Clinical Rheumatology (2019) 38:1873–1880
https://doi.org/10.1007/s10067-019-04481-w

ORIGINAL ARTICLE

When brucellosis met the Assessment of SpondyloArthritis international Society classification criteria for spondyloarthritis: a comparative study

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Received: 3 December 2018 / Revised: 4 February 2019 / Accepted: 14 February 2019 / Published online: 26 February 2019

Abstract

Objectives To distinguish brucellosis patients fulfilling the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for spondyloarthritis (SpA) from SpA patients.

Methods Brucellosis patients diagnosed from September 2012 to December 2017 who met the ASAS classification criteria for SpA were analyzed with clinical characteristics and laboratory and imaging examinations. Axial or peripheral SpA patients were respectively included into the comparative analysis with a 4:1 ratio.

Results Twenty-two brucellosis (10 axial and 12 peripheral) patients (male, 16 cases; 72.72%; mean (S.D.) age, 40.23 (16.49) years) and 88 SpA patients were included. All brucellosis patients had been misdiagnosed or considered as SpA before admission to our center. The brucellosis patients had shorter disease duration (axial, $P = 0.001$; peripheral, $P = 0.108$). More than half (59.09%) of the patients had contact history with livestock. The low back pain (LBP) of brucellosis patients was generally less improved with exercise (axial, $P = 0.001$; peripheral, $P = 0.008$). More brucellosis patients had myalgia (axial, $P < 0.001$; peripheral, $P = 0.071$) or fever (axial, $P < 0.001$; peripheral, $P = 0.107$). None of them had positive HLA-B27. Blood culture tests were performed in all brucellosis patients and only 4 (18.18%) were positive. Twenty (90.91%) brucellosis patients were gold-immunochromatographic assay (GICA) positive. Bone marrow edema and bone erosion in sacroiliac joints were respectively detected in 100% (10/10) and 90% (9/10) axial brucellosis patients by MRI. Adjacent muscle involvement was found in 80% (8/10) of the patients.

Conclusions Indicators including disease duration, contact history of livestock, features of LBP, myalgia, fever, and HLA-B27 can help the differential diagnosis of brucellosis and SpA. GICA test and sacroiliac joints MRI can furtherly confirm the diagnosis of brucellosis.

Keywords Ankylosing spondylitis · Brucellosis · Differential diagnosis · Magnetic resonance imaging · Sacroiliitis · Spondyloarthritis

Introduction

Spondyloarthritis (SpA) encompasses a group of inflammatory disorders: ankylosing spondylitis (AS), psoriatic arthritis, arthritis related to inflammatory bowel disease, reactive arthritis, and juvenile idiopathic arthritis [1]. Besides, according to the main involvement sites, SpA is also divided into two groups: axial SpA and peripheral SpA.

The Assessment of SpondyloArthritis international Society (ASAS) has developed and validated new classification criteria for axial SpA in 2009 [2] and for peripheral SpA in 2011 [3]. Due to the introduction of the concepts of non-radiographic axial SpA and sacroiliitis by magnetic resonance

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imaging (MRI), the sensitivity of the classification criteria has been remarkably improved which enables early diagnosis; however, the diagnostic specificity is decreased in the meanwhile. Hence, knowing the characteristics of the imitators of SpA and how to distinguish SpA from them is very important.

Brucellosis is the most common zoonotic infection worldwide with more than 500,000 new cases annually which may still be largely underestimated [4]. It was once considered as a regional disease, which is mainly prevalent in undeveloped countries of Asia, Eastern Europe, Africa, and Latin America. However, it has also become a common imported disease in the developed countries, and a literature review had identified nearly 1000 brucellosis patients diagnosed within non-endemic areas, mainly North America and Western Europe, due to the international tourism and products importation [4–7].

Brucellosis is a great imitator as it can involve multiple systems and mimic various diseases. Musculoskeletal system, which has a frequency between 23% and 53% in most case series reports [8–14], is the most common focal involvement in brucellosis. In this form, the most common manifestations are arthralgia, myalgia, and low back pain (LBP) [15]. Additionally, a previous study had indicated that some brucellosis patients could be falsely classified as axial SpA [16]. In our clinical practice, we have also found that brucellosis can mimic SpA and even fulfill the ASAS classification criteria either for axial or peripheral SpA.

In this study, to distinguish brucellosis patients fulfilling the ASAS classification criteria for SpA from SpA patients, the demographic characteristics, clinical manifestations, laboratory results, and imaging findings were compared.

Methods

Patients

Hospitalized brucellosis patients diagnosed during September 2012 to December 2017 who met the ASAS classification criteria were included [2, 3]. According to the ASAS classification criteria, patients who had at least 3 months of LBP with sacroiliitis on imaging plus ≥ 1 SpA features were defined as axial brucellosis, while patients with arthritis, enthesitis, or dactylitis plus ≥ 1 main SpA features or ≥ 2 main other SpA features were defined as peripheral brucellosis. Inflammatory LBP was considered and defined according to the ASAS experts' definition [17]. Brucellosis patients with the possible comorbidity of SpA or other rheumatic diseases were excluded.

The data of hospitalized SpA patients were searched from the Electronic Medical Records Database in our hospital based on the ICD-9 code or keywords including SpA, AS, psoriatic arthritis, arthritis related to inflammatory bowel disease, reactive arthritis, and juvenile idiopathic arthritis. Then, axial or peripheral SpA patients were included into the comparative analysis with a 4:1 ratio according to the admission date of brucellosis patients. Patients failing to meet the ASAS classification criteria for SpA or with the comorbidities of other rheumatic or infectious disease were excluded.

This study was approved by the Ethics Committee at Chinese PLA General Hospital (S2016-049-02), and the informed consent was waived due to the retrospective nature of this study.

Data collection

The data of patients were retrieved from the Electronic Medical Records Database. Demographic features including the gender, age, age at onset, and disease duration were collected. The history of contact with livestock including cattle, sheep, or goats before disease onset was questioned at the time of diagnosis which was recorded in the database and was retrieved with the onset time of brucellosis. The pervious misdiagnoses before admission and treatment during the disease duration were analyzed. Clinical manifestations including the involvements of musculoskeletal system and other manifestations were retrieved. Laboratory results including tests of blood culture, gold-immunochromatographic assay (GICA) for *Brucella*, complete blood count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were also retrieved. The imaging of brucellosis patients was reviewed by two rheumatologists together. Sacroiliitis refers to definite radiographic sacroiliitis according to the modified New York criteria [18] or sacroiliitis by MRI according to the ASAS definition [2].

When defining anemia, the lower normal hemoglobin limit in women or children (6–14 years) was 120 g/L and in men was 130 g/L according to the WHO definition [19].

Statistical analysis

All analyses were performed with SPSS version 24.0 (IBM, Armonk, NY, USA). Continuous variables were presented as the mean (S.D.) (with normal distribution) or the median (interquartile range (IQR) (25th percentile, 75th percentile)) (with non-normal distribution). Categorical variables were represented as the frequency and percentages. An independent-samples *t* test was used to compare two groups of continuous variables with normal distribution and equal variances. The Wilcoxon rank-sum test was performed to analyze continuous data with non-normal distribution. Categorical variables were tested with chi-square tests. P values < 0.05 were considered statistically significant.

Results

Patients

Twenty-two brucellosis patients were included in this study. Among them, 10 brucellosis patients fulfilled ASAS classification criteria for axial SpA, while 12 brucellosis patients fulfilled ASAS classification criteria for peripheral SpA. Eighty-eight SpA patients including 40 axial and 48 peripheral SpA patients were included with a 4:1 ratio according to the admission date. The median (IQR) time interval of admission date between each brucellosis patient and matched SpA patient was 6.00 (3.00, 14.75) days, while 4.00 (1.00, 5.75) days for axial forms and 13.00 (5.25, 18.00) days for peripheral forms.

Misdiagnosis and inappropriate treatment

All of these brucellosis patients had ever been misdiagnosed or considered as SpA before admission. Besides that, 11 of them had been misdiagnosed as other diseases for 19 times including lumbar disc herniation, synovitis or bursitis, spinal osteoarthritis, sciatica, fasciitis, osteoporosis, retroperitoneal mass, appendicitis, vasculitis, panniculitis, and rheumatoid arthritis.

Due to the misdiagnosis, 15 patients received non-steroidal anti-inflammatory drugs (NSAIDs) and 9 (60%) of them reported "good response" initially. Among 4 patients ever treated by tumor necrosis factor inhibitor (TNFi) injection (2 subcutaneous, 1 intra-articular, and 1 subcutaneous and intra-articular) before the admission to our center, no good response was observed. Moreover, increased temperature (39.0 °C) and worsened LBP were observed in 1 brucellosis patient after receiving TNFi. Surgeries were performed in 2 patients (1 bilateral shoulder joints arthroscopy and 1 exploratory laparotomy).

After admission, totally, 18 brucellosis patients received combination therapy with two or more antibiotics after admission in our center. The most frequent treatment regimen was the combination of minocycline with moxifloxacin (8 cases), etimicin (4 cases), and levofloxacin (3 cases).

Clinical manifestations

Of the 22 brucellosis patients, 16 (72.72%) were male. The mean (S.D.) age was 40.23 (16.49), ranging from 15 to 69 years. The median (IQR) disease duration was 6 (3, 17) months, ranging from 0.8 to 72 months. Of the cases, 13 (59.09%) had a contact history with livestock. More than half (12 cases, 54.55%) of the patients had disease onset from April to June in total, and another 4 (18.18%) patients had disease onset in October.

Constitutional symptoms such as fever (18 cases, 81.82%) and weight changes (9 cases, 40.91%) were observed in brucellosis patients. For patients with fever, the mean (S.D.) peak temperature was 38.75 (0.69) °C. For weight changes, 7 brucellosis patients had weight loss and 2 had weight gain.

For the involvement of the musculoskeletal system, LBP, myalgia, spinal pain, and other manifestations were observed. Among 22 brucellosis patients, all 10 (45.45%) axial brucellosis patients had current LBP and 2 peripheral brucellosis patients had past LBP. Ten (45.45%) patients had myalgia. Six (27.27%) patients had spinal pain (3 cervical, 2 lumbar, and 1 cervical and lumbar). Peripheral joints pain or swelling was detected in 20 (90.91%) patients (8 axial patients and 12 peripheral patients). Additionally, dactylitis was observed in 3 (13.64%) patients (1 metatarsophalangeal joint, 1 distal and proximal interphalangeal joints, and 1 metacarpophalangeal and proximal interphalangeal joints).

Genital system involvement was observed in 5 (22.73%) patients. Submandibular, axillary, and retroperitoneal lymphadenopathies were respectively detected in one patient.

Laboratory examinations

Only 4 (18.18%) brucellosis patients had positive blood culture results. Twenty (90.91%) brucellosis patients were GICA positive. HLA-27 tests were performed in all of these brucellosis patients after admission and none of them had positive results.

Imaging and pathological examinations

Sacroiliac joints MRI or CT of axial brucellosis patients were reviewed and analyzed. All 10 axial brucellosis patients had underwent sacroiliac joints MRI and 4 patients had underwent sacroiliac joints CT. All patients had sacroiliitis by MRI including 6 bilateral sacroiliitis and 4 unilateral sacroiliitis (3 at right and 1 at left). Except bone marrow edema, which was observed in 100% patients, bone erosion on the articular surfaces of sacroiliac joints was also observed in 9 (90%) patients through MRI and 4 (100%) patients through CT. Besides, T2-hyperintensity lesions in adjacent muscles were found in 8 (80%) patients indicating the muscle involvement. In addition, 1 patient had spondylitis and 2 patients had paravertebral cyst (see Fig. 1).

Six patients had underwent pathological examinations of sacroiliac joint (4 cases), hip (1 cases), or paravertebral cyst (1 case) (see Fig. 1). Proliferation of fibrous tissues with infiltration of lymphocytes, neutrophils, and eosinophils was found.

Comparison between brucellosis and SpA patients

Compared with axial SpA patients, the axial brucellosis patients had shorter disease duration (brucellosis, 5 months; SpA, 87 months; $P = 0.001$), lower frequencies of pain improvement with exercise (brucellosis, 20%; SpA, 80%; $P =$

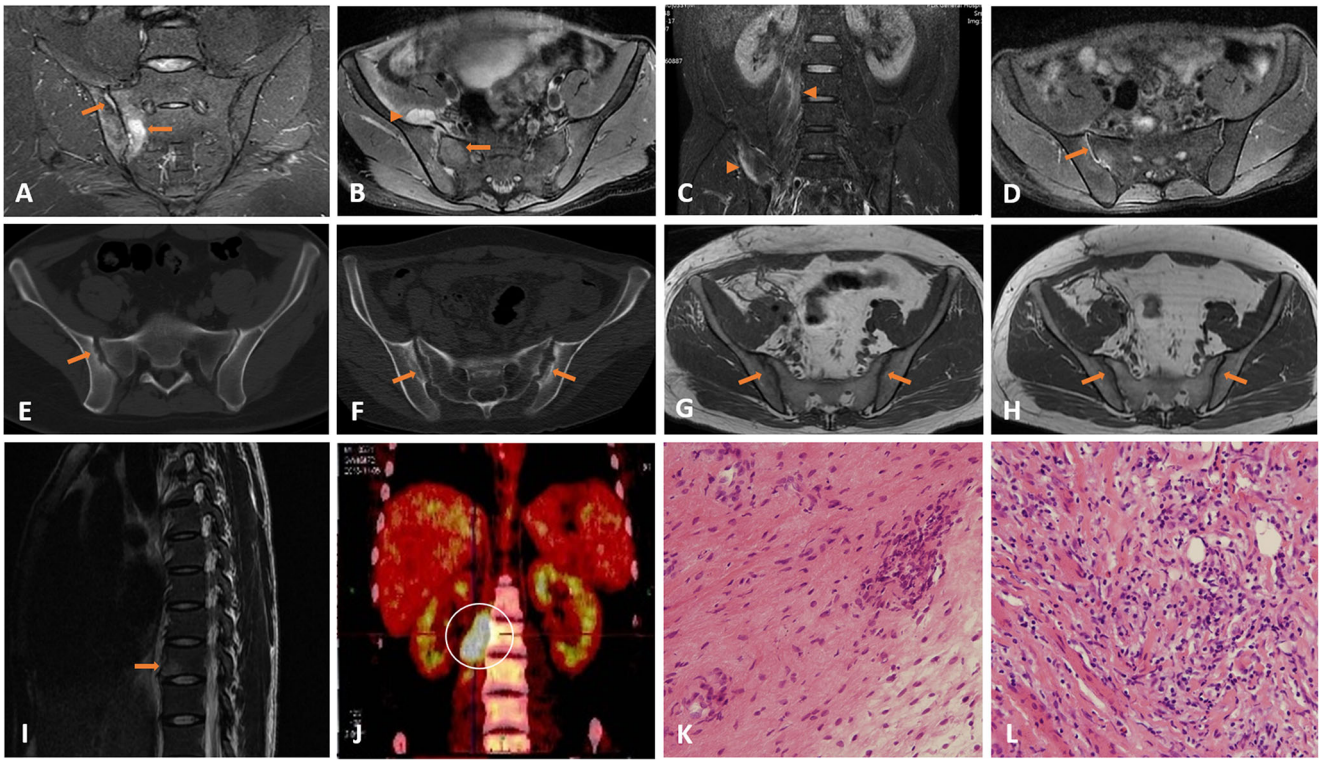

Fig. 1 Imaging and pathological examinations of brucellosis patients. **a** Heterogeneous hyperintense signal (arrow) in T2-weighted image with fat saturation indicating bone marrow edema in sacroiliac joints. **b**, **c** Involvements of sacroiliac joints (arrow) and adjacent muscles (arrow head) detected in axial (**b**) or coronal (**c**) T2-weighted images with fat saturation. **d** Synovitis in right sacroiliac joint in axial T2-weighted image with fat saturation. **e**, **f** Bone erosions on the articular surfaces in axial sacroiliac joint CT images indicating unilateral (**e**) or bilateral (**f**) sacroiliitis. **g**, **h** Axial T1-weighted images of one brucellosis patient. Bilateral sacroiliitis was observed through MRI when the patient was admitted (**g**). After receiving 2 months of antibiotics, this patient had obvious improvement in both sides of the sacroiliac joints (**h**). **i** T2-hyperintensity in the anterior corner of the vertebral body T9 indicating active spondylitis (arrow). **j** Paravertebral cyst shown in positron emission tomography–computed tomography image (circle). **k**, **l** Proliferation of fibrous tissues with infiltration of lymphocytes, neutrophils, and eosinophils sampled from right sacroiliac joint (**k**) and paravertebral cyst (**l**). **f** and **k** are from one patient. **J** and **L** are from one patient

0.001), morning stiffness (brucellosis, 20%; SpA, 70%; $P = 0.012$), good response to NSAIDs (brucellosis, 44.44%; SpA, 87.50%; $P = 0.015$), positive HLA-B27 (brucellosis, 0; SpA, 82.50%; $P < 0.001$), and anemia (brucellosis, 20.00%; SpA, 47.50%; $P = 0.044$), and had higher frequencies of myalgia (brucellosis, 60%; SpA, 7.50%; $P < 0.001$), fever (brucellosis, 90%; SpA, 20%; $P < 0.001$), and fever with chills (brucellosis, 50%; SpA, 2.50%; $P < 0.001$) (see Table 1).

Compared with the peripheral SpA patients, the peripheral brucellosis patients were younger (brucellosis, 48.33 years; SpA, 29.50 years; $P = 0.006$) and had lower frequencies of pain improvement with exercise (brucellosis, 8.33%; SpA, 56.25%; $P = 0.008$), positive HLA-B27 (brucellosis, 0; SpA, 75%; $P < 0.001$), and thrombocytosis (brucellosis, 16.67%; SpA, 58.33%; $P = 0.024$) (see Table 1).

The initial involvements of musculoskeletal system between brucellosis and SpA patients were also compared (see Fig. 2). The most common initial involvement of axial brucellosis and SpA patients was sacroiliac joints (4 cases, 40% vs 20 cases, 50%), while hip pain was the most frequent initial involvement of both peripheral brucellosis (6 cases, 50%) and SpA (17 cases, 35.42%) patients.

Discussion

In clinical practice, many brucellosis patients with the involvement of the musculoskeletal system had been sent to rheumatic centers, and a great proportion of brucellosis patients could be misdiagnosed as inflammatory arthritis, including SpA [16]. In our study, the features of 22 brucellosis patients fulfilling the ASAS classification criteria for SpA were described in clinical manifestations and laboratory and imaging examinations, as well as being compared with those of 88 SpA patients. As a result, some indicators were found to be helpful in distinguishing these brucellosis patients from patients with SpA.

These brucellosis patients included in our study had been previously misdiagnosed or considered as SpA before admission to our center. By analyzing, we found that many

Table 1 Comparison between brucellosis patients fulling ASAS classification criteria for SpA and SpA patients

Parameters	Axial brucellosis ($N = 10$)	Axial SpA ($N = 40$)	P	Peripheral brucellosis ($N = 12$)	Peripheral SpA ($N = 48$)	P
Male, *n* (%)	8 (80)	31 (77.50)	> 0.999	8 (66.67)	33 (68.75)	> 0.999
Age, years, mean (S.D.)	30.50 (13.21)	30.00 (22.25, 41.75)	0.437	48.33 (14.78)	29.50 (20.00, 48.00)	*0.006*
Duration, months, median (IQR)	5 (3.00, 9.50)	87 (38, 144)	*0.001*	10 (3.25, 34.25)	36.00 (3.50, 94.75)	0.108
Fever, *n* (%)	9 (90.00)	8 (20.00)	*< 0.001*	9 (75.00)	21 (43.75)	0.107
Fever with chill, *n* (%)	5 (50.00)	1 (2.50)	*< 0.001*	4 (33.33)	5 (10.42)	0.124
LBP, *n* (%)	10 (100)	40 (100)	NA	2* (16.67)	11* (22.92)	0.938
Spinal pain, *n* (%)	1 (10.00)	20 (50)	0.053	5 (41.67)	7 (14.58)	0.09
Peripheral arthritis, *n* (%)	8 (80.00)	31 (77.50)	> 0.999	12 (100)	48 (100)	NA
Dactylitis, *n* (%)	2 (20.00)	5 (12.50)	0.919	2 (16.67)	15 (31.25)	0.519
Achilles tendinitis, *n* (%)	1 (10.00)	11 (27.50)	0.456	2 (16.67)	15 (31.25)	0.519
Myalgia, *n* (%)	6 (60.00)	3 (7.50)	*< 0.001*	4 (33.33)	4 (8.33)	0.071
Pain at night, *n* (%)	6 (60.00)	24 (60.00)	> 0.999	1 (8.33)	15 (31.25)	0.215
Improved by exercise, *n* (%)	2 (20.00)	32 (80.00)	*0.001*	1 (8.33)	27 (56.25)	*0.008*
Morning stiffness, *n* (%)	2 (20.00)	28 (70.00)	*0.012*	3 (25)	20 (41.67)	0.465
Sacroiliitis, *n* (%)	10 (100)	40 (100)	NA	2 (16.67)	25 (52.08)	0.06
NSAIDs effective, *n* (%)	4/9** (44.44)	35 (87.50)	*0.015*	5/6** (83.33)	38 (79.17)	> 0.999
Anemia, *n* (%)	2 (20.00)	19 (47.50)	*0.044*	5 (41.67)	33 (68.75)	0.16
Leukocytosis ($> 10 \times 10^9$/L), *n* (%)	1 (10.00)	6 (15.00)	> 0.999	0	8 (16.67)	0.296
Thrombocytosis (> 300 × 109/L), *n* (%)	2 (20.00)	17 (42.50)	0.344	2 (16.67)	28 (58.33)	*0.024*
HLA-B27 positive, *n* (%)	0	33 (82.50)	*< 0.001*	0	36 (75.00)	*< 0.001*
Elevated CRP (> 0.8 mg/dl), *n* (%)	7 (70.00)	30/ 39*** (76.92)	0.966	6 (50.00)	30 (62.50)	0.645
Elevated ESR (> 20 mm/h), *n* (%)	6/9*** (66.67)	22/39*** (56.41)	0.851	2/10*** (20.00)	25/47*** (53.19)	0.119

*Past LBP

**Not all patients received NSAIDs

***Not all patients tested with CRP or ESR

NSAIDs: non-steroidal anti-inflammatory drugs; NA: not available; LBP: low back pain; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate. Data with significant differences ($P < 0.05$) were presented in italics

features included in the ASAS classification criteria for axial or peripheral SpA can be detected in brucellosis patients. The age at onset (for axial forms) and gender distribution were very similar between our brucellosis patients and SpA patients. Moreover, brucellosis patients can also have LBP and peripheral arthritis. And, most

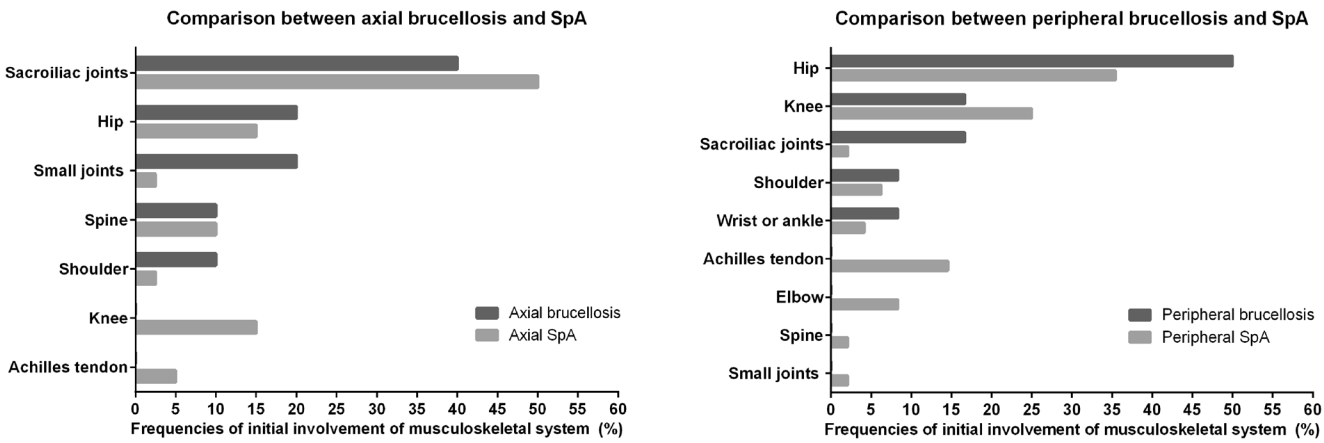

Fig. 2 Comparisons of initial involvement of the musculoskeletal system between axial or peripheral brucellosis and spondyloarthritis (SpA) patients. Small joints refer to the metacarpophalangeal, metatarsophalangeal, and interphalangeal joints

importantly, bone marrow edema and bone erosions in sacroiliac joints were frequently observed in MRI. Therefore, brucellosis can fulfill the ASAS classification criteria for SpA, which is posing a challenge for rheumatologists to differentiate these two diseases.

The improper treatment caused by misdiagnosis may lead to the disease progression. In our study, more than two-thirds (68.18%, 15/22) of the brucellosis patients had been treated with NSAIDs, and 6 of them had received TNFi or surgeries in total. For 8 brucellosis patients with good response to NSAIDs, the misdiagnosis will present continually, and for those without good response, TNFi may be prescribed erroneously. Both of these two situations can lead to treatment delay and even disease exacerbation. Therefore, it is important to find out clues to identify these brucellosis patients from SpA patients.

With comparison, some clues were found and caution was needed when diagnosing SpA even when they could fulfill the ASAS classification criteria. The average disease duration of brucellosis patients was shorter than that of SpA patients, especially for the axial forms (5 months vs 87 months, $P = 0.001$). The contact history with livestock presented in more than half (59.09%) of our brucellosis patients and more brucellosis patients had fever (axial, $P < 0.001$; peripheral, $P = 0.107$) which can remind the physicians considering the diagnosis of brucellosis. Both of the brucellosis patients and SpA patients could have inflammatory LBP; however, the LBP of brucellosis patients was generally less improved with exercise presented as persistent LBP, and the LBP was more intense with the higher rate of walking difficulties. Myalgia was another major musculoskeletal manifestation and presented in nearly half (45.45%) of the brucellosis patients (axial, $P < 0.001$; peripheral, $P = 0.071$). Additionally, none of the brucellosis patients had positive HLA-B27.

After primary judgment based on the above clinical manifestations, further specific tests must be performed before making diagnosis. Since the sensitivity of blood culture was low (18.2%) as *Brucella* from blood could only be detected at an early stage of brucellosis [20, 21], and the blood culture procedures were time-consuming (often takes up to 4 weeks) [22], indirect evidences obtained through serological tests, such as GICA, standard tube agglutination, Rose Bengal test, Coombs' test, and ELISA, were introduced. In our center, GICA was performed and 20 of 22 (90.9%) brucellosis patients were positive.

Based on the results of serological tests, MRI could further help distinguish brucellosis from SpA, but comprehensive interpretation not only bone marrow edema should be stressed. Although, bone marrow edema indicating sacroiliitis by MRI has been introduced as a key diagnostic index in the ASAS classification criteria for SpA, it is not a specific finding for SpA and can be secondary to inflammation, degenerative disorders, infection, or malignancy [23–25]. Misdiagnosed cases of SpA due to the introduction of sacroiliitis by MRI had been mentioned in several articles, including cases with infectious arthritis, neoplastic diseases, and fibromyalgia syndrome [26, 27]. In our study, all axial brucellosis patients were detected with bone marrow edema in sacroiliac joints, and the bone erosions were also frequently observed. However, compared with the general sacroiliac joints MRI features of SpA [28], the bone marrow edema of brucellosis was characterized with higher T2-hyperintensity and usually with the presence of crossing of anatomical border (adjacent muscles involvement). Moreover, it seems that the backfill occurred quickly after the treatment of antibiotics (seen in Fig. 1). The presence of paravertebral cyst may also help to distinguish brucellosis from SpA.

In our study, we discussed the condition that brucellosis can mimic SpA, while, in the clinical practice, brucellosis can also accompany with SpA. In our study, all brucellosis patients had negative HLA-B27 and good response to antibiotics, which can furtherly confirm these brucellosis patients had no company with SpA. However, this condition still needs to be stressed as several articles revealed that brucellosis occurred during the management of SpA and few of them can mimic an exacerbation of SpA [29–31]. Therefore, brucellosis should be considered in the differential diagnosis when new symptoms or worsening of the symptoms occur during the management of SpA. These symptoms could disappear after the treatment of antibiotics.

In our study, the retrospective nature made it difficult to ensure the data integrity; hence, some frequencies may be underestimated. Moreover, the hospitalized patients with a small sample size were incapable of representing the whole population of brucellosis patients. Additionally, GICA was not performed in the patients with SpA because that brucellosis was a relatively rare infection in the clinical practice and was not regularly screened in the management of SpA. The strength of our study is in being the good comparability between brucellosis and SpA patients: (a) all brucellosis patients were included with the reference of the ASAS classification criteria for SpA; and (b) axial and peripheral SpA patients were respectively matched with brucellosis patients according to the admission date.

Conclusions

Indicators including disease duration, contact history of livestock, features of LBP, presence of myalgia, fever, or HLA-B27 negativity can remind the rheumatologists to think of other disorders rather than SpA. Furtherly, results of specific serological tests, such as GICA test, and comprehensive interpretation of sacroiliac joints MRI can help confirm the diagnosis of brucellosis.

Funding This work were supported by the Key Projects in the National Science & Technology Pillar Program during the Twelfth Five-year Plan Period (2014BAI07B05) and the National Basic Research Program of China (973 program) (2014CB541806).

Compliance with ethical standards

This study was approved by the Ethics Committee at Chinese PLA General Hospital (S2016-049-02).

Disclosures None.

References

1. Garg N, van den Bosch F, Deodhar A (2014) The concept of spondyloarthritis: where are we now? Best Pract Res Clin Rheumatol 28:663–672
2. Rudwaleit M, van der Heijde D, Landewe R, Listing J, Akkoc N, Brandt J, Braun J, Chou CT, Collantes-Estevez E, Dougados M, Huang F, Gu J, Khan MA, Kirazli Y, Maksymowych WP, Mielants H, Sorensen IJ, Ozgocmen S, Roussou E, Valle-Onate R, Weber U, Wei J, Sieper J (2009) The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis 68:777–783
3. Rudwaleit M, van der Heijde D, Landewe R, Akkoc N, Brandt J, Chou CT, Dougados M, Huang F, Gu J, Kirazli Y, Van den Bosch F, Olivieri I, Roussou E, Scarpato S, Sorensen IJ, Valle-Onate R, Weber U, Wei J, Sieper J (2011) The Assessment of SpondyloArthritis international Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis 70:25–31
4. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV (2006) The new global map of human brucellosis. Lancet Infect Dis 6:91–99
5. Pappas G, Akritidis N, Bosilkovski M, Tsianos E (2005) Brucellosis. N Engl J Med 352:2325–2336
6. Norman FF, Monge-Maillo B, Chamorro-Tojeiro S, Perez-Molina JA, Lopez-Velez R (2016) Imported brucellosis: a case series and literature review. Travel Med Infect Dis 14:182–199
7. Dean AS, Crump L, Greter H, Schelling E, Zinsstag J (2012) Global burden of human brucellosis: a systematic review of disease frequency. PLoS Negl Trop Dis 6:e1865
8. Buzgan T, Karahocagil MK, Irmak H, Baran AI, Karsen H, Evirgen O, Akdeniz H (2010) Clinical manifestations and complications in 1028 cases of brucellosis: a retrospective evaluation and review of the literature. Int J Infect Dis 14:e469–e478
9. Turan H, Serefhanoglu K, Karadeli E, Togan T, Arslan H (2011) Osteoarticular involvement among 202 brucellosis cases identified in Central Anatolia region of Turkey. Intern Med 50:421–428
10. Mermut G, Ozgenc O, Avci M, Olut AI, Oktem E, Genc VE, Ari A, Coskuner SA (2012) Clinical, diagnostic and therapeutic approaches to complications of brucellosis: an experience of 12 years. Med Princ Pract 21:46–50
11. Guler S, Kokoglu OF, Ucmak H, Gul M, Ozden S, Ozkan F (2014) Human brucellosis in Turkey: different clinical presentations. J Infect Dev Ctries 8:581–588
12. Kazak E, Akalin H, Yilmaz E, Heper Y, Mistik R, Sinirtas M, Ozakin C, Goral G, Helvaci S (2016) Brucellosis: a retrospective evaluation of 164 cases. Singap Med J 57:624–629
13. Ebrahimpour S, Bayani M, Moulana Z, Hasanjani Roushan MR (2017) Skeletal complications of brucellosis: a study of 464 cases in Babol, Iran. Caspian J Intern Med 8:44–48
14. Jia B, Zhang F, Lu Y, Zhang W, Li J, Zhang Y, Ding J (2017) The clinical features of 590 patients with brucellosis in Xinjiang, China with the emphasis on the treatment of complications. PLoS Negl Trop Dis 11:e0005577
15. Dean AS, Crump L, Greter H, Hattendorf J, Schelling E, Zinsstag J (2012) Clinical manifestations of human brucellosis: a systematic review and meta-analysis. PLoS Negl Trop Dis 6:e1929
16. Ye C, Shen GF, Li SX, Dong LL, Yu YK, Tu W, Zhu YZ, Hu SX (2016) Human brucellosis mimicking axial spondyloarthritis: a challenge for rheumatologists when applying the 2009 ASAS criteria. J Huazhong Univ Sci Technolog Med Sci 36:368–371
17. Sieper J, van der Heijde D, Landewe R, Brandt J, Burgos-Vagas R, Collantes-Estevez E, Dijkmans B, Dougados M, Khan MA, Leirisalo-Repo M, van der Linden S, Maksymowych WP, Mielants H, Olivieri I, Rudwaleit M (2009) New criteria for inflammatory back pain in patients with chronic back pain: a real patient exercise by experts from the Assessment of SpondyloArthritis international Society (ASAS). Ann Rheum Dis 68:784–788
18. van der Linden S, Valkenburg HA, Cats A (1984) Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 27:361–368
19. Beutler E, Waalen J (2006) The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? Blood 107:1747–1750
20. Memish Z, Mah MW, Al Mahmoud S, Al Shaalan M, Khan MY (2000) Brucella bacteraemia: clinical and laboratory observations in 160 patients. J Inf Secur 40:59–63
21. Ulu-Kilic A, Metan G, Alp E (2013) Clinical presentations and diagnosis of brucellosis. Recent Pat Antiinfect Drug Discov 8:34–41
22. Yagupsky P (1999) Detection of *Brucellae* in blood cultures. J Clin Microbiol 37:3437–3442
23. Rudwaleit M, Jurik AG, Hermann KG, Landewe R, van der Heijde D, Baraliakos X, Marzo-Ortega H, Ostergaard M, Braun J, Sieper J (2009) Defining active sacroiliitis on magnetic resonance imaging (MRI) for classification of axial spondyloarthritis: a consensual approach by the ASAS/OMERACT MRI group. Ann Rheum Dis 68:1520–1527
24. Patel S (2014) Primary bone marrow oedema syndromes. Rheumatology (Oxford) 53:785–792
25. Eshed I, Lidar M (2017) MRI findings of the sacroiliac joints in patients with low back pain: alternative diagnosis to inflammatory sacroiliitis. Isr Med Assoc J 19:666–669
26. Jin DE, Zhao LD, Yan XP, Hao DL, Liu J, Zhao Y (2013) The re-evaluation of 140 patients diagnosed as ankylosing spondylitis and nonradiographic axial spondyloarthritis. Zhonghua Nei Ke Za Zhi 52:920–923
27. Zhao Z, Wang Y, Jin J, Deng X, Huang F (2014) An analysis of abnormal magnetic resonance imaging of sacroiliac joints in patients misdiagnosed as spondyloarthritis. Zhonghua Nei Ke Za Zhi 53:724–729
28. Baraliakos X (2017) Imaging in axial spondyloarthritis. Isr Med Assoc J 19:712–718

29. Garip Y, Eser F, Erten S, Yilmaz O, Yildirim P (2014) Brucellosis in spondyloarthritis mimicking an exacerbation. Acta Reumatol Port 39:351–352
30. Ozgocmen S, Ardicoglu A, Kocakoc E, Kiris A, Ardicoglu O (2001) Paravertebral abscess formation due to brucellosis in a patient with ankylosing spondylitis. Joint Bone Spine 68:521–524
31. Papagoras CE, Argyropoulou MI, Voulgari PV, Vrabie I, Zikou AK, Drosos AA (2009) A case of *Brucella* spondylitis in a patient with psoriatic arthritis receiving infliximab. Clin Exp Rheumatol 27: 124–127