



Case Report

Ocular Involvement in a Liver Transplant Patient with Brucellosis: A Case Report and Literature Review

Shiva Shabani^{1*}, Shirin Shabani²

¹Department of Infectious Diseases, School of Medicine, Arak University of Medical Sciences, Arak, Iran

²Department of Chemistry, Faculty of Biological Science and Technology, Shahid Rajaee Teacher Training Farhangian University of Isfahan, Iran

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***Corresponding author:**

Shiva Shabani,

Email: drshivashabani@gmail.com

Abstract

Background: Ocular brucellosis is a rare manifestation, and most references in the literature consist of case reports, resulting in a lack of data on the incidence of this condition. This study presents a case of anterior uveitis due to brucellosis in a liver transplant patient. Ocular involvement in organ transplant patients can arise from various causes; however, given the patient's history and occupation, *Brucella*-related ocular involvement was strongly suspected in this case.

Case Presentation: This is the first reported case of uveitis attributed to *Brucella* infection in an organ transplant patient. The patient had undergone a liver transplant 10 years ago due to familial hyperlipidemia and was taking Cellcept and Tacrolimus daily as antirejection medications. Additionally, he had a background as a rancher and farmer and reported a history of consuming small amounts of raw milk, although he had not consumed it so regularly in the past. He was referred for evaluation with a two-month history of fatigue, photophobia, and a mild decrease in visual acuity, presenting in May 2022. The complicated *Brucella* uveitis was diagnosed by a combination of clinical manifestations, including fever, as well as epidemiological and serological findings and ophthalmological examination. The patient was treated with gentamicin, doxycycline, and cotrimoxazole in the first week and was discharged and completed a twelve-week outpatient treatment course with doxycycline 100 mg twice daily, cotrimoxazole 800/160 mg every 12 hours, and ciprofloxacin 500 mg every 12 hours. The patient's symptoms, including ocular discomfort and fever, completely resolved within four weeks. In addition, *Brucella* serology tests demonstrated a decline over three months, with no relapses occurring during the subsequent 24-month follow-up period.

Conclusion: Although uveitis caused by various opportunistic infections is not uncommon among organ transplant patients who are undergoing treatment with immunosuppressive medications, it is important to specifically consider *Brucella* infections in areas where *Brucella* is endemic. In such areas, healthcare providers should perform appropriate investigations for *Brucella* in these cases to ensure accurate diagnosis and appropriate treatment.

Keywords: Zoonotic infection, Rare presentation, Liver transplant patient, Drug interaction, Ocular brucellosis



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Introduction

Brucellosis is a zoonotic infectious disease caused by species of the *Brucella* genus, which are endemic in certain regions worldwide. The primary human pathogens include *Brucella melitensis*, *Brucella abortus*, *Brucella canis*, and *Brucella suis* (1). While brucellosis has been largely eradicated and is well-controlled in most developed countries, it remains a significant health challenge in developing nations, where individuals frequently come into contact with livestock and consume unpasteurized

products from infected animals (2,3).

In summary, pathogenic *Brucella* bacteria enter host cells and employ self-protection mechanisms to avoid degradation by lysosomes. After replication, they advance to the next phase of the infection process to target specific organs. The host's immune system is unable to effectively eliminate the pathogen or block the progression of the infection. Ultimately, *Brucella* disseminates through the systemic lymphatic circulation to various organs within the reticuloendothelial system, including the lungs,



spleen, liver, bone marrow, and even the eyes. Brucellosis is a systemic disease with a broad range of clinical manifestations, and if not diagnosed and treated promptly, it can lead to severe complications (4-6). *Brucella* infections exhibit a range of non-specific symptoms, including fever, joint pain, muscle pain, headaches, and neurological deficits, which complicate diagnosis. If diagnosis or treatment is not appropriately managed, the bacteria can invade and replicate in vital organs, such as the bone marrow, heart, and brain, potentially leading to severe systemic reactions and, in some cases, patient mortality. Therefore, early and accurate diagnosis of brucellosis, along with targeted pharmacological treatment, is of paramount clinical importance and can significantly reduce the risk of serious complications in affected patients (7,8).

Brucellosis appears to be uncommon among organ transplant recipients, even in endemic areas. However, rare cases may be transmitted through bone marrow transplantation and blood transfusions. Studies reporting cases of brucellosis in organ transplant recipients indicate that transmission occurred from the donor, and no ocular infections have been documented in these studies (9).

Ocular brucellosis is a rare manifestation, and most references in the literature contain case reports, leading to a lack of data regarding the incidence of this condition. The current study presents a case of anterior uveitis owing to brucellosis in a liver transplant patient. Ocular involvement in organ transplant patients can result from different causes; nonetheless, in this case, *Brucella*-related ocular involvement was strongly suspected, given the patient's history and occupation. Cases of uveitis, neuritis, optic neuritis, papilledema, keratitis, and other ocular and neurological manifestations associated with brucellosis have been documented so far (7,10). Notably, there is a lack of previous reports regarding ocular brucellosis in liver transplant patients, making this the first documented case of uveitis due to *Brucella* in an organ transplant recipient. While the classical symptoms of brucellosis are well-established, it is essential to recognize rare manifestations, such as ocular brucellosis, to ensure timely intervention and potentially reduce the risk of complications.

Case Presentation

A 19-year-old male was referred for evaluation with a two-month history of fatigue, photophobia, and a mild decrease in visual acuity, presenting in May 2022. He was admitted to the hospital due to the presence of a fever. Initially, a nasopharyngeal sample was collected for a coronavirus disease 19 polymerase chain reaction test due to suspicions of infection. However, the test result was negative, and the patient did not exhibit any upper respiratory symptoms, leading to a consultation with an infectious disease specialist. Upon primary evaluation, the patient showed no signs of musculoskeletal manifestations. He had undergone a liver transplant 10 years ago due to familial hyperlipidemia and was taking Cellcept and

Tacrolimus daily as antirejection medications. Moreover, he had a background as a rancher and farmer and reported a history of consuming small amounts of raw milk, but not so regularly in the past.

Physical examination was normal, and there was only a slight eye redness and photophobia (Figure 1) and fever.

The laboratory results were placed after physical examination. In addition, hematologic and biochemical parameters in initial evaluation were reported, including hemoglobin test: 11 (reference value: 12.5–16.5 g/dL); white blood count: 3,300 (reference value: 4.0–10×1000 mm³); platelet count: 92000 (reference value: 150–450×1000 mm³); erythrocyte sedimentation rate: 24 (reference value: 0–15 mm/h); total bilirubin: 0.75 (0.1–1.2 mg/dL); aspartate aminotransferase: 69 (reference value: up to 40 IU/L); alkaline phosphatase: 178 (reference value: 70–330 IU/L); alanine transaminase: 75 (reference value: up to 37 IU/L), and C-reactive protein positive (Table 1).

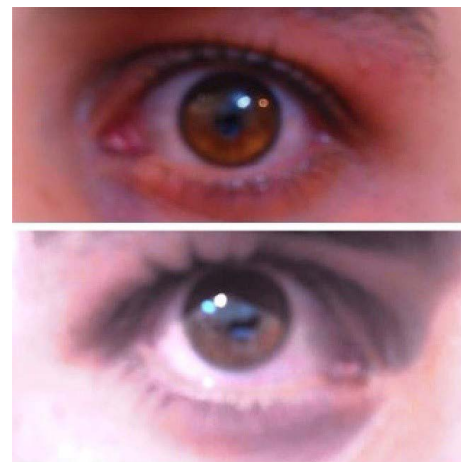


Figure 1. Ocular Involvement

Note. Our patient was a 19-year-old man with anterior uveitis: a red, sore, and inflamed eye with blurred vision and sensitivity to light. He was a livestock farmer and had a history of liver transplants. He was referred with a 2-month history of fatigue, photophobia, and a mild decrease in visual acuity in the eyes in May 2022. He was admitted to the hospital because of a fever.

Table 1. Laboratory Data From the Patient at Different Follow-up Times

Laboratory Data	Admission	Seven Days Later	Two Months Later	Three Months Later
WBC (n × 10 ⁹ /L)	3300	4490	4760	6000
HB (g/dL)	11	10.7	15.1	16
PLT/mm ³	92000	139000	124000	145000
AST (IU/L)	69	30	31	38
ALT (IU/L)	75	54	24	45
ALP (U/L)	178	173	150	244
BIL (mg/dL)	0.75	0.58	0.8	-
ESR (mm/h)	24	-	-	4
WRIGHT TEST	1/320	-	-	Negative
2ME	1/160	-	-	Negative

Note. WBC: White blood cells count; HB: Hemoglobin; PLT: Platelet count; AST: Aspartate aminotransferase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; BIL: Bilirubin; ESR: Erythrocyte sedimentation rate; WRIGHT test and 2ME test; *Brucella* serological diagnostic test.

This change in liver enzymes and pancytopenia was unexpected. The patient had normal liver enzymes and a complete blood count test in the previous two months, and there were no changes to the patient's medication type or dosage, including tacrolimus and CellCept. Further evaluations and ophthalmology consultation were performed because the patient was a livestock farmer with a history of liver transplantation.

According to the history and occupation of the patient, tests related to brucellosis were requested. The Brucella agglutination tests, including Wright: 1/640, 2ME: 1/320, and Coombs Wright: 1/640, were positive (Table 1).

A thorough slit-lamp examination, which is the cornerstone for evaluating anterior uveitis, was conducted to assess the depth and clarity of the anterior chamber. Both the conjunctiva and sclera exhibited hyperemia (redness) with notable injection patterns (Figure 1). No signs of corneal edema or keratitis precipitates were observed. Utilizing a beam of light, the anterior chamber was examined for the presence of cells and flare; no signs of hypopyon were detected. Inflammatory cells were present, quantified using a standardized scale, with a mild inflammation in the anterior chamber (Figure 2). Iritis was noted, characterized by alterations in color. Intraocular pressure measurements were within normal limits. The posterior segment was also evaluated for signs of edema, hemorrhage, or exudates, and the retina appeared intact.

The ophthalmoscopic examination revealed the presence of anterior uveitis, characterized by the inflammation of the iris and ciliary body, along with visible cells and cellular aggregates in the anterior chamber (Figure 2). Although we considered obtaining samples from the anterior chamber for further investigation, we ultimately decided against it due to the patient's lack of consent. To rule out other potential causes of the uveitis, additional tests were ordered, including angiotensin-converting enzyme levels, venereal disease research laboratory tests, and screening for human leukocyte



Figure 2. Photographs of Slit Lamp Findings on Anterior Uveitis Examination. *Note.* Utilizing a beam of light, the anterior chamber was examined for the presence of cells and flare; no signs of hypopyon were detected. Inflammatory cells were present, quantified using a standardized scale, with a count of 1+(1-5 cells), indicating mild inflammation.

antigens (HLA-B27 and HLA-5), as well as rheumatoid factors. All these tests returned normal results. Treatment for brucellosis was initiated based on the results of the tests, examinations, and a comprehensive analysis of the clinical manifestations, epidemiological data, and serological findings. The patient was treated with gentamicin, doxycycline, and cotrimoxazole. However, after one week of treatment, the eye symptoms worsened, leading to a follow-up consultation with ophthalmology. The subsequent ophthalmological examination revealed that the patient's visual acuity in both eyes remained 20/20, and the retinas appeared intact upon ophthalmoscopy. There was no change in the vision or inflammation of the anterior chamber compared to the previous examination. As a result, fluticasone eye drops were initiated.

During subsequent clinical and ophthalmological examinations, the patient's ocular symptoms resolved, and the ophthalmoscopic examination returned normal results. The patient was treated with gentamicin, doxycycline, and cotrimoxazole in the first week. He was discharged and completed a twelve-week outpatient treatment course with doxycycline 100 mg twice daily, cotrimoxazole 800/160 mg every 12 hours, and ciprofloxacin 500 mg every 12 hours.

Results

To our best knowledge, this is the first reported case of uveitis attributed to *Brucella* infection in an organ transplant patient. Although uveitis caused by various opportunistic infections is not uncommon among organ transplant recipients undergoing immunosuppressive therapy, the presence of eye redness in a livestock farmer with a liver transplant living in a brucellosis-endemic region should promptly prompt suspicion of brucellosis. Diagnosis in such cases relies on a combination of clinical manifestations—including fever—as well as epidemiological and serological findings. Based on the standard treatment for complicated brucellosis, the patient underwent a three-month course of a three-drug regimen. Throughout this treatment period, the patient received regular monitoring, which included weekly follow-up visits to assess adherence to the treatment protocol, manage potential side effects or complications arising from the medication, and evaluate the response through clinical and paraclinical examinations. The patient was treated with gentamicin, doxycycline, and cotrimoxazole in the first week and then was discharged and completed a twelve-week outpatient treatment course with doxycycline 100 mg twice daily, cotrimoxazole 800/160 mg every 12 hours, and ciprofloxacin 500 mg every 12 hours. The patient's symptoms, including ocular discomfort and fever, completely resolved within four weeks, with no relapses occurring during the subsequent 24-month follow-up period, which was conducted monthly. Additionally, *Brucella* serology tests demonstrated a decline over three months.

Discussion

Based on the literature review, ocular involvement and ophthalmic manifestations are rare in patients with brucellosis (8, 11-14). Two articles documented the first case of ocular involvement in humans with brucellosis in 1924 (7, 8). Over a span of 26 years, Rolando et al evaluated a total of 1,551 patients diagnosed with brucellosis at Nacional Cayetano Heredia Hospital, among whom 52 individuals presented with ocular brucellosis. Their findings revealed that 7 out of 965 patients with acute brucellosis (0.7%) and 45 out of 570 patients with chronic brucellosis (7.9%) exhibited ocular involvement. Uveitis was the predominant ocular manifestation, affecting 34 (82.7%) of the patients with ocular brucellosis, with posterior uveitis being identified as the most common ocular syndrome. Patients diagnosed with panuveitis showed the poorest visual prognosis (7). In a subsequent study conducted in 2009, Rolando et al analyzed intraocular fluid and biopsy specimens from 12 patients who exhibited clinical and laboratory indicators suggestive of brucellar uveitis. This cohort included seven patients with uveitis from other etiologies who served as control subjects. The results indicated that four patients (33.3%) with ocular brucellosis tested negative for ocular agglutination, while eight (66.7%) demonstrated positive results. Importantly, no positive agglutination results were observed for *B. melitensis* among the control cases. Consequently, the sensitivity of the test was calculated to be 66.7%, with a specificity of 100%. Notably, only one patient exhibited a positive culture for *B. melitensis* in the subretinal fluid (11). The underlying mechanisms contributing to ocular damage in brucellosis may involve the presence of Brucella bacteria during the acute phase of infection. In the chronic phase, such damage may be mediated by specific antibodies and immune complexes, which can disrupt vascular permeability within the uveal tissue (13). This disruption could lead to either temporary or persistent changes, resulting in acute, transient, or recurrent episodes of uveitis (15).

However, some studies reported that after treatment for brucellosis, patients experienced a resolution of symptoms without recurrence. While the overall recovery rate for brucellosis patients with ocular manifestations was relatively low, approximately 37.1% of patients demonstrated significant recovery (14,17).

A diagnosis of ocular brucellosis was typically made through clinical examination and serological tests, while excluding other differential diagnoses (Table 2). The use of anterior chamber fluid to detect Brucella antibodies has been previously employed; however, there may be instances where the volume of fluid is inadequate for precise detection. Current limitations in diagnostic testing underscore the need for alternative approaches. In our patient, the combination of clinical manifestations, epidemiological data, and serological findings suggested a diagnosis of anterior uveitis caused by Brucella.

In most cases of ocular involvement, patients typically present with accompanying systemic symptoms of brucellosis (Table 2). However, our literature review identified a unique case of recurrent uveitis occurring in the absence of systemic symptoms of brucellosis (18). In contrast to these studies, our patient exhibited no musculoskeletal symptoms. To date, there have been no reported cases of ocular involvement in transplant patients with brucellosis in the existing literature. This case represents the first documented instance of uveitis attributed to Brucella in an organ transplant recipient. While ocular involvement in organ transplant patients can arise from a wide variety of causes, the patient's occupational history and clinical presentation raised suspicion for Brucella-related ocular involvement. Upon ruling out other differential diagnoses, Brucella agglutination tests returned positive results, and ophthalmoscopic evaluation confirmed the presence of anterior uveitis. The clinical signs and symptoms of brucellosis are often nonspecific, necessitating a diagnosis based on a comprehensive assessment that includes clinical manifestations, fever, and both epidemiological and serological findings.

Treatment for ocular brucellosis is comparable to that of other forms of brucellosis. However, in organ transplant recipients, it is essential to consider potential drug interactions due to the immunosuppressive medications they are taking to prevent transplant rejection. Rifampin, a medication commonly used for Brucella treatment, can affect the efficacy of anti-rejection drugs. Specifically, rifampin is known to enhance the activity of CYP3A4 and P-glycoprotein enzymes, which may decrease the levels of anti-rejection medications such as tacrolimus (19,20). In this case, rifampin was removed from the brucellosis treatment regimen due to the patient's use of tacrolimus. Therefore, close monitoring of drug interactions is imperative for patients receiving both rifampin and immunosuppressive therapy, or a drug regimen without such interactions should be taken into consideration. The patient was treated with gentamicin, doxycycline, and cotrimoxazole in the first week. He was discharged and completed a twelve-week outpatient treatment course with doxycycline 100 mg twice daily, cotrimoxazole 800/160 mg every 12 hours, and ciprofloxacin 500 mg every 12 hours.

Conclusion

Although uveitis caused by various opportunistic infections is not uncommon among organ transplant patients who are undergoing treatment with immunosuppressive medications, it is important to specifically consider Brucella infections in areas where Brucella is endemic. In such areas, healthcare providers should perform appropriate investigations for Brucella in these cases to ensure accurate diagnosis and appropriate treatment.ase
add conclusion section.

Table 2. Patients With Brucella Uveitis Reviews

Case	Gender/Age	Etiological Diagnosis	Clinical Presentation	2 ME Test	Wright Test
Xi et al (21)					
1	F/57	Acute	Knee and waist pain	–	25
AlMutairi et al (22)					
1	F/31	Acute	Bilateral knee pain, fever, and upper respiratory infection	–	80
Akyol et al (23)					
1	F/28	Subacute	Backache and hip pain		640
Mohammadi et al (24)					
1	F/7	Chronic	Wrist pain, fever, and anorexia	160	160
Hatipoglu et al (25)					
1	F/56	Acute	Fever, knee, and back pain		640
2	M/30	–	–		2560
Akduman et al (26)					
1	F/16	Acute	Fever, sweating, malaise, and joint and muscle pain		20
Walker et al (27)					
1	M/56	Acute	Fevers and night sweats		640
Gasser et al (28)					
1	F/52	Acute	Suspected tumor sited in left breast		320
Tabbara and Al-Kassimi (29)					
1	F/34	Acute	Headache and paravertebral abscess	–	1644
Lidgett and Wilson (30)					
1	M/24	Acute	Fever	–	160
Rolando et al (31)					
1	F/36	Subacute/chronic	Six months of decreased visual acuity	0	0
2	M/13	Subacute/chronic	Diagnosis of brucellosis 7 months ago and 2 months of decreased visual acuity	640	1280
3	M/22	Subacute/chronic	Diagnosis of brucellosis +7 months of decreased visual acuity, red eye, and ocular pain	80	1280
4	F/45	Subacute/chronic	Two months of decreased visual acuity and arthralgia	0	10
5	F/59	Subacute/chronic	Decreased visual acuity and 3 years of low back pain	80	2560
6	F/60	Subacute/chronic	Decreased visual acuity, 6 episodes of recurrent uveitis, and diagnosis of brucellosis 7 years ago	0	160
7	F/19	Subacute/chronic	Red eye and decreased visual acuity	80	640
8	M/28	Subacute/chronic	Red eye and decreased visual acuity and arthralgia	0	0
9	M/36	Subacute/chronic	Eight months of decreased visual acuity	160	1280
10	M/31	Subacute/chronic	Decreased visual acuity	80	640
11	F/28	Subacute/chronic	Eight months of decreased visual acuity	0	640
12	F/53	Subacute/chronic	Two years of progressively decreased visual acuity	40	640

Note. F: Female; M: Male; 2ME: 2-Mercapto Ethanol test.

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Authors' Contribution

Conceptualization: Shiva Shabani.

Data curation: Shiva Shabani.

Investigation: Shiva Shabani, Shirin Shabani.

Methodology: Shiva Shabani.

Validation: Shiva Shabani.

Writing—original draft: Shiva Shabani.

Writing—review & editing: Shiva Shabani.

Competing Interests

The authors declare that they have no competing interests.

Consent Statement

Informed consent has been taken from the authors to publish this report in Journal of clinical case reports. Written informed consent has been obtained from patient to publish this report in accordance with the journal's patient consent policy.

Data Availability Statement

The data during the current study are available from the corresponding author on reasonable request.

Declaration of Patient Consent

Written informed consent has been obtained from patient to publish this report in accordance with the journal's patient consent policy.

Ethical Approval

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