BMC Infectious Diseases

CASE REPORT

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# *Brucella* bloodstream infection mimicking systemic juvenile idiopathic arthritis: a pediatric case report

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## Abstract

**Background** Systemic juvenile idiopathic arthritis (sJIA) accompanied with *Brucella* bloodstream and bone marrow infection is an exceedingly rare occurrence in clinical practice. Owing to the striking similarity in their clinical presentations, there is a propensity for misdiagnosis or underdiagnosis.

**Case presentation** In this case, the pediatric patient underwent medical treatment across five different hospitals over a three-month period before receiving an accurate diagnosis and successful treatment. There are two primary factors contributing to this consequence. To begin with, *Brucella* exhibits slow growth, leading to initial blood cultures producing false negative results due to insufficient cultivation time. Additionally, sJIA and brucellosis present extremely similar clinical symptoms. In addition to arthritis, the child presented with a non-fixed erythematous rash that gradually resolved after fever subsided and was associated with increased IL-6 levels. Furthermore, both blood and bone marrow cultures displayed positive results after four days, and *Brucella* was identified through MALDI-TOF mass spectrometry. Combined with additional laboratory results and clinical symptoms, sJIA accompanied with *Brucella* bloodstream infection was ultimately diagnosed and effectively managed in our hospital.

**Conclusion** It is crucial to emphasize that in cases of brucellosis infection, the identification of sJIA and brucellosis is of vital significance. *Brucella* can be isolated and cultured from blood and bone marrow within approximately two weeks, serving as the definitive indicator for diagnosing *Brucella* bloodstream infection. By reporting this case, we aim to share clinical experience, provide a more accurate and expedited diagnosis, as well as treatment for future patients encountering similar circumstances.

**Keywords** Systemic juvenile idiopathic arthritis, *Brucella*, Bloodstream infection

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## Introduction

Juvenile idiopathic arthritis (JIA) is a chronic inflammatory joint disease characterized by unexplained arthritis lasting for more than six weeks in children under the age of sixteen. Among them, systemic juvenile idiopathic arthritis (sJIA) accounts for 10-20% and is distinguished by prominent symptoms of remittent fever at onset, along with the potential occurrence of joint lesions [1]. The aberrant activation of the innate immune system and excessive secretion of pro-inflammatory cytokines, including interleukin-1 (IL-1), IL-6, and IL-18, constitute the primary immunological characteristics during the initial stage of sJIA disease in the absence of autoantibodies. An increasing number of scholars posit that sJIA is predominantly a polygenic autoimmune inflammatory disorder, in which the interplay between innate and adaptive immunity mechanisms contributes to its pathogenesis [2]. This condition demonstrates significant heterogeneity, and achieving clinical remission through pharmacotherapy may prove to be a challenge for certain pediatric patients. In rare cases, progressive arthritis can lead to joint deformities, while around 10% of affected children may even develop the potentially life-threatening macrophage activation syndrome (MAS) [3].

Brucellosis is a zoonotic infectious disease caused by the invasion of the body by *Brucella* through various routes [4]. The initial discovery of this disease dates back to 1860 when British doctor Marston identified it on the Mediterranean island of Malta, which is why it is also known as Mediterranean fever or Malta fever. The disease was named undulant fever due to its characteristic pattern of recurring fevers resembling waves in certain patients. In 1887, British doctor Bruce successfully isolated and identified the pathogen responsible for this disease, leading to its official renaming as brucellosis in recognition of his significant contribution. The disease is widely prevalent worldwide, particularly in the Mediterranean region, Asia, and Central and South America, which are considered high-risk areas. Patients infected with *Brucella* may present symptoms such as recurrent fever, excessive sweating, arthralgia, lumbago, fatigue, and hepatosplenomegaly [5, 6]. The transmission of brucellosis to humans can occur through various routes, including contact or ingestion of secretions, body fluids, corpses, contaminated meat and milk from infected animals, inhalation of bacterial dust or entry of bacteria into the conjunctiva, as well as tick bites. Additionally, research has demonstrated person-to-person transmission of brucellosis [7]. The majority of brucellosis cases can be effectively treated, but if left untreated, it may progress into a chronic infection, leading to complex conditions and unfavorable treatment outcomes, the neglected cases have the potential to result in fatality [5, 8]. Therefore, proactive management of *Brucella* infection is of immense significance.

In clinical practice, the coexistence of sJIA and *Brucella* infection is an extremely rare occurrence. Due to the striking similarity in their clinical manifestations, misdiagnosis or failure to diagnose is prone to occur. This case presents a pediatric patient with concurrent sJIA accompanied with *Brucella* bloodstream and bone marrow infections, aiming to provide clinical practitioners with diagnostic and therapeutic insights, expedite the process of disease identification and management, mitigate the detrimental consequences and economic burden associated with misdiagnosis or failure to diagnose for patients.

## Case presentation

The patient, a three-year-old boy from Qinghai Province, presented with persistent and recurrent fever reaching a peak temperature of 41 ℃ three months prior to admission. Despite receiving oral antipyretic medication, his body temperature remained elevated and he experienced repeated episodes approximately twice daily. Initial treatment at a local clinic for three days yielded no improvement, leading to his subsequent transfer to Yushu People's Hospital for further management where he was diagnosed with community-acquired pneumonia. Two months prior to admission, the child experienced intermittent pain in the right knee joint of unknown etiology, accompanied with a fever peaking at 39 ℃. The oral administration of ibuprofen did not succeed in normalizing body temperature, with episodes occurring every three to four days, mainly during noon or early morning hours. The pain and fever lasted for several hours before resolving spontaneously. During painful episodes, there was an associated increase in local joint skin temperature, and the child exhibited a refusal to ambulate. Following the resolution of symptoms, normal walking and movement were observed. However, the pain progressively worsened over time throughout the course of the disease. Subsequently, the patient was referred to Qinghai University Affiliated Hospital for advanced management. Ultrasound examination of the left knee joint revealed no evident abnormalities, blood culture results were negative, while C-reactive protein (CRP) showed 11.9 mg/L (reference value: <0–8 mg/L). Upon returning home, the patient once again experienced pain and fever in the right knee joint.

The patient had been experiencing persistent pain and fever in the right knee joint for one month before admitted, along with fluctuating body temperature of around 40 ℃. Additionally, there was edema observed in the lower part of the right thigh and within the affected knee joint, accompanied with localized dermal hyperthermia. The patient sought medical attention at Yushu People's Hospital in Qinghai Province, where an MRI examination

revealed minimal fluid accumulation in both the suprapatellar bursa and articular cavity of their affected right knee joint. Following this evaluation period, there was a gradual improvement in pain intensity as well as resolution of fever and edema affecting both the lower thigh region and afflicted knee over a span of one week. After a two-week interval, six days prior to hospital admission, the patient experienced recurrent pain in the right hip joint along with fever and tenderness. The pattern and frequency of symptoms were consistent with previous episodes. The patient then sought medical attention at West China Hospital of Sichuan University, where a plain scan revealed a cystic low-density lesion with marginal sclerosis located in the inner portion of the distal femoral epiphysis on the right side. It was recommended that they be transferred to our hospital for further treatment.

Upon admission, the child had exhibited pyrexia and had a body temperature of approximately 39 ℃. Absence of associated rigors or tremors was observed, however, localized warmth was noted in the right knee joint accompanied by pain resembling previous episodes. Furthermore, during this period, erythematous rashes measuring about 1–2 mm in diameter emerged on the extremities. These rashes were non-pruritic and gradually resolved after the fever subsided. Due to an undetermined etiology for both febrile illness and arthralgia, further evaluation is being sought at our hospital. Following admission, the pediatric patient consistently presented with nocturnal fever, reaching a peak temperature of 40 ℃. Pain in the right knee and hip joints was observed, which resolved on its own once the fever subsided. Laboratory tests displayed procalcitonin 0.11 ng/mL (reference value: <0.1 ng/mL), aspartate aminotransferase 110 U/L (reference value: <40 U/L) and alanine aminotransferase 135 U/L (reference value: <49 U/L), both twice higher than normal values. Hypersensitive CRP was measured at 11.7 mg/L (reference value: <0–8 mg/L), platelet count $212 \times 10^9$/L (reference value: $100–300 \times 10^9$/L), white blood cell count at $16 \times 10^9$/L (reference value: $9–30 \times 10^9$/L), and eosinophils count at $0.57 \times 10^9$/L (reference value: $<0.45 \times 10^9$/L) were recorded. IL-6 level was found to be 22.73 pg/mL on analysis, with reference values ranging from 0.373 pg/mL to 0.463 pg/mL. Chest radiography demonstrated bilateral axillary lymphadenopathy, while magnetic resonance imaging (MRI) results indicated involvement of the hip joint and right knee joint. Abnormal signal intensity was observed in the upper segment of the right femur, particularly evident in the femoral head, greater trochanter epiphysis, and metaphyseal end with associated muscular edema (Fig. 1A and B). Additionally, there was enhancement of synovial thickening in both hip joints (Fig. 1C). The distal metaphysis of the right femur exhibited abnormal signal intensity, accompanied with mild synovial thickening and enhancement in the right knee joint (Fig. 1D). No other abnormalities were found in the remaining findings. Subsequently, improvements were made to the bone marrow culture technique, and dual bottle blood cultures were obtained during episodes of high fever which displayed negative in former blood cultures. In conclusion, based on the following six indications in the patient, a diagnosis of sJIA can be established: (1) The three-year-old patient exhibits a daily temperature fluctuation range of 36 to 41 ℃, which characterized by abrupt increments and decrements and is different from the typical undulant fever of brucellosis, is the so called peak fever. (2) During a high fever, accompanying symptoms such as chills, fatigue, and muscle pain may manifest. Once the fever subsides, normal activities can be resumed. (3) The non-fixed erythematous rash gradually resolves subsequent to the resolution of fever. (4) The enhanced MRI findings of the hip joint and right knee joint suggest the presence of arthritis. (5) Elevated IL-6 levels were observed. The elevated IL-6 levels are consistent with sJIA, it can also occur in infections like *Brucella*. IL-6 levels is an important auxiliary examination indicators for diagnosing sJIA, while it isn't the critical indicators for diagnosing brucellosis. (6) The disease course extended beyond two months, surpassing a duration of six weeks, while the joint pain persisted for over two weeks. Here, we should pay attention to the importance of considering infectious causes, such as *Brucella*, in patients presenting with fever and arthritis before concluding a diagnosis of sJIA. Following a definitive diagnosis, the patient received combination therapy comprising ibuprofen (150 mg, po, tid) and methotrexate (8 mg, po, qw). Subsequently, folic acid supplementation was administered on the following day to mitigate potential adverse reactions. It is notable that recent evidence supports IL-1 inhibitors (e.g., anakinra) as a first-line treatment for sJIA due to their rapid efficacy in systemic inflammation, so IL-1 inhibitors may be an alternative approach.

On the seventh day of hospitalization, both blood and bone marrow cultures displayed positive results after four days. Gram staining and Giemsa staining revealed the presence of gram-negative coccobacilli. These microorganisms appeared as small red rod-shaped structures in the Gram staining (Fig. 2A and B). The morphology observed with Giemsa staining was similar to that seen with Gram staining, revealing fine sand-like, clumplike clusters, but exhibited a blue hue (Fig. 2C and D). At the same time, the culture medium was extracted and inoculated in Columbia blood medium and chocolate medium without vancomycin, then placed in an incubator containing 5% $CO_2$ at 35 ℃. Colonies gradually appeared after 24 h of incubation. After 48 h of culture, small smooth non-hemolytic off-white colonies could be seen on the medium (Fig. 2E-H). Subsequently, *Brucella* was

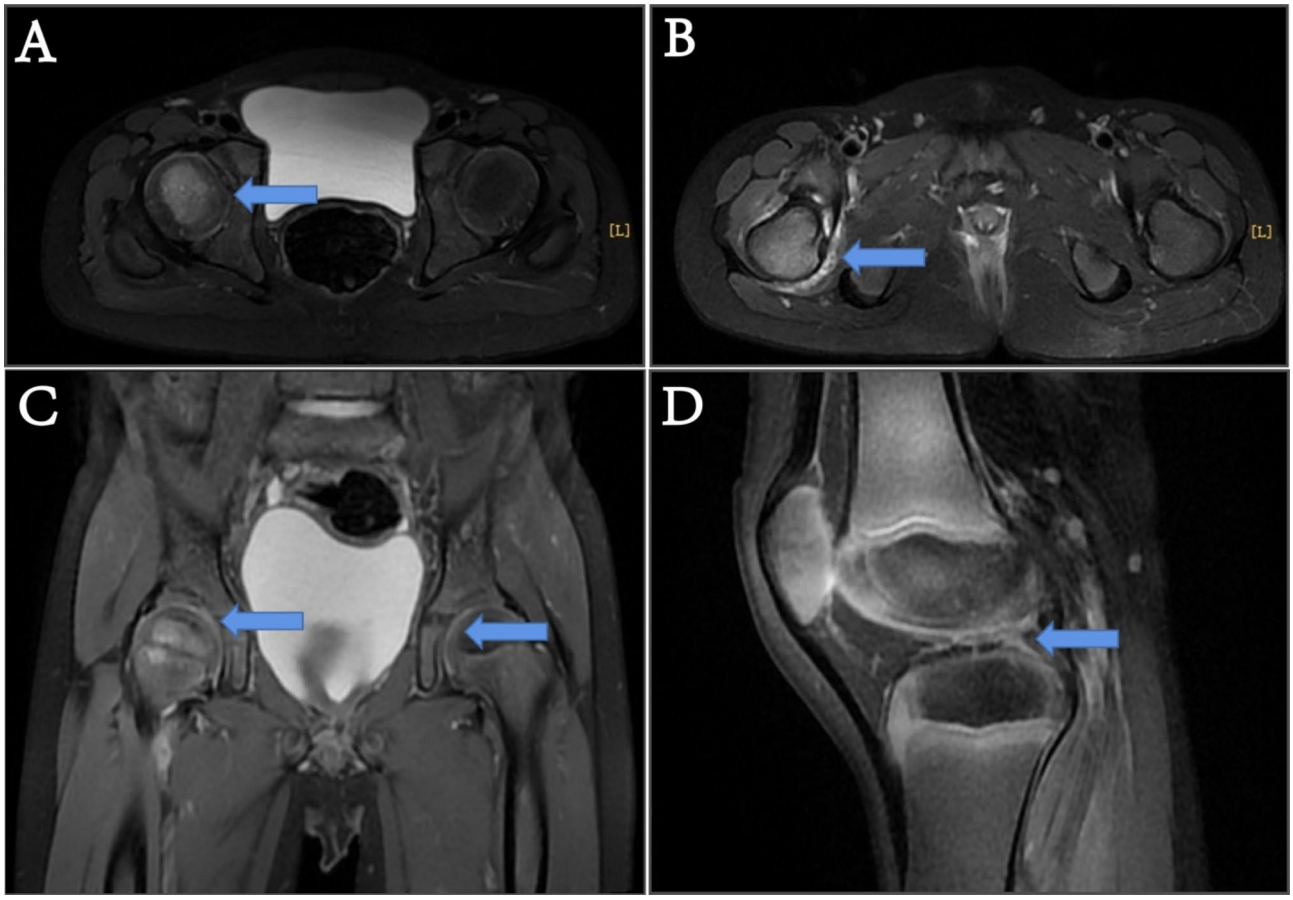


**Fig. 1** Magnetic resonance imaging of the hip and right knee articulations. (**A**) The occurrence of edema within the bone marrow of the proximal femur. (**B**) Reactive hypertrophy of the musculature surrounding the proximal femur. (**C**) Bilateral hip synovial membrane thickening and reinforcement. (**D**) The synovial membrane in the right knee exhibits thickening

detected through identification using mass spectrometry indicating a diagnosis of sJIA accompanied with *Brucella* bloodstream infection upon further investigation into the patient's medical history which revealed previous exposure to cattle and sheep. Treatment commenced with compound sulfamethoxazole tablets (0.48 g, po, bid) and rifampicin (0.3 g, po, qd) for anti-infective therapy.

After a twelve-day hospitalization, the child's fever subsided and there was a reduction in reported pain in both the right knee and hip joints. No tenderness was detected upon examination of these joints. Subsequent evaluation revealed gradual normalization across all indicators, with notable improvement observed specifically in liver function markers. Blood test results indicated a white blood cell count of $5.8 \times 10^9$/L, hemoglobin level at 98 g/L, platelet count measuring at $278 \times 10^9$/L, along with a CRP level reading of 7 mg/L. Consequently, based on these findings, the attending physician authorized the patient's discharge. Upon discharge, the patient will be prescribed methotrexate (8 mg, po, qw) and instructed to take 5 mg of folic acid on the following day. Additionally, compound sulfamethoxazole tablets (0.48 g, po, bid) and rifampicin (0.3 g, po, qd) for six weeks duration will be prescribed to the patient. The patient will also receive advice to return to the hospital for a follow-up examination in two weeks. During this follow-up vist, the patient's liver function gradually returned to normal and is currently in a satisfactory condition, displaying no evidence of recurrence or chronic infection. To provide a more comprehensive overview of this case, a general timeline of the pediatric patient's clinical presentation and relevant tests has been created and is shown in Fig. 3.

## Discussion

*Brucella* infection is a significant public health concern due to its diverse clinical manifestations and potential complications. Several case reports have highlighted the various presentations of *Brucella* infection in different anatomical locations and patient populations. Willems reported a case of a ruptured aneurysm of the common iliac artery caused by *Brucella* melitensis, emphasizing the importance of considering *Brucella* as a potential etiology in vascular complications [9]. Song presented a case of co-infection with *Rickettsia burneti* and *Brucella*

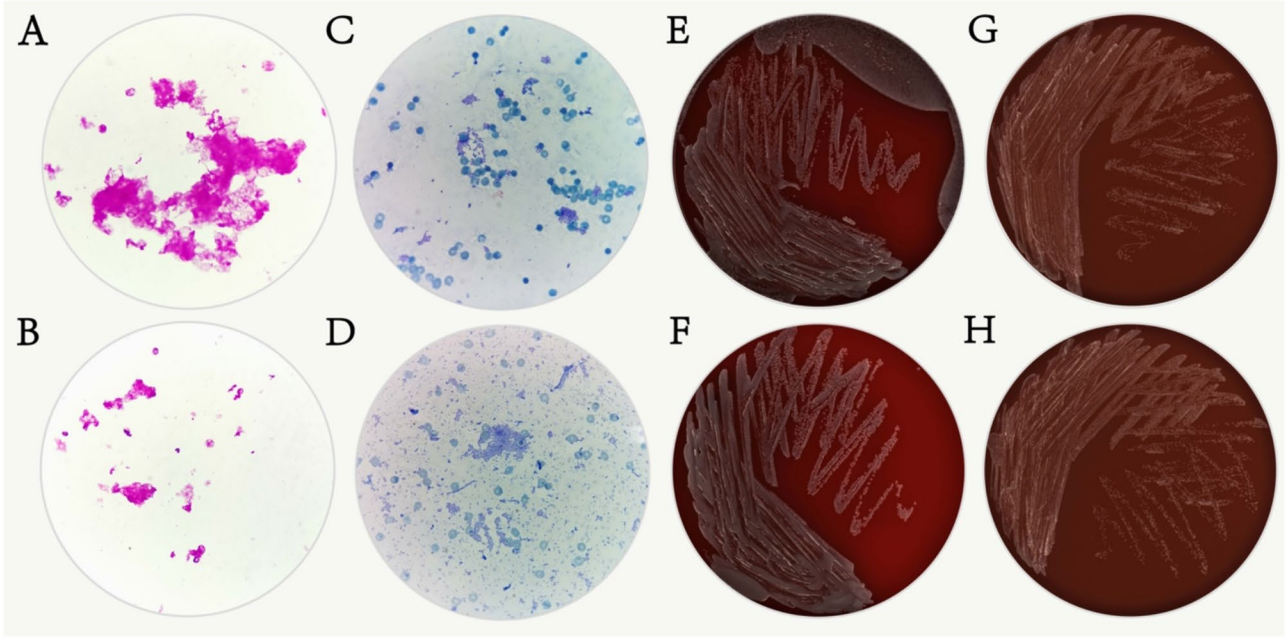


**Fig. 2** Morphological characteristics of *Brucella*. (**A** and **B**) Gram staining and (**C** and **D**) Giemsa staining of *Brucella* demonstrate fine sand-like, clumplike clusters (magnification 10 × 100). (E-H) Morphological characteristics of *Brucella* after 48 h of culture on Columbia blood medium and chocolate medium without vancomycin. (The pictures of upper row were all from positive blood culture bottle, and the lower row were from positive bone marrow culture bottle.)

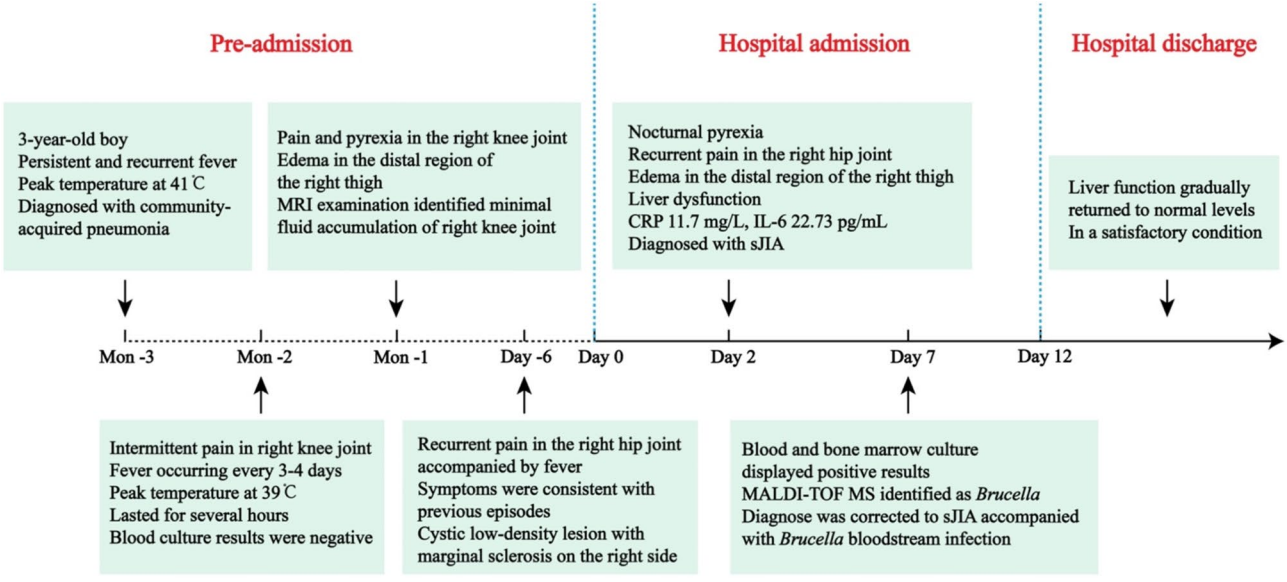


**Fig. 3** Timeline of the pediatric patient's clinical presentation and relevant tests

melitensis, underscoring the need for routine detection of multiple pathogens to prevent missed diagnoses [10]. Furthermore, Shebli described a rare presentation of peripheral edema and ascites in a 10-year-old child with Brucellosis, highlighting the diverse clinical manifestations of the infection [11]. An immune thrombocytopenic purpura associated with *Brucella* infection case was reported, demonstrating the immune-mediated complications that can arise from *Brucella* infection [12]. In 2023, a case of spine infection with *Brucella* melitensis in a non-endemic area, showcasing the importance of considering *Brucella* as a potential pathogen even in regions with low prevalence and a case of aortoduodenal fistula and abdominal aortic aneurysm as complications of *Brucella* aortitis, highlighting the potential serious vascular complications of *Brucella* infection [13,

14]. Moreover, a case of neurobrucellosis complicated by primary pyogenic ventriculitis was reported, emphasizing the neurological manifestations that can arise from *Brucella* infection last year and an unusual case of *Brucella* melitensis-related wound infection was presented, illustrating the diverse clinical presentations of *Brucella* infection [15, 16]. Lastly, report of the first human case of molecularly confirmed co-infection of *Brucella* melitensis and *Coxiella burnetii*, highlighting the importance of considering multiple pathogens in cases of suspected *Brucella* infection [17]. And Abdulrahman described a case of femoral head avascular necrosis due to *Brucella* infection, underscoring the potential musculoskeletal complications associated with *Brucella* infection [18]. In conclusion, the literature on *Brucella* infection case reports demonstrates the diverse clinical manifestations and potential complications of this infectious disease. Healthcare providers should maintain a high index of suspicion for *Brucella* infection in patients presenting with a wide range of symptoms, especially in endemic regions or in cases of unusual clinical presentations.

By investigating this case, we not only enhanced our comprehension of *Brucella* infection but also acquired valuable expertise in the diagnosis and treatment of *Brucella* infection combined with sJIA. During the diagnostic and therapeutic process, we discovered that sJIA and brucellosis exhibit remarkably similar clinical symptoms. Inadequate clinical experience or professional knowledge can easily lead to misdiagnosis or missed diagnosis.

In this particular case, the pediatric patient underwent medical treatment across five distinct hospitals over a three-month period before receiving an accurate diagnosis and successful treatment. There are two primary factors contributing to this consequence. To begin with, *Brucella* exhibits slow growth, leading to initial blood cultures producing false negative results due to insufficient cultivation time. Additionally, sJIA and brucellosis present extremely similar clinical symptoms. In addition to arthritis, the child presented with a non-fixed erythematous rash that gradually resolved after fever subsided and was associated with increased IL-6 levels. Furthermore, both blood and bone marrow cultures displayed positive results after four days, and *Brucella* was identified through MALDI-TOF mass spectrometry. Combined with additional laboratory results and clinical symptoms, sJIA accompanied with *Brucella* bloodstream infection was ultimately diagnosed and effectively managed in our hospital. Moreover, it is imperative to note that *Brucella* can be isolated and cultured from the blood and bone marrow within approximately two weeks following a brucellosis infection, which serves as the definitive basis for diagnosing brucellosis. In summary, these aforementioned factors contributed to the delayed diagnosis and treatment of this particular case.

For sJIA, the management and treatment of refractory disease courses, such as refractory arthritis, recurrent macrophage activation syndrome, and chronic lung disease, present significant challenges [19]. Studies have also investigated the incidence and risk factors for eosinophilia and lung disease in children with sJIA exposed to biologics, with a focus on IL-1/IL-6 inhibitors as effective therapeutic options [20]. In recent research on *Brucella* infections, Cabello et al. demonstrated that *Brucella* exploits the EP Rhg1 to reprogram the host N-glycome and promote bacterial intracellular parasitism [21]. Gomes revealed the regulatory role of STING in metabolic reprogramming of macrophages during *Brucella* infection, leading to an inflammatory M1-like macrophage profile that aids in controlling bacterial replication [22]. Additionally, Demars' team identified the involvement of aconitate decarboxylase 1 in controlling pulmonary *Brucella* infection in mice, highlighting the importance of specific genes in host defense mechanisms against *Brucella* [23]. Regarding vaccine development against *Brucella* melitensis and *Brucella* abortus infection, Sadeghi explored the use of mannosylated chitosan nanoparticles loaded with FliC antigen as a novel vaccine candidate [24]. These studies contribute to ongoing efforts aimed at developing effective preventive measures against *Brucella* infections.

The precise targeting of *Brucella* during the initial stage of infection is crucial for effective intervention [25]. The recent advancements in automated blood culture systems have significantly improved the sensitivity of blood culture, leading to a reduction in the time required for detecting fastidious strains such as *Brucella* [26]. Currently, more than 95% of blood culture samples obtained from patients with acute brucellosis can successfully identify pathogens within the standard one-week incubation period without the need for further subculture [27]. In patients with a continuous duration of infection or local complications, prolonged cultivation and routine transfer of the liquid from the culture bottle to Columbia medium are still necessary. The implementation of MALDI-TOF mass spectrometry technology, serological tests, nucleic acid amplification tests, and metagenomic sequencing enables rapid, precise, and secure identification and determination of pathogenic bacteria isolated from patients [27–29]. It is crucial to note that *Brucella* can remain viable on inanimate surfaces for extended periods, ranging from weeks to even months. Additionally, manual laboratory procedures have the potential to generate hazardous aerosols and contaminate culture media, or result in reagent spills. Therefore, when conducting laboratory operations involving *Brucella*, it is imperative to perform them within a biosafety cabinet while implementing appropriate protective measures. Subsequently, upon completion of the experiment,

prompt sterilization of the bacterial strain under high pressure should be carried out.

## Conclusion

The specific diagnostic challenges and the importance of early infectious disease evaluation in similar cases would be particularly useful. If similar cases are encountered in the future, it is imperative to enhance epidemiological investigations during consultations in order to achieve efficient diagnosis and treatment. When conducting blood/bone marrow culture, the culture time can be appropriately extended or metagenomic sequencing can be directly adopted for more accurate and expedited identification of pathogens. This approach holds significant value for clinical diagnosis and treatment, particularly for microorganisms with slow growth and high pathogenicity. Simultaneously, reinforcing professional knowledge acquisition and upholding professional ethics is essential in order to provide patients with more precise and prompt diagnosis and treatment when faced with such cases, thereby contributing to their health.

### Abbreviations

| | |
|---|---|
| JIA | Juvenile idiopathic arthritis |
| sJIA | Systemic juvenile idiopathic arthritis |
| IL-1 | Interleukin-1 |
| MAS | Macrophage activation syndrome |
| CRP | C-reactive protein |
| MRI | Magnetic resonance imaging |

### Acknowledgements

Not applicable.

### Author contributions

All authors have made significant contributions to the work and approved the final version of the manuscript. XXL contributed the original idea, WZ and YMJ provided the case description, XGL offered magnetic resonance imaging guidance, WJW collected clinical data and illustrated figures for this work, JJL (Jiaji Ling) wrote the final version of the manuscripts with assistance from JJL (Jingjing Luo), JJL, XXL and LHK provided open access funding for this work.

### Funding

Open access funding was supported by the Province Natural Science Foundation of Sichuan Province No. 2023NSFSC1699 to Linghan Kuang, No. 2024NSFSC1942 to Xingxin Liu and No. 2025ZNSFSC1740 to Jiaji Ling.

### Data availability

Data is provided within the manuscript or supplementary information files.

## Declarations

### Ethics approval and consent to participate

The publication of the case was approved by the Ethics committee of West China Second University Hospital. Informed consent to participate was obtained from the patient's parents.

### Consent for publication

Written informed consent for publication of identifying images and clinical details was obtained from the patient's parents.

### Clinical trial

Not applicable.

### Competing interests

The authors declare no competing interests.

Received: 2 November 2024 / Accepted: 12 February 2025
Published online: 18 February 2025

### References

1. Martini A, Lovell DJ, Albani S, Brunner HI, Hyrich KL, Thompson SD, Ruperto N. Juvenile idiopathic arthritis. Nat Rev Dis Primers. 2022;8(1):5.
2. Szekanecz Z, McInnes IB, Schett G, Szamosi S, Benko S, Szucs G. Autoinflammation and autoimmunity across rheumatic and musculoskeletal diseases. Nat Rev Rheumatol. 2021;17(10):585–95.
3. Henderson LA, Cron RQ. Macrophage activation syndrome and secondary Hemophagocytic Lymphohistiocytosis in Childhood Inflammatory disorders: diagnosis and management. Paediatr Drugs. 2020;22(1):29–44.
4. Qureshi KA, Parvez A, Fahmy NA, Abdel Hady BH, Kumar S, Ganguly A, Atiya A, Elhassan GO, Alfadly SO, Parkkila S, et al. Brucellosis: epidemiology, pathogenesis, diagnosis and treatment-a comprehensive review. Ann Med. 2023;55(2):2295398.
5. Franco MP, Mulder M, Gilman RH, Smits HL. Human brucellosis. Lancet Infect Dis. 2007;7(12):775–86.
6. Qie C, Cui J, Liu Y, Li Y, Wu H, Mi Y. Epidemiological and clinical characteristics of bacteremic brucellosis. J Int Med Res. 2020;48(7):300060520936829.
7. Tuon FF, Gondolfo RB, Cerchiari N. Human-to-human transmission of *Brucella* - a systematic review. Trop Med Int Health. 2017;22(5):539–46.
8. Bosilkovski M, Siskova D, Spasovska K, Vidinic I, Dimzova M. The influence of illness duration before diagnosis on clinical characteristics and outcome in human brucellosis. Trop Doct. 2019;49(3):177–81.
9. Willems SA, Buntinx M, Gelinck LBS, van Schaik J, Eefting D. Ruptured aneurysm of the common iliac artery caused by *Brucella* melitensis: a Case Report. EJVES Vasc Forum. 2021;52:26–9.
10. Song J, Hu X, Li X, Chen Y, Yan X, Zhu W, Ding Y, Zhou J. Rickettsia burneti and *Brucella* melitensis co-infection: a case report and literature review. BMC Microbiol. 2021;21(1):270.
11. Shebli B, Batal R, Chihab M, Zammar L, Warrak B, Allouzi S, Abdullah M. A rare presentation of peripheral edema and ascites in a 10-year-old child with brucellosis: a case report. Ann Med Surg (Lond). 2022;73:103196.
12. Qiu Z, Yang F, Zhang S. Immune Thrombocytopenic Purpura and its Rare Association with a *Brucella* infection: a Case Report. Cureus. 2022;14(10):e30049.
13. Du J, Tao Y, Yang J, Cai J, Zhou H, Zhang R, Hu Y. Case Report: metagenomic next-generation sequencing confirmed a case of spine infection with *Brucella* melitensis in non-endemic area. Infect Drug Resist. 2023;16:7219–25.
14. Hosseinzadeh A, Zehra J, Davarpanah MA, Farsani MM, Gorji MG, Shahriarirad R. Aortoduodenal fistula and abdominal aortic aneurysm as a complication of *Brucella* Aortitis managed with Insitu aortic aneurysm repair: a case report. Clin Case Rep. 2023;11(12):e8269.
15. Alhatou M, Joudeh AI, Alhatou A, Ghamoodi M. Neurobrucellosis complicated by primary pyogenic ventriculitis: a case report. Oxf Med Case Rep. 2024;2024(1):omad149.
16. Bilik OA, Ince FM, Ozcan N, Ayaydin Z. An unusual case of *Brucella* melitensis-related wound infection. Infez Med. 2024;32(1):99–102.
17. Mangkalamanee O, Rotcheewaphan S, Phuensan P, Ponpinit T, Hemachudha T, Torvorapanit P. The first human case report of molecularly confirmed co-infection of *Brucella* melitensis and Coxiella burnetii: a case report. Heliyon. 2024;10(8):e29685.
18. Abdulrahman BB, Sadq BN, Shareef FU, Abdul Aziz JM, Rasheed MK. Femoral Head Avascular Necrosis due to *Brucella* infection: a Case Report. Cureus. 2024;16(7):e65740.
19. Erkens R, Esteban Y, Towe C, Schulert G, Vastert S. Pathogenesis and treatment of Refractory Disease courses in systemic juvenile idiopathic arthritis: refractory arthritis, recurrent macrophage activation syndrome and chronic lung disease. Rheum Dis Clin North Am. 2021;47(4):585–606.
20. Onel KB, Horton DB, Lovell DJ, Shenoi S, Cuello CA, Angeles-Han ST, Becker ML, Cron RQ, Feldman BM, Ferguson PJ, et al. 2021 American College of Rheumatology Guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for Oligoarthritis, Temporomandibular Joint Arthritis, and systemic juvenile idiopathic arthritis. Arthritis Rheumatol. 2022;74(4):553–69.

21. Cabello AL, Wells K, Peng W, Feng HQ, Wang J, Meyer DF, Noroy C, Zhao ES, Zhang H, Li X, et al. *Brucella*-driven host N-glycome remodeling controls infection. Cell Host Microbe. 2024;32(4):588–e605589.
22. Gomes MTR, Guimaraes ES, Marinho FV, Macedo I, Aguiar E, Barber GN, Moraes-Vieira PMM, Alves-Filho JC, Oliveira SC. STING regulates metabolic reprogramming in macrophages via HIF-1alpha during *Brucella* infection. PLoS Pathog. 2021;17(5):e1009597.
23. Demars A, Vitali A, Comein A, Carlier E, Azouz A, Goriely S, Smout J, Flamand V, Van Gysel M, Wouters J, et al. Aconitate decarboxylase 1 participates in the control of pulmonary *Brucella* infection in mice. PLoS Pathog. 2021;17(9):e1009887.
24. Sadeghi Z, Fasihi-Ramandi M, Azizi M, Bouzari S. Mannosylated chitosan nanoparticles loaded with FliC antigen as a novel vaccine candidate against *Brucella* melitensis and *Brucella* abortus infection. J Biotechnol. 2020;310:89–96.
25. Spera JM, Guaimas F, Czibener C, Ugalde JE. *Brucella* Egresseshostmcells exploitingomultivesicularibodiesBodies. mBio. 2023;14(1):e0333822.
26. Mantur BG, Mulimani MS, Bidari LH, Akki AS, Tikare NV. Bacteremia is as unpredictable as clinical manifestations in human brucellosis. Int J Infect Dis. 2008;12(3):303–7.
27. Yagupsky P, Morata P, Colmenero JD. Laboratory diagnosis of human brucellosis. Clin Microbiol Rev 2019, 33(1).
28. El-Ashry AH, Saad K, Obiedallah AA, Elhoufey A, Dailah HG, Hussein MSA. Molecular and Serological Diagnostic Approach to define the Microbiological Origin of Blood Culture-negative infective endocarditis. Pathogens 2022, 11(11).
29. Abuawad A, Ashhab Y, Offenhausser A, Krause HJ. DNA sensor for the detection of *Brucella* Spp. Based on magnetic nanoparticle markers. Int J Mol Sci 2023, 24(24).

## Publisher's note