of culture according to specimen sources were as follows: 78.8% (52/66) from intraoperative specimens, 67.3% (37/55) from aspiration or biopsy specimens, and 28.0% (33/118) from blood cultures.

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Table 1. Demographics, underlying disease/conditions, and clinical characteristics of patients with community-onset pyomyositis

Variable	Patients, n (%)			
	Total (N = 140)	Community-acquired (n = 102)	Healthcare-associated infection[a] (n = 38)	*P*-value
Demographics				
Median age, year (IQR)	58 (45 – 73)	57 (46 – 70)	67 (51 – 77)	0.04
Sex, male	81 (57.9)	61 (59.8)	20 (52.6)	0.45
Underlying diseases or conditions				
Diabetes mellitus	47 (33.6)	30 (29.4)	17 (47.2)	0.07
Solid tumor	14 (10.0)	9 (8.8)	5 (13.9)	0.52
Alcoholism	11 (7.9)	9 (8.8)	2 (5.6)	0.73
Liver cirrhosis	8 (5.7)	7 (6.9)	1 (2.8)	0.68
Immunocompromised[b]	5 (3.6)	3 (3.0)	2 (6.3)	0.59
End-stage renal disease	4 (2.9)	0	4 (11.1)	0.004
Hematologic malignancy	2 (1.4)	0	2 (5.6)	0.07
Site of infection				
Lower extremity	77 (55.0)	62 (60.8)	15 (39.5)	0.04
Upper extremity	14 (10.0)	11 (10.8)	3 (7.9)	0.76
Other[c]	49 (35.0)	29 (28.4)	20 (52.6)	0.01
Severity				
ICU admission during hospitalization	34 (24.3)	18 (17.6)	16 (43.2)	0.003
Septic shock	17 (12.1)	11 (10.9)	6 (16.7)	0.39
Laboratory findings at the time of admission, median (IQR)				
White blood cell count, /mm^3	12,100 (8,600 – 16,852)	11,750 (8,482 – 15,117)	15,170 (10,525 – 20,772)	0.02
Platelet count, /mm^3	234,500 (163,500 – 313,000)	225,500 (161,750 – 297,000)	263,000 (146,000 – 368,250)	0.53
Creatinine level, mg/dL	0.8 (0.7 – 1.1)	0.8 (0.7 – 1.0)	0.8 (0.7 – 1.3)	0.19
C-reactive protein, mg/dL	12.24 (3.90 – 21.54)	11.85 (3.17 – 21.64)	13.6 (7.61 – 20.15)	0.55
Surgery	73 (52.1)	52 (51.0)	21 (56.8)	0.57
In-hospital mortality	12 (8.6)	5 (4.9)	7 (18.9)	0.02

[a]Healthcare-associated infection comprised 28 (20.0%) patients previously admitted within 3 months for more than 2 days before the episode, 17 (12.1%) patients previously receiving intravenous antibiotics, chemotherapy, or nursing care at home within 1 month of the episode, 5 (3.6%) patients who were in a nursing facility, and 3 (2.1%) patients on hemodialysis within 1 month of the episode.
[b]Patients were deemed immunocompromised if they had human immunodeficiency virus or had acquired immunodeficiency syndrome; or if they had received solid organ or hematopoietic stem-cell transplantation, chemotherapy within 6 weeks, systemic steroids ≥20 mg of prednisone for 2 weeks, or other immunosuppressive agents within 2 weeks before hospitalization. [c]25 (17.9%) patients in the paravertebral area, 18 (12.9%) patients in buttock area, 3 (2.1%) patients in the chest wall area, 2 (1.4%) patients in the abdominal wall area, and 1 (7.1%) patient in the face.
IQR, interquartile range; ICU, intensive care unit.

S. aureus (n = 38 patients, 27.1%) was the most common pathogen, followed by streptococci (n = 24 patients, 17.1%). There were only four (2.7%) of the methicillin-resistant *S. aureus* (MRSA) isolates identified in all patients with PM and it comprised 10.5% (4/38) of isolates of *S. aureus*. Four isolates of coagulase-negative staphylococci were considered as pathogens, because these were cultured in sterile aspiration or intra-operative specimens. We identified enteric Gram-negative rods in 27 (19.3%) patients. Of these isolates, 77.8% (21/26), 87.0% (20/23), 87.0% (20/23), and 77.8% (21/26) were susceptible to ceftriaxone, cefepime, piperacillin/tazobactam, and quinolone, respectively.

Isolates of enterococci were found only in HCA PM; there was no difference in the proportion of MRSA isolates in the CA and HCA PM groups. In 83 patients with PM infected by monomicrobial pathogens, isolates of Gram-negative organisms were more commonly found in the HCA PM subgroup than in CA PM subgroup (20.7% [12/58] of patients with CA PM *vs.* 47.6% [10/21] of patients with HCA PM; $P = 0.01$).

DISCUSSION

Our findings show that *S. aureus* was the most common etiology in community-onset PM, followed by enteric Gram-negative organisms, and streptococci. MRSA was detected in only

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Table 2. Identified microbial etiologies in patients with community-onset pyomyositis

Variables	Patients, n (%)			
	Community-acquired (n = 102)	Healthcare-associated (n = 38)	*P*-value	Total (N = 140)[a]
Any pathogen	67 (65.7)	29 (76.3)	0.31	96 (68.6)
Aerobic Gram-positive organisms	53 (52.0)	18 (47.4)	0.71	71 (50.7)
Staphylococcus aureus	31 (30.4)	7 (18.4)	0.2	38 (27.1)
Methicillin-susceptible *S. aureus*	29 (28.4)	5 (13.2)	0.08	34 (24.3)
Methicillin-resistant *S. aureus*	2 (2.0)	2 (5.3)	0.3	4 (2.9)
Streptococci	18 (17.6)	6 (15.8)	>0.99	24 (17.1)
Viridans streptococci	8 (7.8)	2 (5.3)	0.73	10 (13.6)
Group A, C, G streptococci	4 (3.9)	2 (5.3)	0.66	6 (4.3)
Group B streptococci	6 (5.9)	2 (5.3)	>0.99	8 (5.7)
Coagulase-negative staphylococci	4 (3.9)	0	0.57	4 (2.9)
Enterococci	0	4 (10.5)	0.004	4 (2.9)
Aerobic Gram-negative organisms	14 (13.7)	16 (42.1)	<0.001	30 (21.4)
Enteric Gram-negative rod	14 (13.7)	13 (34.2)	0.01	27 (19.3)
Escherichia coli	5 (4.9)	6 (15.8)	0.07	11 (7.9)
Klebsiella species	6 (5.9)	1 (2.6)	0.67	7 (5.0)
Enterobacter species	1 (1.0)	2 (5.3)	0.18	3 (2.1)
Citrobacter species	0	2 (5.3)	0.07	2 (1.4)
Serratia species	1 (1.0)	1 (2.6)	0.47	2 (1.4)
Proteus species	1 (1.0)	1 (2.6)	0.47	2 (1.4)
Non-enteric Gram-negative rod	0	4 (10.5)	0.005	4 (2.9)
Acinetobacter species	0	2 (5.3)	0.07	2 (1.4)
Pseudomonas species	0	1 (2.6)	0.27	1 (0.7)
Aeromonas species	0	1 (2.6)	0.27	1 (0.7)
Anaerobe[b] and *Candida* species	4 (3.9)	4 (10.5)	0.21	8 (5.7)
Mycobacterium	1 (1.0)	1 (2.6)	0.47	2 (1.4)

[a]Percentage denominator is the total number of enrolled patients. A total of 111 organisms were isolated from 96 (68.6%) patients, and polymicrobial infections were found in 12 of 96 (12.5%) patients. Microbiologic tests were conducted in 131 (93.6%) patients: 118 for blood culture, 66 for intraoperative specimens, and 55 for aspiration or biopsy. The positive rates of culture according to specimen source were as follows: 78.8% (52/66) from intraoperative specimens, 67.3% (37/55) from aspiration or biopsy specimens, and 28.0% (33/118) from blood cultures.
[b]Three isolates of *Corynebacterium* species, one isolate of *Bacteroides fragilis*, one isolate of *Bacillus* species, one isolate of *Parvimonas micra*, one isolate of *Lactobacillus*.

2.9% (4/140) patients with community-onset PM. In hospital mortality occurred in roughly 10% of patients with community-onset PM. This study is the largest multicenter investigation of current microbial etiology, clinical characteristics, and outcomes of community-onset PM in Korea. We expect that this study can be used to develop treatment strategies for community-onset PM in this region.

MRSA is a concerning pathogen in community-onset skin and soft tissue infections; however, in PM, epidemiologic studies are lacking. A retrospective study in the United States, for example, found that MRSA was commonly isolated in patients with PM [5]. Additionally, there have been reports on MRSA-induced PM in the pediatric setting [10]. Based on these experiences, glycopeptides against MRSA are recommended in skin and soft tissue infection guidelines of the Infectious Diseases Society of America. However, with the exception of India, which detected MRSA infection in 12.9% (8/62) of patients with PM [11], MRSA has rarely been idenfitied. For example, a retrospective study conducted in Taiwan found only two MRSA isoles in 32 patients [12], whereas in Brazil, there was no detection of MRSA in a total of 13 adult patients with PM [13]. This study suggests that it may not be appropriate to choose glycopeptides as an empirical regimen for PM in Korea, because MRSA was identified in only 2.9% of the patient population.

When choosing empirical antibiotics, it is important to assess the benefits of administering appropriate antibiotics for improved outcomes against the risk of antibiotic overuse that

could cause antimicrobial resistance and unnecessary adverse drug reactions. In PM, empirical antibiotics against methicillin-susceptible *S. aureus* and streptococci, rather than against MRSA, should be considered. Moreover, enteric Gram-negative rods should be covered in some situations. While most pathogens in the tropics were *S. aureus*, Gram-negative rods comprised 30% in temperate regions [3, 4]. Additionally, in a patient with liver cirrhosis, the major pathogen identified was *Klebsiella pneumoniae* [14]. Older age was also associated with an etiology independent of the *S. aureus* infection [5]. In our study, Gram-negative rods were more commonly found in HCA PM. It is therefore reasonable to choose cefepime or piperacillin/tazobactam as empirical regimens for PM treatment, as recommended in the skin and soft tissue infection guideline published by the Korean Society for Antimicrobial Therapy [15].

This study has some limitations. First, it is possible that some isolates such as coagulase-negative staphylococci were a wound colonizer rather than pathogens. Second, data on therapeutic investigations such as antibiotics usage were not fully investigated, because this would have fallen outside the scopy of the study. Further investigation on the effect of surgical intervention and appropriate use of antibiotics on mortality will be important.

In conclusion, Gram-positive cocci such as *S. aureus* and streptococci were dominant etiologies in community-onset PM. MRSA appears to be uncommon as a causative organism of PM in Korea; however, enteric Gram-negative organisms should also be considered as major etiologies, especially in HCA PM in Korea.

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The list of the membership of the Korean SSTI study group is identical to the list of the authors.

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