Case Report

Journal of Iranian Medical Council, Volume 10, Issue no. 1
http://dx.doi.org/10.18502/jimc.v10i1.23287

Check for updates

The Diagnostic Challenge: A Case Report of Mycoplasma Septic Arthritis in the Setting of Common Variable Immunodeficiency

Sara Ghaderkhani[1], Mohammadreza Salehi[1], Mohammad Mehdi Ebrahiminasab[2], Hossein Khalili[3], Seyed Sajjad Mousavi Zad[4] and Ensiyeh Rahimi[5*]

1. Department of Infectious Diseases and Topical Medicine, School of Medicine, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Orthopedic Surgery, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
3. Pharmacotherapy Department, Tehran University of Medical Sciences, Tehran, Iran
4. School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
5. Iranian Research Center for HIV/AIDS, School of Medicine, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

*** Corresponding author**
Ensiyeh Rahimi, MD
Iranian Research Center for HIV/AIDS, School of Medicine, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
Email:
ensiyehrahimi@gmail.com

Received: 24 Sept 2025
Accepted: 10 Dec 2025

Citation to this article
Ghaderkhani S, Salehi Mr, Ebrahiminasab MM, Khalili H, Mousavi Zad SS, Rahimi E. The Diagnostic Challenge: A Case Report of Mycoplasma Septic Arthritis in the Setting of Common Variable Immunodeficiency. *J Iran Med Counc*. 2027;10(1):300-6.

Abstract

Background: Common Variable Immunodeficiency (CVID) is a heterogeneous disorder and a primary immunodeficiency with variable clinical manifestations characterized by hypogammaglobulinemia and increased susceptibility to recurrent bacterial infections (1). *Mycoplasma hominis*, a commensal organism of the genitourinary tract, can cause serious infections such as septic arthritis in immunocompromised individuals, particularly those with disruptions in mucosal integrity or underlying immune deficiencies (2).

Case Presentation: A 26-year-old male with CVID presented with left knee swelling after trauma. Multiple arthrotomies and synovial fluid analyses were initially negative for pathogens. Standard antibiotics (vancomycin, cefepime) failed. PCR eventually identified M. hominis, and treatment with doxycycline and moxifloxacin led to clinical improvement despite joint damage. Later, a knee abscess with osteomyelitis grew Pseudomonas aeruginosa, treated with cefepime, levofloxacin, and doxycycline.

Conclusion: This case highlights the importance of considering atypical pathogens like M. hominis in immunocompromised patients with culture-negative septic arthritis and emphasizes early molecular testing to guide effective therapy.

Keywords: Common variable immunodeficiency, Immunocompromised patients, *Mycoplasma hominis*, Septic arthritis

Copyright © 2027, Journal of Iranian Medical Council.
This work is licensed under a Creative Commons Attribution–NonCommercial 4.0 International License.

Introduction

Common Variable Immunodeficiency (CVID) is a heterogeneous disorder characterized by hypogammaglobulinemia and increased susceptibility to recurrent bacterial infections (1). *Mycoplasma hominis* (*M. hominis*) is typically found as a commensal organism in the genitourinary tracts of sexually active individuals (2). Multiple immunocompromising conditions have been recognized as contributing factors to the onset of septic arthritis, with notably low levels of Immunoglobulin G (IgG) identified as a significant risk factor (3).

However, it has the potential to spread to other areas of the body, particularly when there is a breach in the mucosal barriers or when the immune system is compromised. This is commonly observed in transplant patients and individuals with autoimmune diseases, such as Systemic Lupus Erythematosus (SLE) or hypogammaglobulinemia (4).

M. hominis is part of the flora of the genitourinary tract of healthy individuals with colonization rates ranging between 21% and 53%. However, it is potentially pathogenic and can cause genitourinary, maternal, and neonatal infections (6). *M. hominis* is known for its slow growth and necessitates particular media and specific incubation environments for culture; this is not part of standard testing protocols (5). Moreover, standard gram staining often yields negative results due to the bacterium's lack of a cell wall, which complicates the identification process (6). Since *M. hominis* requires prolonged culture periods, specialized media, or PCR methods, it is rarely included in routine testing, causing delays in both diagnosis and appropriate treatment (2).

Although there is no notable difference in sensitivity between traditional bacterial culture methods and *M. hominis*-specific real-time PCR, the latter significantly shortens the diagnosis timeframe from several days to just a few hours (7). This case highlights the diagnostic challenges of culture-negative septic arthritis in immunocompromised individuals, emphasizing the need for early molecular testing.

Case Presentation

A 26-year-old male patient with a history of CVID presented with complaints of swelling in the left knee joint. The patient has a history of underlying conditions since childhood. At the age of 2, he experienced jaundice and hemolysis. Six months later, he was hospitalized due to severe thrombocytopenia and received Intravenous Immunoglobulin (IVIG) treatment. IVIG therapy continued until the age of 7 and was then discontinued. At the age of 13, he was diagnosed with autoimmune hemolytic anemia (Coombs positive) and was treated with rituximab for 8 weeks (one dose per week).

At the age of 22, he visited a rheumatologist due to complaints of joint pain and stiffness and was diagnosed with rheumatoid arthritis. He was treated with 5 *mg* of prednisolone daily for two years, during which his symptoms improved.

In the laboratory tests performed in 2023, immunoglobulin levels were found to be low, and further investigations led to the diagnosis of CVID. He was started on a monthly IVIG regimen of 40 *g*. In June 2023, the patient experienced trauma following a fall, injuring his left knee against a vehicle's bumper. At first, an arthrocentesis was performed, and synovial fluid analysis was inflammatory and septic arthritis was not considered for the patient. The patient was admitted to the rheumatology service and examined for rheumatological diseases. All the rheumatological tests of the patient were negative.

Fifteen days later, in July 2023, he presented to another hospital with severe pain and swelling in the left knee where he was diagnosed with septic arthritis. An arthrocentesis was performed, and synovial fluid analysis was negative for culture. The patient was prescribed vancomycin for 10 days. Then he returned to Imam Khomeini Hospital in Tehran with recurrent symptoms, where he underwent a surgical arthrotomy and Arthrocentesis, receiving treatment with vancomycin and cefepime. The synovial fluid culture remained negative.

Due to inadequate response to treatment, the patient underwent arthrotomy and Arthrocentesis again two weeks later. Fluid samples were sent for PCR of tuberculosis and brucellosis, which were negative. From July to December 2023, he underwent joint lavage and arthrotomy eight times due to recurrent symptoms. The patient underwent repeated examinations for 6 months. The patient presented in early December 2023 with exacerbation of symptoms. Joint fluid culture reported the presence

of *Pseudomonas aeruginosa* (*P. aeruginosa*). The patient was treated with cefepime for three weeks. Despite receiving appropriate antibiotics based on the antibiogram sensitivity results, the patient remained symptomatic and had elevated inflammatory markers (Table 1).

Considering the background of CVID disease and the lack of response to treatment and the persistence of the patient's symptoms, the patient was a candidate for arthrotomy, and microbial samples were sent and MRI was performed. Consequently, a PCR test of the joint fluid was performed for the patient. Ultimately, in December 2023, *M. hominis* was identified from the joint fluid culture, leading to a change in the antibiotic regimen to doxycycline 100 *mg* twice daily and moxifloxacin 400 *mg* once daily (Tables 2 and 3). Below is the patient's first MRI Report done in November 2023 (Figure 1).

Moderate joint effusion is observed; however, the synovial surfaces of the joint are significantly thickened with considerable enhancement, indicating edema and inflammation that has spread to the surrounding soft tissues. This finding suggests active septic arthritis.

The spread of inflammation and soft tissue collections in the anterior and medial aspects of the knee, as well as the anterior and lateral aspects, have reached the skin surface in the form of draining sinuses. This finding may be due to recent surgery and irrigation.

Nevertheless, active inflammation in the joint is still

Table 1. Laboratory results

	WBC $\times 10^3/\mu l$	ESR *mm/hr*	CRP *mg/L*	C3 *mg/dL*	C4 *mg/dL*	IgA *mg/dL*	IgM *mg/dL*	IgG *mg/dL*
Reference range	4-11	<20	<5	90-180	10-40	70-400	40-230	700-1600
6 .8.2023	4	94	122	177	49	10	17	15
13.9.2023	8.5	100	85	-	-	-	-	-
22.10.2024	6	30	74	-	-	-	-	-
25.6.2024	11	107	97	-	-	-	-	-

Table 2. Synovial fluid analysis

	Color	Appearance	Glucose (*mg/dL*)	WBC ($\times 10^3/\mu l$)	Poly (%)	Lymph (%)	Bk smear
Reference range	Clear	Clear	Similar to serum	<200	>25%	<75%	Neg.
6.8. 2023	Yellow	Turbid	61	10,000	20%	80%	Neg.
13.9.2023	Milky	Turbid	15	23,000	65%	35%	Neg.
6.12.2023	Milky	Turbid	30	46,000	90%	10%	Neg.

Table 3. Synovial culture or PCR

6 August 2023	Culture: No growth after 72 *hr*
13 September 2023	Culture: No growth after 72 *hr*
1 December 2023	Culture: *P. aeruginosa* sensitive to Cephalosporines
25 December 2023	PCR: M. hominis
25 June 2024	Culture: *P. aeruginosa* sensitive to cephalosporines

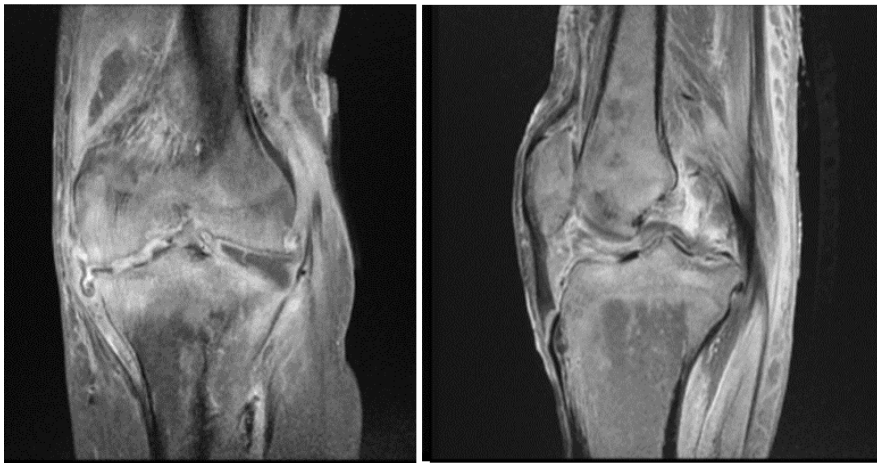


Figure 1. Knee MRI in November 2023.

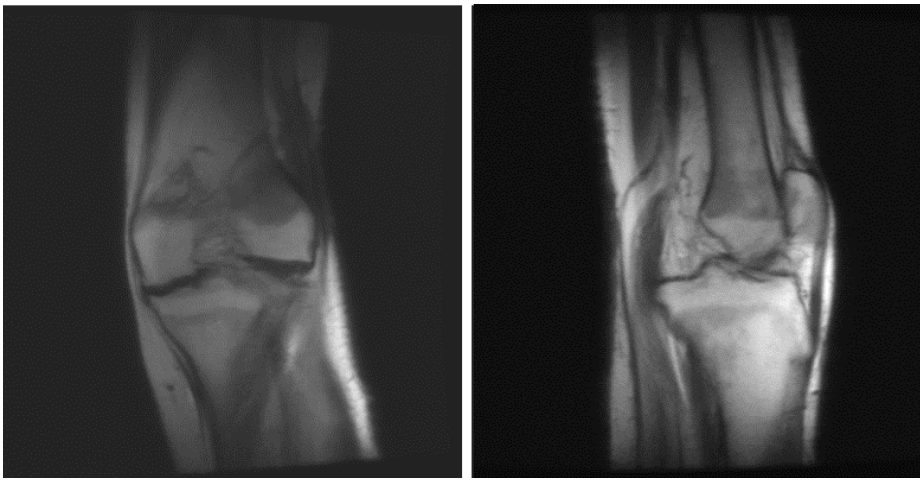


Figure 2. Knee MRI in June 2024.

present, and the juxta-articular bone is also inflamed, with signals suggesting juxta-articular osteomyelitis.

The next MRI was done 6 months later in June 2024 (Figure 2).

The current MRI was compared with the MRI performed about three months ago .The swelling and inflammation around the knee have decreased compared to previous imaging, and the previously noted loculated collections appear successfully drained. There is no evidence of osteomyelitis, although degenerative changes and significant damage to the menisci, cruciate ligaments, and capsular structures persist.

The patient showed significant improvement, and symptoms were controlled, although the joint had sustained considerable damage.

Due to adjacent osteomyelitis occurring alongside septic arthritis, the patient received oral treatment with doxycycline and moxifloxacin for 5 months.

In June 2024, the patient referred with an abscess behind the knee, which was subsequently drained. The culture from the abscess revealed *P. aeruginosa* sensitive to Cephalosporines, prompting a change in the antibiotic regimen to cefepime (2 *g* TDS), levofloxacin (500 *mg* Daily), and doxycycline (100 *mg* BD). The patient's symptoms were controlled following this treatment plan.

At the one-year follow-up, the patient was in good general condition. He had joint destruction, and orthopedic evaluation indicated that he was a candidate for total knee arthroplasty.

The flowchart summarizes the patient's clinical journey, including their medical history, complications, treatment timeline, and outcomes effectively, providing a clear overview of the case progression.

1. Injury (June 2023) **⬇** **Left knee swelling after fall** **⬇** **Initial Evaluation (July 2023)**
• Septic arthritis suspected
• Arthrocentesis performed
• Started: Vancomycin (1*g* BD) + Cefepime (2 *g* TDS) **⬇** **Partial response but persistent symptoms** **⬇** **Re-evaluation (Dec 2023)**
• *Mycoplasma hominis* identified
• Revised treatment: Doxycycline (100 *mg* BD) + Moxifloxacin (400 *mg* daily) **⬇** **Further improvement** **⬇** **IVIG restarted at age 25 (CVID management)** **⬇** **Complication (June 2024)**
• New abscess behind knee and osteomyelitis
• Drainage performed
• Culture: *Pseudomonas aeruginosa* sensitive to Cephalosporines **⬇** **Treatment for Abscess and osteomyelitis**
• Cefepime (2 *g* TDS) + Levofloxacin (500 *mg* daily) + Doxycycline (100 *mg* BD) **⬇** **Outcome**
• Symptoms improved and controlled.

Flowchart. Patient's clinical journey.

Conclusion

In the present study, the immunocompromised patient presented with septic arthritis symptoms. The joint fluid culture of the patient was negative. The patient did not respond to routine antibiotic therapy for negative culture septic arthritis. Finally, after 6 months, he was diagnosed with mycoplasma septic arthritis. Therefore, testing for atypical organisms including *M. hominis* should be performed routinely in immunocompromised patients with septic arthritis (8).

In the study by Ali *et al*, 15 cases of *M. hominis* native joint septic arthritis immunocompromising conditions were observed in more than two-thirds of cases with hypogammaglobulinemia (9). The patient of this study also had CVID and hypogammaglobulinemia.

In this study, after the diagnosis of mycoplasma septic arthritis, the patient responded dramatically to the treatment. Although mycoplasma septic arthritis responds well to its specific antibiotic treatment, delay in diagnosis and lack of response to empiric treatment causes complications and damage (10).

In the Chen *et al*, study 34 cases of mycoplasma septic arthritis and eight of them were periprosthetic joint infection (PJI). Twenty-four patients (70.6%) were immunocompromised. The possibility of mycoplasma septic arthritis should be considered if patients with joint infections have a history of

immunocompromised, repeated negative cultures, and poor empiric antibiotic treatment results (3).

The optimal management of native joint septic arthritis caused by *M. hominis* remains inadequately defined, primarily due to its infrequent occurrence. Two active agents, particularly fluoroquinolones, have been recommended due to their excellent penetration into bone tissue (11). Intrinsic resistance to macrolides in Gram-negative bacteria is primarily attributed to the low permeability of the outer membrane, though the underlying genetic and molecular mechanisms remain to be fully elucidated (12). Additionally, other effective agents include tetracyclines and clindamycin, with treatment durations typically ranging from several weeks to a few months (13).

Similar to the current study in a septic polyarthropathy caused by *M. hominis* that was resistant to multiple drugs. The patient eventually responded to treatment with doxycycline and fluoroquinolone (14).

Recurrent surgeries likely increased risk of Pseudomonas superinfection including iatrogenic factors. The present report emphasized the need for heightened awareness and diagnostic vigilance for atypical organisms in immunocompromised patients, facilitating timely and effective treatment strategies that can improve patient outcomes.

Culture-negative septic arthritis in immunocompromised patients warrants consideration of atypical pathogens. Early PCR testing can improve outcomes and reduce joint damage.

Antibiotic regimens should be tailored to identified pathogens and patient-specific factors.

Funding

Not applicable.

Ethical approval

This study has been approved by the ethics committee of Tehran University of Medical Sciences and adheres to the Declaration of Helsinki, with informed consent obtained from the patient for publication. The consent form is signed by the patient.

Consent for publication

The consent form for publication was signed by All authors.

Conflict of Interest

The authors declare that they have no competing interests.

References

1. Yazdani R, Habibi S, Sharifi L, Azizi G, Abolhassani H, Olbrich P, Aghamohammadi A. Common variable immunodeficiency: epidemiology, pathogenesis, clinical manifestations, diagnosis, classification, and management. J Investig Allergol Clin Immunol 2020;30(1):14-34.

2. Bozo N, Ravn C, Stenz Justesen U, Dahlerup Rasmussen L. Mycoplasma hominis septic arthritis in a patient with hypogammaglobinaemia and rheumatoid arthritis. BMJ Case Rep 2021 Jan 19;14(1):e237798.

3. Chen Y, Huang Z, Fang X, Li W, Yang B, Zhang W. Diagnosis and treatment of mycoplasmal septic arthritis: a systematic review. Int Orthop 2020 Feb;44(2):199-213.

4. Franz A, Furr PM, Taylor-Robinson D. Mycoplasmal arthritis in patients with primary immunoglobulin deficiency: clinical features and outcome in 18 patients. Br J Rheumatol 1997;36:661-8.

5. Luttrell LM, Kanj SS, Corey GR, Lins RE, Spinner RJ, Mallon WJ, et al. Mycoplasma hominis septic arthritis: two case reports and review. Clin Infect Dis 1994 Dec;19(6):1067-70.

6. Waites KB, Xiao L, Paralanov V, Viscardi RM, Glass JI. Molecular methods for the detection of mycoplasma and Ureaplasma infections in humans: a paper from the 2011 William Beaumont Hospital symposium on molecular pathology. J Mol Diagn 2012;14(5):437-50.

7. Cunningham SA, Mandrekar JN, Rosenblatt JE, Patel R. Rapid PCR detection of Mycoplasma hominis, Ureaplasma

urealyticum and Ureaplasma parvum. Int J Bacteriol 2013;2013:1-7.

8. Hum RM, Iftikhar H, Tang E, Ho P. Septic arthritis caused by Mycoplasma hominis in a patient with systemic lupus erythematosus. BMJ Case Rep 2022 Jan 19;15(1):e247675.

9. Ali GA, Goravey W, Hamad A, Ibrahim EB, Hasan MR, Al Maslamani M, et al. An enemy in shadows—Mycoplasma hominis septic arthritis and iliopsoas abscess: case report and review of the literature. IDCases 2021;26:e01260.

10. Karabay O, Topcuoglu A, Kocoglu E, Gurel S, Gurel H, Ince NK. Prevalence and antibiotic susceptibility of genital Mycoplasma hominis and Ureaplasma urealyticum in a university hospital in Turkey. Clin Exp Obstet Gynecol 2006;33(1):36-8.

11. Ma Y, Pirolo M, Jana B, Mebus VH, Guardabassi L. The intrinsic macrolide resistome of Escherichia coli. Antimicrob Agents Chemother 2024 Aug 7;68(8):e0045224.

12. Waites KB, Taylor-Robinson D. Manual of Clinical Microbiology. 11th ed. Washington DC: ASM Press; 2015. Chapter 62, Mycoplasma and Ureaplasma; p. 1088-105.

13. Ahmed J, Rawre J, Dhawan N, Khanna N, Dhawan B. Mycoplasma hominis: an under-recognized pathogen. Indian J Med Microbiol 2021;39:88-97.

14. Clough W, Cassell GH, Duffy LB, Rinaldi RZ, Bluestone R, Morgan MA, et al. Septic arthritis and bacteremia due to Mycoplasma resistant to antimicrobial therapy in a patient with systemic lupus erythematosus. Clin Infect Dis 1992;15:402-7.