Hepatosplenic brucella abscesses on computed tomography and magnetic resonance imaging
Case series
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Abstract
Introduction: Because of its infrequent and the lack of clinical data and image finding, the management of acute infections with the hepatosplenic brucella abscesses is challenging.

Methods: There were 10 serologically diagnosed cases with this brucella infection. All patients had fever, 50% patients had upper abdominal pain. Ninety percent patients lived in an urban environment. The localization of lesions included: 30% hepatosplenic, 30% liver, and 40% spleen.

Results: Abdominal computed tomography (CT) scans and magnetic resonance imaging (MRI) demonstrated hepatosplenomegaly, with multiple small abscess lesions of various sizes in the acute stage of brucellosis, with the largest diameter of 1.5 cm in the liver. After contrast-enhanced CT and MRI findings, the arterial phase in which the enhancing area of lesions was thick, revealed multifocal hypodense or hypointense lesions of various sizes. These lesions manifested distinct boundary, which was intensified obviously in portal venous phase.

Conclusion: Our results indicate that early CT or MRI dynamic contrast enhancement of suspected cases could improve rapid diagnosis. However, diagnostic criteria remain problematic and diagnosis is mostly based on a combination of clinical suspicion, serologic markers, and radiologic findings.

Abbreviations: CBC = complete blood count, CRP = C-reactive protein, CT = computed tomography, ESR = erythrocyte sedimentation rate, MRI = magnetic resonance imaging, RBT = rose Bengal Test, SAT = standard agglutination test.

Keywords: abscess, brucellosis, imaging features, liver, spleen

1. Introduction
Brucellosis may occur in almost any organ or system of the human body, by far the most common sites of localization being osteoarticular systems. The other less common complications affect genitourinary, respiratory, cardiovascular, and central nervous systems. Although diffuse involvement of liver and spleen is frequently seen in human cases, hepatosplenic abscesses are rare.

This was partly because of the difficulty in making the diagnosis without imaging techniques such as those available today. The pattern of complications depends on the strain of Brucella, and complicated cases that are admitted to the hospitals.

Because of its rare and protean presentation and the lack of clinical data and image finding, the management of acute infections with hepatosplenic brucella abscesses is challenging. There were 10 serologically diagnosed cases with this hepatosplenic brucella abscesses in China, Xinjiang.

2. Methods
We conducted a retrospective and descriptive study in the First Affiliated Hospital of Xinjiang Medical University Between January 1, 2007 and December 31, 2016. 10 new cases of hepatosplenic brucella abscesses were admitted during the study period. Ethical approval for the study was obtained from the Ethical Review Committee of the First Affiliated Hospital of Xinjiang Medical University (No.20170214-111). All participants provided written informed consent, and the procedures were performed as per the guidelines of Declaration of Helsinki 2013. All cases which diagnosed by culture were negative was not performed molecular methodology. All cases were serologically diagnosed by Standard agglutination test (SAT) and rose Bengal test (RBT). The diagnostic criteria were clinical findings in accordance with SAT ≥1/160 with brucellosis. The diagnostic criteria was the positive results of RBT.

The laboratory tests for these patients included complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), globulin, procalcitonin, albumin, red cell distribution widt, hematokrit, hemoglobin, platelet count, leucocyte count, mononuclear cell, neutrophil, lymphocyte, red blood cell count, platelet distribution width.

Computed tomography (CT) images were obtained using a 64-slice Spiral CT system (Light speed VCT; GE Healthcare, United
Table 1
Summary of demographic and clinic characteristics patients (n=10) with hepatosplenic brucella abscesses.

| Case No. | Sex | Age  | Ethnicity | RBT | SAT | Symptoms                  | Temperature | Duration of symptoms | Location | Treatment (w) |
|---------|-----|------|-----------|-----|-----|---------------------------|-------------|----------------------|----------|---------------|
| 1       | M   | 29   | Uighurs   | +   | 1:160 | Fever+abdominal pain       | 40°C        | 2W                  | Liver + spleen | 12             |
| 2       | F   | 47   | Kazak     | +   | 1:160 | Fever+abdominal pain       | 39°C        | 1W                  | Liver + spleen | 10             |
| 3       | M   | 58   | Xibo      | +   | 1:320 | Fever                     | 41°C        | 3W                  | Liver + spleen | 11             |
| 4       | F   | 63   | Uighurs   | +   | 1:160 | Fever                     | 40.5°C      | 5W                  | Liver        | 14             |
| 5       | M   | 79   | Han       | +   | 1:400 | Fever+abdominal pain       | 39.5°C      | 2W                  | Liver        | 19             |
| 6       | M   | 49   | Han       | +   | 1:320 | Fever                     | 40°C        | 3W                  | Liver        | 15             |
| 7       | F   | 48   | Xibo      | +   | 1:160 | Fever                     | 38.5°C      | 4W                  | Spleen       | 17             |
| 8       | M   | 58   | Han       | +   | 1:320 | Fever+abdominal pain       | 41°C        | 3W                  | Spleen       | 18             |
| 9       | M   | 56   | Han       | +   | 1:160 | Fever+abdominal pain       | 39°C        | 7W                  | Spleen       | 20             |
| 10      | F   | 17   | Uighurs   | +   | 1:160 | Fever+abdominal pain       | 41°C        | 2W                  | Spleen       | 17             |

+ = positive, F = False, M = Male, RBT = rose Bengal test, SAT = standard agglutination test.

3. Results

3.1. Demographic, epidemiological, and clinical variables
We identified 10 hepatosplenic brucella abscess cases during the study period. Six patients were men and 4 women. Mean age was 50 years (range: 17–79 years). Nine patients came from rural areas (90%). Other relevant clinical data are shown in Table 1. The duration of the symptoms before diagnosis was 2.2 ± 3.5 weeks (range: 1–7 weeks). All the patients had fever for 38.5°C to 41°C (average 40°C), either continuously or intermittently, during the course of the disease. The presentation in 5 patients had abdominal pain of varying duration.

3.2. Laboratory studies
Before treatment, all cases were serologically diagnosed by SAT and RBT, and 6 cases were performed by brucella culture test. The results were negative for 6 patients in brucella culture test, and positive for all patients in RBT. The SAT result 1/160 accounted for 30.0%, 1/320 accounted for 10.0%, and RBT, and 6 cases were performed by brucella culture test. The results were negative for 6 patients in brucella culture test, and positive for all patients in RBT. The SAT result 1/160 accounted for 60.0%, 1/320 accounted for 30.0%, 1/400 accounted for 10.0%. Serological test results in blood are detailed in Table 1. Before treatment, the laboratory data are shown in Table 2.

Table 2
Laboratory findings of hepatosplenic brucella abscesses.

| Parameters                  | Mean ± SD  | Range      | High  | Normal (n) | Low (n) |
|-----------------------------|------------|------------|-------|------------|--------|
| Leukocyte count, K/µL       | 5.33 ± 2.59| 2.50–8.93  | 0     | 6          | 4      |
| Neutrophil, 10³/µL          | 3.66 ± 2.12| 1.54–6.99  | 2     | 4          | 4      |
| Lymphocyte, 10³/µL          | 1.50 ± 0.99| 0.60–4.19  | 1     | 5          | 4      |
| Mononuclear cell            | 0.34 ± 0.17| 0.07–0.54  | 0     | 9          | 1      |
| Red blood cell count        | 3.91 ± 0.89| 2.65–5.12  | 2     | 4          | 4      |
| Hemoglobin, g/dL            | 111.40 ± 20.03| 73.00–140.00| 0   | 2          | 8      |
| HCT (hematocrit)            | 0.33 ± 0.06| 0.22–0.42  | 0     | 1          | 9      |
| Platelet count, K/µL        | 126.80 ± 71.60| 23.00–229.00| 0   | 5          | 5      |
| Thrombocytocrit             | 0.13 ± 0.08| 0.02–0.25  | 0     | 5          | 5      |
| Procalcitonin               | 1.32 ± 2.46| 0.12–8.27  | 8     | 2          | 0      |
| Total protein               | 66.17 ± 4.91| 58.80–74.76| 2     | 8          | 0      |
| Albumin                     | 29.15 ± 4.97| 22.12–35.12| 0     | 3          | 7      |
| Globulin                    | 36.99 ± 5.59| 26.64–45.00| 7     | 3          | 0      |
| PDW,%                       | 13.84 ± 4.13| 8.00–18.40 | 1     | 5          | 4      |
| RDW,%                       | 14.91 ± 2.87| 12.70–20.90| 3     | 7          | 0      |
| CRP, mg/L                   | 36.28 ± 40.57| 7.30–127.00| 10   | 0          | 0      |
| ESR, mm/h                   | 42.40 ± 27.95| 10.00–90.00| 10   | 0          | 0      |

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, PDW = platelet distribution width, RDW = red cell distribution width, SD = standard deviation.
lesions, 2 liver lesions, and 2 spleen lesions with multifocal hypodense lesions of various sizes. The venous phase of enhanced CT revealed multifocal hypodense lesions of various sizes, with the largest diameter of 1.5 cm in the liver (Case 1, Fig. 1A). The enhancing area of majority lesions was thick in the arterial phase (Case 1, Fig. 1B). These lesions manifested distinct boundary, which was intensified obviously in portal venous phase. Table 3 showed that there were more lesions in contrast-enhanced CT scans when compared to CT scans. The localization of lesions included: 30% hepatosplenic, 30% liver, and 40% spleen.

Only 2 of all cases were studied with MRI scanning. One case showed 12 lesions in liver and 5 lesions in spleen with a hyperintense signal on T2-weighted images (Case 1, Fig. 1C). After contrast-enhanced MRI findings, there were 18 small lesions in liver and 8 lesions in spleen with the largest diameter 1.5 cm of various sizes. There were 13 lesions in liver and 6 lesions in spleen which manifested thick (≥3–5 mm) wall edge reinforcement with a hypointense signal on T1-weighted images. Enhanced MRI had 8 lesions and 6 thick wall (≥3–5 mm) edge reinforcement, with the largest diameter of not >1 cm. Two cases demonstrated hepatosplenomegaly multiple lesions with a hyperintense signal on diffusion-weighted images (Case 1, Fig. 1E).

### 3.4. Treatment and follow-up

The specific treatment time was shown in Table 1. On the 10 to 20 weeks (average 15.3 weeks) of the treatment with a combination of doxycycline and rifampicin, clinical condition of all patients improved gradually and all the lesions disappeared by the end of treatment on follow-up 8 cases ultrasound and 2 cases CT examinations (Case 9, Fig. 2A and B). The patients remained asymptomatic without any signs or symptoms of disease recurrence at 1 year after the completion of treatment, all patients were no >1/160 results of SAT, and all patients were the negative results of RBT.

### 4. Discussion

Brucellosis is a multisystemic disease; all systems and organs can be affected by the complications.[8] The disease is epidemic in North China, and particularly in Xinjiang. Hepatosplenic brucella abscesses result from the caseous necrosis of granulomatous tissue that is induced by persistent brucella in macrophages.[9] It is a remarkably rare complication,[10] and the incidence of this illness ranges worldwide from 2% to 3%.[11,12]

In recent years, with the development of China’s animal husbandry and tourism industries, the incidence of this illness in China is increasing, and patients and doctors should be caused the attention.

The mean age of the patients was 50 years (range 17–79 years) and 60% were men. Similar findings had also been reported by Mesut Yilmaz.[13] Ninety percent came from rural areas. Hepatic and/or splenic involvement during the course of brucellosis was very common and presents with hepatospleno-megaly. Hepatic and splenic involvement in patients affected by brucellosis is usually asymptomatic, although it was almost constant and diffuse, owing to the crucial role of these organs in defending against Brucella infections.[14] In this study, all patients had a prolonged fever, and the body temperature was 38.5°C to 41°C (average 40°C). Similar study had also been reported by Erdem et al.[11] Five of all patients had abdominal pain. The study by Ibis et al.[15] was similar with ours. As a multisystem disease, brucellosis can often be a diagnostic dilemma as the disease was associated with a wide variety of signs and symptoms. Our
patient had a duration of symptoms of average 2.2 weeks (ranged from 1 to 7 weeks) on presentation.

Most scholars believed that blood culture was the criterion standard for the diagnosis of brucellosis. However, in clinical practice, brucellosis culture required a long incubation period and specific conditions. In addition, brucellosis culture did not always produce a positive bacterial culture, making it unsuitable to serve as a conventional detection method. Negative bacterial cultures were obtained for 6 of the 10 patients with diagnosed hepatosplenic brucella abscesses. Therefore, in the absence of bacteriologic confirmation, positive serology for brucella to be SAT result ≥1/160 was needed for definite diagnosis.\textsuperscript{[5,6]} In this study, SAT result was 1/160 or higher. Blood serums for Brucella detection were performed for all patients and the results of RBT were positive.

Increases in CRP and ESR levels would also occur in these patients. In this study, the CRP levels ranged from 7.30 to 127.00 mg/dL (average 36.28 mg/dL), and the ESR ranged from 10 to 96 mm/h (average 42.4 mm/h). However, increased CRP and ESR were observed in all case reports, which may represent a useful measure for assessing the response to therapy. The constant presence of an elevated ESR and/or elevated levels of and CRP suggested the existence of an active, focal inflammatory process. Routine laboratory findings in brucellosis were not usually diagnostic that may include anemia, leukopenia, pancytopenia, thrombocytopenia, and mild-to-moderate elevation of liver...
function tests.[6,16] There were fewer laboratory tests on hepatosplenic brucella abscesses. In the present study of 10 patients with brucellosis, the ESR and CRP levels of all patients increased, globulin of 80.0% patients increased, procalcitonin of 70.0% patients increased, red cell distribution width of 30.0% patients increased; hematokrit of 90.0% patients decreased, hemoglobin of 80.0% patients decreased, albumin of 70.0% patients decreased, platelet count of 50.0% patients decreased; 40.0% patients decreased including to leukocyte count, neutrophil, lymphocyte, red blood cell count, and platelet distribution width.

Imaging played an important role in identifying the liver and/or spleen lesion usually some time after the primary infection and in a clinical feature that was generally poor. CT and MRI had also been used in the diagnostic workup of a brucellar abscess.\[15,17]\n
The CT evaluation provided further information about the exact location and extension of the lesion. However, owing to the small lesion, CT scan may show no abnormalities. In this study, we encountered 3 cases. Enhanced CT revealed multiple hypodense nodules representing small abscesses in the hepatic and/or parenchyma in the acute stage of brucellosis. The localization of lesions was 30% hepatosplenic, 30% liver, and 40% spleen. Multiple smaller abscesses frequently involved the spleen. In this study, CT scan revealed multiple hypodense nodules or normal in the hepatic and/or splenic parenchyma. The venous phase of enhanced CT revealed multifocal hypodense lesions of various sizes, with the largest diameter of 1.5 cm in the liver in the acute stage of brucellosis. The enhancing area of lesions was thick in the arterial phase. These lesions manifested distinct boundary, which was intensified obviously in portal venous phase, whereby it was suggested that CT contrast enhancement scan may improve the detection rate. Heller et al\[18\] studied the report was similar with our findings. In this study, all brucellosis patients were acute and multiple abscess. Two similar findings had also been reported by others.\[19,20\] Solitary abscess had calcification, but multiple smaller abscesses showed few calcifications.\[18\] Our study reported CT examination showed no calcification with multiple smaller abscesses in the spleen or liver. Similar findings had also been reported by others.\[19,21\]

MRI is extremely sensitive tool with which to diagnosis early liver and spleen infections, and it should be considered as a way of early detection. Multiple small abscesses may be present, and hepatosplenic involvement was also possible. In this study, MRI showed elements similar to pyogenic hepatic and splenic abscess including a group of cystic lesions of various sizes with a hypointense signal on T1-weighted images and a hyperintense signal on T2-weighted images.\[22\] Because of dispersion constraints, multiple small abscess lesions manifested a hyperintense signal on diffusion-weighted images. In addition to case 1, all lesions was found the largest diameter of no >1.5 cm. Similar findings have also been reported by Yilmaza et al and Heller et al.\[15,18\] After contrast-enhanced MRI findings, the walls during the arterial phase persisted during the delayed phase as well as enhancement of the adjacent liver parenchyma during the arterial phase because of inflammation. A hypovascular area peripheral to the abscess was observed in some cases and may represent edema or decreased venous perfusion. They manifested thick wall edge reinforcement of majority lesions in liver and spleen with a hypointense signal on T1-weighted images. This study also noticed that in the arterial phase, the enhancing area was thick (≈3–5 mm), a finding that could be related to the type of host inflammatory response to a brucellar infection. Peripheral enhancement can be seen after intravenous administration of gadolinium. These findings were similar to those described for CT. The contrast-enhanced scans revealed more number of lesions than CT or MRI scan.

Hepatosplenic brucella abscesses often needed to be differentiated from hepatosplenic military tuberculosis, pyogenic abscesses, hepatosplenic cyst and hepatosplenic metastases. The image of hepatosplenic military tuberculosis was similar to that of hepatosplenic brucella abscesses, but it was characterized by low fever and night sweats, and the brucellosis was high fever. Contrast-enhanced MRI findings in pyogenic abscesses had been described previously. Typical pyogenic abscesses appeared as partially enhancing lesions with a rim of marked enhancement and a persistently hypointense center. Wash-out was seen in the portal phase. Hepatosplenic cyst had no inflammatory response, and MRI was diffused as low signal. Hepatosplenic metastases generally had primary lesions, and metastases were generally larger.

In the acute phase, hepatosplenic brucella abscess achieved good therapeutic outcomes with drug treatment.\[23\] In this study, all patients received conservative drug treatment consisting of a combination 10 to 20 weeks regimen of doxycycline and rifampicin. The best therapeutic approach for hepatosplenic
abscess because of brucella was not clearly established. However, this modality appeared to be successful only in the early stages of the disease when there was no calcification in the lesions.\textsuperscript{[13,23]} As all patients had acute brucellosis and no calcification, they responded well to the standard duration 12 weeks of treatment. However, follow-up at 12 months revealed no recurrence.

5. Study limitations

This study had several limitations. In the first place, a small number of patients was included. There was 1 more point: none of the patients underwent biopsy. Lastly, further studies with more patients were needed to confirm our findings.

6. Conclusions

In conclusion, with the increased availability of cross-sectional imaging techniques, reports become more frequent. CT or MRI contrast enhancement may be used to better characterize a brucellar multiple small abscesses and help differentiate it from other hepatic disease, and MRI may be more superior to CT scan. Our results indicate that early CT or MRI contrast enhancement of suspected cases could improve rapid diagnosis. However, diagnostic criteria remain problematic and diagnosis is mostly based on a combination of clinical suspicion, serologic markers, and radiologic findings.

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