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Original Article

Impact of underlying diseases on the clinical characteristics and outcome of primary pyomyositis

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Background and Purpose: Primary pyomyositis is increasingly recognized in non-tropical areas, its incidence seeming to mirror the increase in immunocompromised populations. In this study, we sought to analyze the differences in clinical characteristics, causative organisms, treatment and outcome between pyomyositis patients with and without underlying diseases.

Methods: Thirty five patients with a diagnosis of primary pyomyositis seen in our hospital between July 1989 and July 2006 were enrolled. Descriptive information concerning age, gender, clinical features, underlying comorbid diseases, results of blood tests, blood culture, muscle or pus culture, disease severity and clinical stages at the time of diagnosis, therapy, and outcome were collected by review of medical charts.

Results: Of the 23 cases with underlying diseases, the mean age was 47.8 years (range, 24 to 79 years). Of the 12 patients without underlying diseases, the mean age was 26.2 years (range, 2 to 72 years). The lower extremities was the most common site of involvement. *Staphylococcus aureus* was the most frequent causative organism. Gram-negative organisms were isolated in 30.4% of patients with underlying diseases and in none of the patients without underlying diseases (p=0.07). Positive blood culture was significantly more common in patients with underlying diseases than in patients without underlying diseases (52.2% vs 8.3%, p=0.013). The mortality rate was higher in patients with underlying diseases than in patients without underlying diseases (39.1% vs 0.0%, p=0.015). White blood cell count (p=0.017), Acute Physiology and Chronic Health Evaluation (APACHE) II score (p<0.001), recurrence (p=0.004), and presence of underlying diseases (p=0.015) were significant prognostic factors for mortality by univariate analysis. APACHE II score (odds ratio, 1.57; 95% confidence interval, 1.13 to 2.20; p=0.008) was found to be a significant independent risk factor for mortality in multivariate logistic regression analysis. For prediction of mortality, the best cut-off point in APACHE II score was 16 (sensitivity, 77.8%; specificity, 92.3%; accuracy, 88.6%).

Conclusions: Patients with primary pyomyositis should be treated with appropriate broad-spectrum antibiotics and be monitored closely for complications. This study found that patients who suffered from primary pyomyositis with underlying diseases had a higher rate of Gram-negative bacterial infections, bacteremia and mortality. The APACHE II score at diagnosis was found to be an independent prognostic factor for mortality.

Key words: APACHE; Comorbidity; Mortality; Pyomyositis; Risk factors

Introduction

Primary pyomyositis, an intramuscular abscess of the large skeletal muscle groups, was originally described as pyomyositis tropicans [1]. Initially, the disease was thought to occur predominately in the tropics, but it is now increasingly recognized in non-tropical areas; its incidence appears to mirror increases in the number of immunocompromised persons, in association with diabetes mellitus, malignancy, human immunodeficiency virus infection, autoimmune disease, chronic liver diseases, rheumatologic conditions and history of intravenous drug abuse [2-5]. Because of its rarity

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and often vague clinical presentation, the diagnosis of pyomyositis might be delayed if the affected muscle is deeply situated and local signs are not apparent. This delay in diagnosis may result in a compartment syndrome, extension into and destruction of an adjacent joint, sepsis and occasionally death [6-9]. This study was conducted to evaluate the differences in clinical presentation, causative organism, treatment and outcome between pyomyositis patients with and without underlying diseases.

Methods

The charts of all patients with a discharge diagnosis of primary pyomyositis seen in our hospital, a medical center at Taipei City in Taiwan, between July 1989 and July 2006 were reviewed retrospectively. A primary pyomyositis was defined as tenderness and edema of striated muscle combined with intramuscular pus collection found by imaging or operative findings, and those secondary to infection of adjacent skin, soft tissue or bone were excluded [10,11]. The clinical stages of pyomyositis at presentation were defined previously [10]. In the first (invasive) stage, the muscle was increasingly edematous and painful due to bacterial seeding, but without abscess formation. The second stage, the suppurative phase, was characterized by abscess formation. The final stage was characterized by septicemia, metastatic abscesses, and multiorgan dysfunction.

Information concerning age, gender, clinical features, underlying comorbid diseases, results of routine blood tests, blood culture, muscle or pus culture, disease severity and clinical stages at the time of diagnosis, therapy, and outcome was obtained from the charts. Patients were categorized into two groups by the presence or absence of underlying diseases. Underlying disease refers to any disease that may have predisposed the patient to pyomyositis [2,12]. The initial antibiotic therapy was defined as the first antibiotic regimen started within 24 h for this diagnosis. The definitive antibiotic therapy was the antibiotic regimen which was adjusted according to the culture results and susceptibility tests. Inappropriate initial antibiotic therapy was defined as resistance of the pathogenic bacteria to the initial antibiotic therapy.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows (Version 14.0; SPSS, Chicago, IL, USA) software package. Univariate analysis was performed by Student's *t* test or Mann-Whitney test for continuous variables, and chi-squared test for categorical variables. Multivariate logistic regression analysis was performed on the independently significant variables from the univariate analyses, to identify the prognostic factors associated with mortality. The forward stepwise (likelihood ratio) method was used to select variables for the model. Odds ratio (OR) and 95% confidence interval (CI) values were estimated in the logistic regression model. A value of $p<0.05$ was considered statistically significant in all analyses.

Results

Demographic data and underlying conditions

There were 35 cases of primary pyomyositis identified at our hospital during the study period. Of the 35 cases, 23 had underlying medical diseases and the other 12 cases did not. The male-to-female ratio was 1.7:1.0. The mean age was significantly older in the patients with underlying disease (51.3 ± 13.6 years vs 26.2 ± 24.4 years, $p=0.005$) [Table 1]. Of the 23 patients with underlying diseases, 9 had type 2 diabetes mellitus, 4 had hematological disorders (2 aplastic anemia, 2 acute myeloid leukemia, 1 myelodysplastic syndrome), 3 had solid organ malignancy (1 breast carcinoma, 1 colon carcinoma, 1 glottic carcinoma), 3 had liver disease (1 hepatitis C, 1 hepatitis C-related cirrhosis of liver, 1 alcoholic liver disease), 2 had rheumatoid disease (1 Sjögren's syndrome, 1 rheumatoid arthritis), 1 had acquired immunodeficiency syndrome and 1 had hypothyroidism. One patient had concomitant hepatitis C and intravenous drug abuse.

Clinical and laboratory features

The most common symptoms and signs were fever, chills, pain, tenderness, swelling and redness (Table 1). The lower extremities were the most common site of involvement, specifically the thigh. None of the patients with underlying diseases had blunt trauma, as compared with 33.3% of patients without underlying disease ($p=0.009$). In both groups most patients had leukocytosis at the time of diagnosis. Eighty three percent of patients (29/35) presented in the second clinical stage. Patients with underlying diseases presented at a later stage ($p=0.024$).

Several imaging methods were used. Computed tomography was performed in 17 patients (48.6%), ultrasonography was performed in six patients (17.1%),

Table 1. Demographic data, clinical characteristics and laboratory features at initial presentation of pyomyositis patients with and without underlying medical conditions

Variable	Patients with underlying medical conditions (n = 23) No. (%)	Patients without underlying medical conditions (n = 12) No. (%)	*p*
Gender			0.726[a]
Male	15 (65.2)	7 (58.3)	
Female	8 (34.8)	5 (41.7)	
Age (years; mean ± SD) [range]	51.3 ± 13.5 (24-79)	26.2 ± 24.4 (2-72)	0.005[b]
Location			0.24[c]
Lower extremity	13 (56.5)	10 (83.0)	
Gluteal	3 (13.0)	4 (33.3)	
Thigh	7 (30.4)	2 (16.7)	
Calf	3 (13.0)	4 (33.3)	
Upper extremity	5 (21.7)	1 (8.3)	
Psoas	3 (13.0)	0 (0.0)	
Neck	1 (4.3)	0 (0.0)	
Facial	1 (4.3)	0 (0.0)	
Multifocal infection	0 (0.0)	1 (8.3)	
Blunt trauma	0 (0.0)	4 (33.3)	0.009[a]
Symptoms			
Fever	18 (78.3)	9 (75.0)	
Chills	14 (60.9)	9 (75.0)	
Pain	16 (69.6)	10 (83.3)	
Weight loss	3 (13.0)	1 (8.3)	
Lethargy	3 (13.0)	0 (0.0)	
Signs			
Tenderness	19 (82.6)	11 (91.7)	
Swelling	12 (52.2)	10 (83.3)	
Redness	10 (43.5)	7 (58.3)	
Warmth	9 (39.1)	6 (50.0)	
WBC count (/mm^3; mean ± SD) [range]	16,090 ± 11,022 (360-38,200)	14,615 ± 5011 (6800-23,500)	0.591[d]
Leukocytosis (WBC ≥10,500/mm^3)	15 (65.2)	9 (75.0)	0.709[a]
Leukopenia (WBC ≤3000/mm^3)	3 (13.0)	0 (0.0)	0.536[a]
CK (≥174 U/L) [n = 10]	3/6 (50.0)	2/4 (50.0)	1.000[a]
Stage at presentation			0.024[c]
First stage	0 (0.0)	3 (25.0)	
Second stage	20 (87.0)	9 (75.0)	
Final stage	3 (13.0)	0 (0.0)	

Abbreviations: SD = standard deviation; WBC = white blood cell; CK = creatine kinase

[a]Fisher's exact test.

[b]Mann-Whitney test.

[c]Pearson chi-squared test.

[d]Independent two-sample *t* test.

and nuclear imaging with gallium 67-labeled leukocytes was performed in two patients (5.7%). Magnetic resonance imaging was performed in combination with other studies in two patients (5.7%) and was used alone in seven patients (20.0%).

Causative organisms and underlying diseases

The causative microorganisms are shown in Table 2. Twenty seven patients (27/35, 77.1%) had a positive culture from the muscle specimen. Patients with underlying diseases had a higher proportion of Gram-negative bacteria isolated compared with patients without underlying diseases (30.4% vs 0.0%), but statistical significance was not obtained (p=0.07).

Among the four patients with hematological malignancy, three patients were diagnosed as pyomyositis in the status of neutropenia that was secondary to aggressive chemotherapy. These three cases were all caused

Table 2. Characteristics of microorganisms isolated in pyomyositis patients with and without underlying conditions

Variable	Patients with underlying medical conditions (n = 23) No. (%)	Patients without underlying medical conditions (n = 12) No. (%)	*p*
Culture-positive[a]	20 (87.0)	7 (58.3)	0.091[c]
Organisms[b]			
Gram-positive	12 (52.2)	6 (50.0)	1.000[d]
Staphylococcus aureus	8 (34.8)	5 (41.7)	
Coagulase-negative staphylococci	1 (4.3)	1 (8.3)	
Viridans *Streptococcus*	2 (8.7)	1 (8.3)	
Entercoccus spp.	2 (8.7)	0 (0.0)	
Gram-negative	7 (30.4)	0 (0.0)	0.07[c]
Klebsiella pneumoniae	3 (13.0)	0 (0.0)	
Samonella spp.	1 (4.3)	0 (0.0)	
Escherichia coli	3 (13.0)	0 (0.0)	
Stenotrophomonas maltophilia	1 (3.6)	0 (0.0)	
Pseudomonas aeruginosa	1 (3.6)	0 (0.0)	
Acinetobacter anitratus	1 (3.6)	0 (0.0)	
Mycobacterium	1 (3.6)	0 (0.0)	
Anaerobes	2 (8.7)	1 (8.3)	
Candida spp.	2 (8.7)	0 (0.0)	
Polymicrobial	3 (13.0)	1 (8.3)	
Positive blood culture	12 (52.2)	1 (8.3)	0.013[c]

[a]Either pus or blood culture.

[b]Some cases had more than one organism isolated.

[c]Fisher's exact test.

[d]Chi-squared test with Yates' continuity correction.

by Gram-negative organisms (1 *Stenotrophomonas maltophilia*, 1 extended-spectrum beta-lactamases producing *Escherichia coli* and 1 polymicrobial infection).

Thirteen strains of *Staphylococcus aureus* were isolated in our series. Two strains were methicillin-resistant *S. aureus*. One strain of methicillin-resistant *S. aureus* isolated from a nine-year-old girl was considered as community-acquired methicillin-resistant *S. aureus*, based on the clinical history and antibiogram [13]. It was resistant to oxacillin and clindamycin, but susceptible to gentamicin, sulfamethoxazole-trimethoprim, ciprofloxacin, vancomycin and teicoplanin.

Three cases with underlying diseases had polymicrobial infection (1 with *S. aureus* and coagulase-negative *Staphylococcus*; 1 with *Klebsiella pneumoniae*, *E. coli*, *Candida* spp. and *Bacteroides fragilis*; 1 with *Entercoccus* spp., *E. coli, Pseudomonas aeruginosa* and *Acinetobacter anitratus*). One patient without underlying diseases had polymicrobial infection (*S. aureus* and coagulase-negative *Staphylococcus*).

Blood cultures were positive in thirteen patients (13/35, 37.1%) in this study. Patients with underlying diseases had a significantly higher rate of positive blood culture compared with those without underlying diseases (50.2% vs 8.5%, p=0.013). Among the patients with positive blood cultures, four patients had *S. aureus* bacteremia, two had viridans *Streptococcus* bacteremia, two had *K. pneumoniae* bacteremia, two had *E. coli* bacteremia, one had candidemia, one had *Provetella* bacteremia and one had *S. maltophilia* bacteremia.

Treatment and outcome

The Acute Physiology and Chronic Health Evaluation (APACHE) II score at the time of diagnosis was significantly higher in patients with underlying diseases (13.9 ± 4.9 vs 3.8 ± 2.3, p<0.001) [Table 3].

All patients received effectively definitive antibiotic therapy. Initial antibiotic therapy among patients with underlying diseases included: oxacillin in 12 cases, first-generation cephalosporin plus gentamicin in three cases, third-generation cephalosporin in four cases, oxacillin plus gentamicin in one case, third-generation cephalosporin plus metronidazole in one case, clindamycin plus gentamicin in one case, and antituberculous therapy in one case. Initial antibiotic treatments among patients without underlying diseases included: oxacillin in eight cases, oxacillin plus gentamicin in

Table 3. Acute Physiology and Chronic Health Evaluation (APACHE) II score, treatment and outcome in pyomyositis patients with and without underlying conditions

Variable	Patients with underlying medical conditions (n = 23) No. (%)	Patients without underlying medical conditions (n = 12) No. (%)	*p*
APACHE II at diagnosis (mean ± SD)	13.9 ± 4.9	3.8 ± 2.3	<0.001[b]
Treatment			1.000[c]
Antibiotic treatment combined with surgical intervention	18 (78.3)	9 (75.0)	
Antibiotic treatment alone	5 (21.7)	3 (25.0)	
Initial inappropriate antibiotic treatment	8 (34.8)	2 (16.7)	0.434[c]
Mortality[a]			
Yes	9 (39.1)	0 (0.0)	0.015[c]
No	14 (60.1)	12 (100.0)	
Recurrence			
Yes	4 (17.4)	0 (0.0)	0.275[c]
No	19 (82.6)	12 (100.0)	

Abbreviation: SD = standard deviation

[a]Due to infection.

[b]Independent two-sample *t* test.

[c]Fisher's exact test.

two cases, penicillin in one case and first-generation cephalosporin in one case. Eight patients in the group with underlying diseases and two patients without underlying diseases had inappropriate initial antibiotic therapy (34.8% vs 16.7%, p=0.434).

Among the patients with underlying diseases, 5 patients (22%) were treated with antibiotics alone and 18 patients (78%) were treated with antibiotics plus surgical procedures. Among patients without underlying diseases, 3 patients (25%) were treated with antibiotics alone and 9 patients (75%) were treated with antibiotics plus surgical approaches. Twenty seven patients were treated with surgical intervention (4 fasciotomy, 9 incision and drainage and 14 debridement) combined with antibiotics. Recurrence developed in 4 patients in the group with underlying diseases but in none of the patients without underlying diseases. The overall mortality rate of patients with pyomyositis was 25.7% (9/35). The mortality rate in the group with underlying diseases was higher than in the group without underlying diseases (39.1% vs 0.0%, p=0.015).

Prognostic factors for mortality

A comparison of variables between survivors and non-survivors is shown in Table 4. Compared with the survivors, non-survivors had a higher white blood cell count (WBC; 2183.2/μL vs 13421.9/μL, p=0.017) and higher APACHE II score (17.6 vs 8.0, p<0.001). Recurrence (33.8% vs 3.8%, p=0.004) and presence of underlying diseases (100.0% vs 53.8%, p=0.015) were significant prognostic factors for mortality by univariate analysis. These significant prognostic factors (WBC, APACHE II score, recurrence, presence of underlying diseases) were included in a multivariate logistic regression analysis. The APACHE II score (OR, 1.57; 95% CI, 1.13 to 2.20; p=0.008) was found to be a significant independent risk factor for mortality.

The sensitivity, specificity and accuracy of prediction of mortality for different cut-off points in APACHE II score were calculated from the two-by-two table in SPSS. The best cut-off point was determined as the point yielding the best specificity and sensitivity. For prediction of mortality, 16 was the best cut-off point (sensitivity, 77.8%; specificity, 92.3%; accuracy, 88.6%).

Discussion

In this study, we found that patients with underlying diseases had a higher rate of Gram-negative bacterial infection, a higher rate of bacteremia, and a higher rate of mortality.

S. aureus was the most common causative organism in this study as well as previous reports [14,15]. Several other organisms that have been implicated include Gram-negative organisms, other Gram-positive organisms (predominantly *Streptococcus*), anaerobes, mycobacteria (*Mycobacterium avium* complex and *Mycobacterium tuberculosis*), microsporidia, and fungi (*Cryptococcus neoformans*, *Aspergillus*, *Candida*, *Fusarium*, *Pneumocystis jiroveci*) [10,16-22].

Table 4. Comparison of survivors and non-survivors among 35 patients with pyomyositis

Variable	Survivors (n = 26) No. (%)	Non-survivors (n = 9) No. (%)	*p*
Gender			0.698[a]
Male	17 (65.4)	5 (55.6)	
Female	9 (34.6)	4 (44.4)	
Age (years; mean ± SD)	42.3 ± 23.9	43.7 ± 12.2	0.777[b]
APACHE II at diagnosis (mean ± SD)	8.0 ± 5.1	17.6 ± 4.0	<0.001[b]
Location			
Lower extremity			
Gluteal	5 (19.2)	2 (22.2)	
Thigh	6 (23.1)	3 (33.3)	
Calf	7 (26.9)	0 (0.0)	
Upper extremity	6 (23.1)	0 (0.0)	
Psoas	1 (3.8)	2 (22.2)	
Neck	0 (0.0)	1 (11.1)	
Facial	0 (0.0)	1 (11.1)	
Multifocal infection	1 (3.8)	0 (0.0)	
Trauma	4 (15.4)	0 (0.0)	0.553[a]
Fever	18 (69.2)	9 (100.0)	0.081[a]
WBC count (/mm^3; mean ± SD)	13,422 ± 7128	21,832 ± 12,364	0.017[b]
WBC ≥10,500/mm^3	17 (65.4)	7 (77.8)	0.685[a]
WBC ≤3000/mm^3	2 (7.7)	1 (11.1)	1.000[a]
Stage at presentation			0.156[c]
First stage	3 (11.5)	0 (0.0)	
Second stage	22 (84.6)	7 (77.8)	
Final stage	1 (3.8)	2 (22.2)	
Culture-positive (n)	18 (69.2)	9 (100.0)	0.081[a]
Monomicrobial	16 (61.5)	7 (77.8)	
Gram-positive	10 (62.5)	4 (57.1)	1.000[a]
Gram-negative	4 (25.0)	1 (14.3)	1.000[a]
Mycobacterium	0 (0.0)	1 (14.3)	
Anaerobes	1 (6.3)	1 (14.3)	
Candida spp.	1 (6.3)	0 (0.0)	
Polymicrobial	2 (7.7)	2 (22.2)	
Positive blood culture	8 (30.8)	5 (55.6)	0.243[a]
Treatment			
Antibiotic treatment combined with surgical intervention	19 (73.1)	8 (88.9)	0.648[a]
Antibiotic treatment alone	7 (26.9)	1 (11.1)	
Initially inappropriate antibiotic treatment	5 (19.2)	5 (55.6)	0.081[a]
Recurrence	1 (3.8)	3 (33.8)	0.044[a]
Underlying disease	14 (53.8)	9 (100.0)	0.015[a]

Abbreviations: SD = standard deviation; APACHE = Acute Physiology and Chronic Health Evaluation; WBC = white blood cell

[a]Fisher's exact test.

[b]Independent two-sample *t* test.

[c]Pearson chi-squared test.

It is postulated that subclinical myopathy, immunosuppression secondary to malignancy, or chemotherapeutic drugs and preceding bacteremia may predispose to pyomyositis [20]. Pyomyositis should be considered as a rare but important complication in patients with hematological malignancy undergoing chemotherapy. Diabetic and other immunocompromised patients are particularly susceptible to pyomyositis due to neutrophil dysfunction, specifically defective oxidative metabolism that predisposes to catalase-positive organisms such as *S. aureus* [2,3].

Blood cultures are reported to be positive in 5% of cases from the tropics, reflecting both the transient nature of the initial bacteremia and perhaps the poor

sensitivity of blood cultures in these areas [23]. However, blood cultures in non-tropical areas are positive in approximately 30% of cases [1,12]. Our study further demonstrated that the rate of positive blood culture was higher in patients with underlying diseases than in patients without underlying diseases (52.5% vs 8.3%, p=0.013). The higher rate of positive blood cultures in non-tropical areas may reflect the fact that patients are often immunosuppressed, have Gram-negative infections, and may present later in the course of illness due to subtle clinical presentation [1,12].

Primary pyomyositis is believed to be caused by transient bacteremia because it develops without an obvious penetrating injury or any other clear portal of entry in the majority of cases [24]. Despite the frequency of bacteremia, it rarely leads to muscle infection since the musculature is relatively resistant to infection [25]. It has been hypothesized that intensive exercise or trauma alters local muscle tissue structure, thereby creating a portal of entry for implantation of bacteria from a subsequent, untreated bacteremic episode [4,5,10]. Among the 35 patients in this series, four sustained minor trauma events (11% of all cases) before acute infection, such as fall in one case, strain of muscle in one case and Chinese medical manipulation with massage in two cases. The role of minor muscle trauma may be important in the pathogenesis of pyomyositis in immunocompetent hosts, since the four patients with trauma history were immunocompetent. Other disease conditions, including diabetes mellitus, as well as malignancies treated with chemotherapeutic agents and steroids, may also induce muscular injury [3,26]. Such unrecognized muscle damage has also been suggested to be an inciting event.

Primary pyomyositis is considered to have three clinical stages [10]. Pus formation occurs 10 to 21 days after the initial invasive seeding of bacteria on the muscle. The final stage is characterized by septicemia, metastatic abscesses, and multiorgan dysfunction, and is associated with high mortality [2,10]. In our series, we saw the full spectrum of these three stages; 82.9% of patients presented at the second stage. Patients with underlying diseases presented at a later stage — early diagnosis requires a high index of suspicion and confirmation with ultrasound, computed tomography, or magnetic resonance imaging [2]. Magnetic resonance imaging is better than other imaging diagnostic modalities for early detection of pyomyositis [4,27,28].

Laboratory findings during pyomyositis are nonspecific. Levels of creatine kinase, aldolase, and serum aspartate aminotransferase are typically normal, despite cases of extensive muscle involvement and pathologic evidence of muscle necrosis [3,29].

The overall mortality of this series was 25.7%. In other studies, mortality rates have ranged from 1.5 to 27.0% [10,30]. Mortality is rare in healthy patients, but rises in patients with underlying diseases, especially diabetic patients and those with hematological disorders. The APACHE II score at the time of diagnosis was significantly higher in non-survivors compared with surviving patients (17.6 vs 8.0, p<0.001). Facing patients diagnosed as pyomyositis with higher disease severity, physicians should exercise particular care in management because of the high risk of mortality.

Early diagnosis, complete drainage of purulent material and the use of appropriate antibiotic therapy are the key determinants of successful treatment, and lead to complete resolution in the vast majority of cases [31]. If the disease is recognized early, i.e., at the first stage, antibiotic therapy alone is usually sufficient. Initial therapy should include a broad-spectrum agent with good *S. aureus* coverage and should subsequently be modified based on culture and sensitivity results. Coverage of Gram-negative organisms should be included empirically in the treatment of immunocompromised patients. In case of primary pyomyositis, treatment with an intravenous agent followed by an oral agent (when clinical improvement has occurred) for a total of 21 to 28 days seems to be appropriate [9]. The immune status of the host, clinical course, and number of abscesses should be considered when determining the length of therapy [2].

In conclusion**,** compared with healthy persons, patients with underlying medical diseases have a higher rate of Gram-negative bacterial infections, bacteremia and mortality, and thus should promptly receive appropriate broad-spectrum antibiotics and be monitored closely for infectious complications. The APACHE II score at diagnosis was found to be a significant prognostic factor for mortality.

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