Discrimination between tuberculous and bacterial pyomyositis in magnetic resonance features

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ABSTRACT

Purpose: The purpose of this study was to assess the differences of magnetic resonance features between tuberculous and bacterial pyomyositis.

Method: This is a retrospective study of patients with bacterial and tuberculous pyomyositis. We excluded patients with pyomyositis caused by actinomycosis, non-tuberculous mycobacterium, fungi, unknown of causative organism, or inadequate imaging for analysis. Magnetic resonance imaging was independently reviewed by two radiologists.

Results: Of the 136 pyomyositis patients, 71 (52.2 %) patients had bacterial pyomyositis while 65 (47.8 %) patients had tuberculous pyomyositis. Seventy-seven patients (56.6 %) had intramuscular abscess. On multivariable analysis, bacterial pyomyositis was associated with diabetes mellitus (odds ratio [OR] 3.17, 95 % confidence interval [CI] 1.30–8.24) and bone marrow involvement (OR 5.02, 95 % CI 1.21–34.4). Spinal involvement had a significantly lower likelihood of bacterial pyomyositis (OR 0.25, 95 %CI 0.11–0.54). In patients with intramuscular abscess, diabetes mellitus and hyperintense on T2-weighted images at the abscess wall had a significantly higher likelihood of bacterial pyomyositis (OR 5.21, 95 %CI 1.33–25.42 and OR 5.34, 95 %CI 1.36–24.71, respectively), whereas spinal involvement had a significantly lower likelihood of bacterial pyomyositis (OR 0.09, 95 %CI 0.02–0.30).

Conclusions: Magnetic resonance imaging has modest accuracy for differentiation of tuberculous and bacterial pyomyositis. Diabetes mellitus and extraspinal pyomyositis were the predictors of bacterial pyomyositis. Presence of T2 hyperintense wall of intramuscular abscess was also the predictor of bacterial pyomyositis.

1. Introduction

Infectious pyomyositis is an infection of skeletal muscles endemic in tropical climates and becoming more common in outside the tropics [1]. Most commonly, infectious pyomyositis is caused by bacteria, predominantly Staphylococcus aureus, whereas tuberculous and nonbacterial pyomyositis including virus, fungi and parasites are rare [1–6]. The etiology of pyomyositis is classified into primary and secondary pyomyositis. Primary pyomyositis is an infection of skeletal muscle itself, while secondary pyomyositis is a contiguous infection from the adjacent structures such as bone, joint or soft tissue [2].

Magnetic resonance imaging (MRI) is the most useful imaging modality for diagnosis of pyomyositis with high sensitivity and specificity. It most clearly demonstrates diffuse muscle inflammation as well as any subsequent abscess formation [2]. Moreover, MRI can demonstrate the extent of disease and associated conditions such as osteomyelitis and septic arthritis [1,2,7,8].

To reduce the risk of progression of pyomyositis to sepsis and mortality, it is important to differentiate tuberculous and bacterial pyomyositis for the proper treatment at the early stage of the disease. However, there is a paucity of literature discussing how to differentiate between these two causative organisms. This study aims to assess the magnetic resonance imaging features to differentiate tuberculous and bacterial pyomyositis.
2. Methods

2.1. Study design

2.1.1. Patient population

We retrospectively reviewed 355 patients who were diagnosed with pyomyositis or the following conditions of septic arthritis, osteomyelitis and spondylodiscitis and have undergone MRI between August 2013 and April 2019. We excluded the patients who had diagnosis of septic arthritis, osteomyelitis and spondylodiscitis with no muscle involvement in 55 patients. We excluded the patients who had chronic bacterial infection (Actinomyces, Mycobacterium abscessus, Mycobacterium avium complex) or fungal infection (Eumycetoma, Cryptococcus neoformans) in 8 patients, and inadequate imaging for analysis in 2 patients. One hundred fifty-four patients were also excluded because they did not have data documents about the causative organisms, and they were referred for only imaging studies. A total of 136 patients were included in Fig. 1. This study was approved (Approval number HE611541) by the Ethics Committee for Human Research.

Patients were classified into tuberculous and bacterial pyomyositis based on the evidence of skeletal muscle infection [1] and by reviewing the tissue or fluid culture, hemoculture, polymerase chain reaction, Acid-Fast Bacilli stain, histopathology, the medical records of the causative organisms or based on responsiveness of antibiotics or anti-tuberculous therapy.

2.1.2. Imaging protocol

MRI was performed on 1.5 T system (Magnetom Aera, Siemens Medical Solutions, Erlangen, Germany) or 3 T system (Philips Achieva, Philips Medical System, Netherland, B.V.). MRI protocol included a combination of axial, sagittal and/or coronal images using T1-weighted (T1WI) fast spin echo (FSE) with TR/TE range of 400–680/8–12, T2-weighted (T2WI) FSE with TR/TE range of 3000–5360/78–100 and Short Tau Inversion Recovery (STIR) or Spectral Attenuated Inversion Recovery (SPAIR); matrix size 256 × 160 to 384 × 216. Contrast enhanced images of axial, sagittal and/or coronal planes were obtained using T1WI FSE sequence with fat suppression after 0.1 mmol/kg of body weight of gadolinium injection. Field of view, slice thickness, and interslice gap varied along with diseased region.

2.1.3. Imaging analysis

The MR images were analyzed on Picture Archiving and Communication System (PACS). Two musculoskeletal radiologists, who had experiences about 10 and 20 years, were independently reviewed under blind condition to patient’s information and the diagnosis of causative organisms. The data were collected as double data entry. The discrepancy findings between radiologists were given in a consensus.

The extension of abnormalities was classified into two categories; a lesion in the isolated muscle alone or a muscle lesion with involvement of adjacent structures including bone marrow, joint, fistula, and spine. For more precise evaluation, the location of pyomyositis (lower extremity, upper extremity, neck, psoas muscle, pelvic iliacus muscle, paravertebral muscle, thoracic wall, buttock or others), the number of affected muscles (single or multiple muscles), muscle contour (normal or enlarged), characters of the affected muscles including signal intensity (hypointense, isointense, or hyperintense on T1-weighted images and T2-weighted images in comparison with normal skeletal muscle) and feathery muscle edema were taken in account. The presence of intramuscular gas was assessed in case of absent history of biopsy, drainage or fistula. The cellulitis was also evaluated.

Regarding to the presence of intramuscular abscess, which was defined by a mass with the signal intensity of fluid collection and a peripheral rim enhancement after intravenous gadolinium injection. We characterized the abscess in terms of the location (lower extremity, upper extremity, neck, psoas muscle, pelvic iliacus muscle, paravertebral muscle, thoracic wall, buttck, or others), the number of abscess (single or multiple abscesses), the abscess volume [by the ellipsoid volume formula $\frac{4}{3} \times \pi \times (height/2) \times (width/2) \times (depth/2)$] [9], signal intensity of the abscess wall (hypointense, isointense, or hyperintense on T1-weighted images and T2-weighted images in comparison with normal skeletal muscle), signal intensity of internal abscess content (hypointense, isointense, or hyperintense on T1-weighted images and T2-weighted images in comparison with normal skeletal muscle), the character of abscess wall (smooth or irregular wall was defined as less than or equal to or more than 3 mm, difference from each side of the abscess wall), the thickness of abscess wall (thick wall was defined as $\geq$ 3 mm thickness) and the presence of internal abscess enhancement. When there was more than one abscess, the largest abscess was evaluated.

Study data were collected and managed using Research Electronic Data Capture (REDCap) [10].

2.2. Statistical analysis

Continuous variables were presented as mean (standard deviation)
or median (interquartile range [IQR], as appropriate. Categorical variables were reported as number (percentage). Continuous variables were compared between two groups (bacterial group vs tuberculosis group) using two sample t-test or Wilcoxon rank-sum as appropriate. Chi-square test or Fischer’s exact test were used for categorical variables.

Binary logistic regression was used for analyzing the predictors associated with bacterial pyomyositis. To build a multivariable regression model, univariable regression was first analyzed. The variables significant at $p < 0.1$ in univariable analysis were identified as potential factors variables and entered into a multivariable regression model. Four-fold cross validation was used in estimating the generalization error and model performance. Area under the receiver operating characteristic (ROC) were calculated from cross-validation for determination the model performance. We performed a sub-group analysis on patients who had the abscess then developed the predictive model for bacterial pyomyositis. All the statistical analyses were performed using R software version 3.5.2. The level of statistical significance was set at $p < 0.05$ (two tailed).

3. Results

A total of 136 patients were diagnosed as having pyomyositis. Of these patients, 71 patients (52.2 %) were bacterial pyomyositis and 65 patients (47.8 %) were tuberculosis pyomyositis. Among 136 patients, 77 (56.6 %) of them had abscess. Thirty-seven (52.1 %) of 71 bacterial pyomyositis patients were males while 32 (49.2 %) of 65 tuberculous pyomyositis patients were males. The median age of both groups were 77 (56.6 %) vs 77 (42-65) years, $p = 0.30$. The pathogenic organisms detected by culture were Staphylococcus spp. in 3 patients (7.5 %), Salmonella spp. in 5 patients (12.5 %), Burkholderia pseudomallei in 9 patients (22.5 %), Escherichia coli in 4 patients (10 %), Pseudomonas aeruginosa in 2 patients (5 %), and 1 patient (2.5 %) each with Klebsiella pneumonia, Aeromonas veronii, and Acinetobacter baumannii. The patients with history of diabetes mellitus were more frequent in bacterial pyomyositis group than in tuberculosis pyomyositis group (15/56 [26.8 %] vs 2/61 [3.3 %], $p < 0.001$) (Table 1).

### 3.1. MRI findings of pyomyositis

Pyomyositis at lower extremities were more frequent in bacterial pyomyositis group compared to tuberculosis pyomyositis group (29 [40.8 %]) vs 10 [15.4 %], $p < 0.001$). The psoas muscle involvement was more common in tuberculosis pyomyositis group compared to bacterial pyomyositis (39 [60 %] vs 29 [40.8 %]), $p = 0.03$. The majority of patients in both bacterial and tuberculosis pyomyositis groups had involvement of muscle and other structures with predominant involvement of spines. Spinal involvement was more common in tuberculosis pyomyositis than in bacterial pyomyositis (46/61 [75.4 %] vs 24/56 [42.9 %], $p < 0.001$) (Table 2). Other less

### Table 1
Demographic Data between Pyogenic and Tuberculous Pyomyositis.

| Characteristics                  | Tuberculous pyomyositis(n=65) | Pyogenic pyomyositis(n=71) | P-value |
|----------------------------------|--------------------------------|---------------------------|---------|
| Age, median (IQR), years         | 57 (42.65)                     | 53 (43.5-61.5)            | 0.30    |
| Male, n (%)                      | 32 (49.2)                      | 37 (52.1)                 | 0.74    |
| Comorbidities, n (%)             |                               |                           |         |
| Diabetes mellitus                | 10 (15.4)                      | 22 (31)                   | 0.03    |
| Malignancy                       | 2 (3.1)                        | 8 (11.3)                  | 0.10    |
| Chronic kidney disease           | 5 (7.7)                        | 5 (7)                     | 1.00    |
| Connective tissue disease        | 4 (6.2)                        | 5 (7)                     | 1.00    |
| History of muscle trauma         | 1 (1.5)                        | 5 (7)                     | 0.21    |
| HIV infection                    | 2 (3.1)                        | 1 (1.4)                   | 0.61    |
| Cirrhosis                        | 2 (3.1)                        | 1 (1.4)                   | 0.61    |

Note—HIV = human immunodeficiency virus, IQR = interquartile range.

### Table 2
Magnetic Resonance Imaging Findings of Pyogenic and Tuberculous Pyomyositis in All Patients.

| Findings                          | Tuberculous pyomyositis (n=65) | Pyogenic pyomyositis (n=71) | P-value |
|-----------------------------------|--------------------------------|---------------------------|---------|
| Intramuscular gas, n (%)          | 2 (3.2)                        | 2 (2.8)                   | 1.00    |
| Location, n (%)                   |                               |                           |         |
| Psoas muscle                      | 39 (60)                        | 29 (40.8)                 | 0.03    |
| Paravertebral muscle              | 34 (52.3)                      | 29 (40.8)                 | 0.18    |
| Lower extremity                   | 10 (15.4)                      | 29 (40.8)                 | < 0.001 |
| Buttock                           | 19 (29.2)                      | 24 (33.8)                 | 0.57    |
| Pelvic iliacus muscle             | 25 (38.5)                      | 22 (31)                   | 0.36    |
| Upper extremity                   | 4 (6.2)                        | 3 (4.2)                   | 0.71    |
| Neck                              | 3 (4.6)                        | 1 (1.4)                   | 0.35    |
| Thoracic wall                     | 3 (4.6)                        | 1 (1.4)                   | 0.35    |
| Other                             | 2 (3.1)                        | 7 (9.9)                   | 0.17    |
| Extension of the abnormalities, n (%) |                      |                           |         |
| Isolated muscles                  | 4 (6.2)                        | 15 (21.1)                 | 0.01    |
| Muscle and bone marrow            | 2 (3.3)                        | 15 (26.8)                 | < 0.001 |
| Muscle and joint                  | 15 (24.6)                      | 17 (30.4)                 | 0.48    |
| Muscle and fistula                | 2 (3.3)                        | 3 (5.4)                   | 0.67    |
| Muscle and spine                  | 46 (75.4)                      | 24 (42.9)                 | < 0.001 |
| Number of affected muscles, n (%) |                                 |                           |         |
| Single muscle                     | 2 (3.1)                        | 6 (8.5)                   | 0.28    |
| Multiple muscles                  | 63 (96.9)                      | 65 (91.5)                 | 0.80    |
| Enlarged muscle contour, n (%)    | 52 (80)                        | 58 (81.7)                 | 0.98    |
| Muscle signal intensity on TIWI, n (%) |                    |                           |         |
| Hypointense                       | 2 (3.1)                        | 0 (0)                     | 0.26    |
| Isointense                        | 57 (87.7)                      | 67 (94.4)                 | 1.00    |
| Hypertintense                     | 6 (9.2)                        | 4 (5.6)                   |         |
| Muscle signal intensity on T2WI, n (%) |                    |                           |         |
| Hypointense                       | 0 (0)                          | 0 (0)                     |         |
| Isointense                        | 0 (0)                          | 1 (1.4)                   |         |
| Hypertintense                     | 65 (100)                       | 70 (98.6)                 |         |
| Feathery muscle edema, n (%)      | 54 (84.4)                      | 60 (84.5)                 | 0.98    |
| Cellulitis, n (%)                 | 32 (49.2)                      | 44 (62)                   | 0.14    |
| Intramuscular abscess, n (%)      | 37 (56.9)                      | 40 (56.3)                 | 0.95    |

Note—IQR = interquartile range, TIWI = T1-weighted image, T2WI = T2-weighted image.

frequently involved structures were the joint, bone marrow and fistula tract. Pyomyositis with bone marrow involvement was more frequent in patients with bacterial pyomyositis compared to tuberculosis pyomyositis (15/56 [26.8 %] vs 2/61 [3.3 %], $p < 0.001$). An isolated muscle infection was more common in bacterial pyomyositis than in
Table 3
Magnetic Resonance Imaging Findings of Pyogenic and Tuberculous Pyomyositis in Patients with Intramuscular Abscesses.

| Findings                                      | Tuberculous pyomyositis (n = 27) | Pyogenic pyomyositis (n = 40) | P-value |
|-----------------------------------------------|----------------------------------|--------------------------------|---------|
| Intramuscular gas, n (%)                      | 1 (−2.9)                        | 1 (−2.5)                       | 1.00    |
| Location, n (%)                               | 25 (−67.6)                      | 19 (−47.5)                     | 0.08    |
| Psas muscle                                   | 19 (−51.4)                      | 13 (−32.5)                     | 0.09    |
| Lower extremity                               | 6 (−16.2)                       | 16 (−40)                       | 0.02    |
| Buttock                                       | 13 (−35.1)                      | 23 (−57.5)                     | 0.05    |
| Pelvis ilacus muscle                          | 15 (−40.5)                      | 18 (−45)                       | 0.69    |
| Upper extremity                               | 1 (−2.7)                        | 3 (−7.5)                       | 0.62    |
| Neck                                          | 1 (−3.7)                        | 1 (−2.5)                       | 1.00    |
| Thoracic wall                                 | 3 (−8.1)                        | 0 (0)                          | 0.11    |
| Other                                         | 2 (−5.4)                        | 6 (−15)                        | 0.27    |

Table 4
Factors Associated with Pyogenic Pyomyositis.

| Variables                                      | Odds ratio | 95% confidence interval | P-value |
|------------------------------------------------|------------|--------------------------|---------|
| All patients<sup>a</sup>                       | History of diabetes mellitus | 3.17 | 1.30 to 8.24 | 0.01 |
| Muscle and spine involvement                   | 0.25 | 0.11 to 0.54 | < 0.001 |
| Muscle and bone marrow involvement             | 5.02 | 1.21 to 20.4 | 0.05 |
| Patients with intramuscular abscesses<sup>b</sup> | History of diabetes mellitus | 5.21 | 1.33 to 25.42 | 0.03 |
| Muscle and spine involvement                   | 0.09 | 0.02 to 0.30 | < 0.001 |
| Abscess wall signal intensity on T2WI           | Hypoointense | 2.50 | 0.60 to 11.07 | 0.21 |
| Isointense                                    | Ref | Ref | Ref |
| Hyperintense                                  | 5.32 | 1.36 to 24.71 | 0.02 |

Note—Ref = reference, T2WI = T2-weighted image.

<sup>a</sup> Area under the receiver operating characteristic curve = 0.70 (95 %CI 0.61–0.79).
<sup>b</sup> Area under the receiver operating characteristic curve = 0.77 (95 %CI 0.66–0.88).

tuberculous pyomyositis (15 [21.1 %] vs 4 [6.2 %], p = 0.01).

3.2. MRI findings of pyomyositis with intramuscular abscess

Among the patients who have pyomyositis with abscesses formation, involvement of lower extremities was significantly more frequent in bacterial pyomyositis group than in tuberculous pyomyositis group (16 [40 %] vs 6 [16.2 %], p = 0.02). Similarly, involvement of buttow was more common in patients with bacterial pyomyositis with abscesses compared to tuberculous pyomyositis with abscess (23 [57.5 %] vs 13 [35.1 %], p = 0.05). Isolated muscle involvement was also significantly more common in bacterial than tuberculous pyomyositis with abscess (11 [27.5 %] vs 3 [8.1 %], p = 0.03). Bone marrow involvement was significantly higher in bacterial pyomyositis with abscess compared to that in tuberculous pyomyositis with abscess (7/29 [24.1 %] vs 1/34 [2.9 %], p = 0.02). In contrast, patients with spine involvement were more common in tuberculous pyomyositis with abscess, compared to those in bacterial pyomyositis with abscess (27/34 [79.4 %] vs 10/29 [34.5 %], p < 0.001) (Table 3).

3.3. Factors associated with bacterial pyomyositis

On multivariable analysis, bacterial pyomyositis showed significant association with the history of diabetes mellitus (odds ratio [OR] 3.17, 95 % confidence interval [CI] 1.30–8.24, p = 0.01) and bone marrow involvement (OR 5.02, 95 %CI 1.21–20.4, p = 0.05), although spinal involvement had a significantly lower association with bacterial pyomyositis (OR 0.25, 95 %CI 0.21–0.54, p < 0.001) (Table 4). The area under the receiver operating characteristic curve (95 %CI) of this multivariable analysis was 0.7 (95 %CI 0.61–0.79).

On multivariable analysis for the sub-group of patients with intramuscular abscess, a history of diabetes mellitus had a significantly higher likelihood of bacterial pyomyositis (OR 5.21, 95 %CI 1.33–25.42, p = 0.03) whereas spinal involvement had a significantly lower likelihood of bacterial pyomyositis (OR 0.09, 95 %CI 0.02–0.30, p < 0.001). In addition, hyperintensity on T2-weighted image at the abscess wall was a significant predictor of bacterial pyomyositis (OR 5.32, 95 %CI 1.36–24.71, p = 0.02) (Table 4). The area under the receiver operating characteristic curve (95 %CI) of this multivariable analysis was 0.77 (95 %CI 0.66–0.88).

4. Discussion

Differentiation between bacterial and tuberculous pyomyositis is
crucial. Our study revealed that patients with a history of diabetes mellitus were strongly associated with bacterial pyomyositis. Site and extension of infection from MR imaging were important for differential diagnosis between bacterial and tuberculous pyomyositis. Patients with bone marrow involvement were associated with bacterial pyomyositis while patients with spine involvement were associated with tuberculous pyomyositis. Among patients who developed intramuscular abscess, hyperintensity of abscess wall on T2-weighed images was associated with bacterial pyomyositis.

There are many comorbidities that might impair the immune system.
of patients with pyomyositis such as diabetes mellitus, human immunodeficiency virus infection, liver cirrhosis, malignancy, autoimmune disease, connective tissue disease or chronic kidney disease [1,2,7]. In our study, diabetes mellitus was the significant predictive factor for development of bacterial pyomyositis. This supported the previous studies that diabetes mellitus was a predisposing factor for pyogenic spondylodiskitis [7,11,12].

In the previous series of MRI study, characteristic features of pyomyositis were described as muscle enlargement, with increased signal intensity on T2-weighted images, usually associated with subcutaneous fat stranding and edema along the fascial planes [1,3–7]. Similar to our patients, all cases showed increased signal intensity on the T2-weighted images at the muscles and most of cases had enlarged muscle contours, and there were no differences between bacterial and tuberculous pyomyositis groups.

On T1-weighted images, the intramuscular abscess is often characterized by hyperintense which was found in both bacterial and tuberculous pyomyositis in our study. This finding was consistent with the others [1,7,13] and it is postulated that hyperintense rim could be related to the presence of paramagnetic materials in the abscess wall such as blood product, bacterial or macrophage sequestration of iron or free radicals. In addition, in this study we have found that hyperintense rim on T2-weighted images of the intramuscular abscess wall was a significant predictor of bacterial pyomyositis as shown in Fig. 2. In the previous report of Stavroula et al. [13], the abscess wall was hypointense on T2-weighted images in the bacterial pyomyositis in patients with local muscle trauma. Likewise, Kim et al. [5] reported that the abscess wall was hypointense on T2-weighted images in tuberculous pyomyositis. These findings in the previous studies are not conclusive. We assume that these findings are related to the age of blood product and vascularized granulation tissue in the abscess wall as shown in Fig. 3 here. According to the nature of disease, tuberculosis is more chronic than bacterial infection. In bacterial pyomyositis, earlier stage of blood production, more vascularized granulation tissue and less fibrotic tissue component give rise MR imaging of hyperintense rim on T2-weighted images at the abscess wall.
The location of pyomyositis usually involves the larger muscle groups located around the pelvic girdle and lower extremities [1]. Similar to our results, the lower extremities muscles were the one of the most commonly affected location in bacterial pyomyositis. In addition, muscular lesion with bone marrow involvement was significantly more common in bacterial pyomyositis group than in tuberculosis group. In contrast, patients with spine involvement were associated with a lower likelihood of bacterial pyomyositis as shown in Fig. 4. To our knowledge, there is no previous report mentioned statistically about this information.

In the present study, data quality was assured by double data entry and was given consensus from two radiologists. In addition, we used the modern machine learning techniques for estimating the model performances. However, there are limitations due to small sample size of study populations. Moreover, we included patients who responded to antimicrobial therapy alone, so that severe cases may have been unintentionally excluded if their treatment failed. Future study should evaluate the relationship between MRI findings and histopathological findings in patients with intramuscular abscess.

5. Conclusion

MRI has modest accuracy for differentiation of bacterial and tuberculous pyomyositis. Diabetes mellitus and extraspinal pyomyositis were the predictors of bacterial pyomyositis with and without intramuscular abscess, compared to those of tuberculous pyomyositis. Presence of T2 hyperintense wall of intramuscular abscess was the predictor of bacterial pyomyositis.

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Declaration of Competing Interest

None.

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