

A rare presentation of retinal vasculitis with Roth spot in a brucellosis patient without endocarditis

Ecem Önder Tokuç¹, Özlem Güler², Hatice Ceren Kabaoğulları¹, Levent Karabaş¹

ABSTRACT

Purpose: Brucellosis is a zoonotic infection that can manifest in various forms, including neurobrucellosis. This case study aims to highlight a rare ocular involvement of brucellosis in a young, previously healthy male, specifically focusing on a unique presentation of severe vision loss, retinal vasculitis, and Roth's spot.

Methods: Single-center, case report.

Results: This case study reports on a 25-year-old male patient who was previously healthy and presented with severe vision loss, optic disc edema, extensive vasculitis, and Roth spot in a single eye due to ocular involvement associated with brucellosis. The diagnosis of brucellosis was confirmed through laboratory tests, including the tube agglutination test, which had a positive titer of 1/160. The patient was administered systemic antibiotics, including doxycycline, rifampin, and ceftriaxone, along with steroids. The treatment resulted in an improvement in the patient's vision and the resolution of ocular lesions within three months.

Conclusion: Roth spots are primarily associated with subacute infective endocarditis. Our case is unique as *Brucella*-induced Roth's spot without endocarditis has not been previously reported.

Key Words: *Brucella*, Retinal vasculitis, Retinal hemorrhage, Papilledema

INTRODUCTION

Brucellosis is the most prevalent zoonotic disease in the world and is endemic in the Mediterranean region, Eastern Europe, the Middle East, Africa, South and Central America, and Asia (1). It is caused by a gram-negative bacterium of the genus *Brucella*, which is transmitted by consuming unpasteurised dairy products and improperly cooked meat (2,3). It can also be transmitted by contact with abrasions of the skin, conjunctiva of the eye, or inhalation of aerosols (4). The diagnosis of brucellosis can be challenging because it does not have any distinguishing features and can be observed in various clinical forms (3). Brucellosis has a wide range of disease expression, from acute febrile

illness to chronic infection, most commonly infecting the central nervous system, the cardiovascular system, or the skeletal system (1). Although ocular involvement is rare, any ocular structure can be affected (5). The diverse ocular manifestations of both acute and chronic infections extend to include uveitis, keratitis, conjunctivitis, papillitis, cataracts, maculopathies, glaucoma, and muscle paresis (5). In this case study, we report the case of a young male adult who experienced severe vision loss, optic disc edema, extensive vasculitis, and Roth spot in a single eye due to ocular involvement associated with brucellosis. Our case is noteworthy because there are no reports in the literature of brucellosis presenting with Roth spots, and in this context,

1 Kocaeli University School of Medicine, Ophthalmology, Kocaeli, Türkiye

2 Kocaeli University School of Medicine, Infectious Diseases and Clinical Microbiology, Kocaeli, Türkiye

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Correspondence author:

Ecem Önder Tokuç

Email: drecem@yandex.com

the Roth spots observed in our patient may be considered secondary to occlusive retinal vasculitis.

CASE PRESENTATION

A 25-year-old male patient presented with a rapid loss of vision in the left eye. The patient reported caring for goats and consuming raw goat milk. He had no history of additional diseases, except for experiencing arthralgia for the past four months. Ocular examination showed a visual acuity of 20/20 in the right eye and hand motion in the left eye, with normal pupillary light reflexes and intraocular pressures. Anterior segment examinations were unremarkable bilaterally.

Posterior segment examination revealed moderate cells in the posterior vitreous, preretinal hemorrhage with peripapillary flame-shaped nerve fiber layer hemorrhage, optic disc infiltration, and Roth spots in the left eye (Figure 1a). These Roth spots suggested that they had developed secondary to occlusive retinal vasculitis, as supported by the associated vascular findings. Perivascular sheathing was particularly noticeable in the veins of the lower nasal quadrant of the optic disc. Fundus Fluorescence angiography (FFA) revealed vascular narrowing in the same vessel. Optical coherence tomography (OCT) revealed subretinal fluid and cystoid macular edema at the fovea, along with optic disc edema (Figure 1b, 1c). FFA also revealed staining of the vascular wall, hypofluorescence due to bleeding blockage, and late leakage along the inferior retinal venula (Figure 2).

Laboratory tests indicated a sedimentation rate (ESR) of 20 mm/h and highly positive C-reactive protein (CRP) level (74 mg/dL), suggestive of a generalized inflammatory process. The total leukocyte count was 12,500/mm³ and the neutrophil count was 8,870/mm³. Imaging studies, including chest radiography and brain computerized tomography (CT), were unremarkable, and echocardiography ruled out infective endocarditis. A peripheral blood smear revealed no atypical cells.

Tests for rheumatoid factor (RF), antinuclear antibodies (ANA), antinuclear cytoplasmic antibodies (ANCA), and anti-DNA antibodies were negative, ruling out collagen vascular disease. The PPD test result was 5 mm, and the patient had a BCG vaccination scar in the left arm deltoid region. The interferon gamma release assay (IGRA) was negative; therefore, latent and active tuberculosis were excluded from the patient. In addition, no findings in favor of tuberculosis were observed in the patient's PAAG. Serum ACE and lysozyme levels were within normal ranges, as were blood calcium and 24-hour urine calcium levels. Tests for *Borrelia burgdorferi* and *Bartonella henselae* IgG and IgM yielded negative results. Meanwhile, the patient's Brucella tube agglutination test titer increased fourfold within ten days, and brucellosis was finally accepted as the etiology of the present clinical picture. VDRL-RPR, syphilis ELISA, and TPHA test results were negative for syphilis. Further tests for Lyme disease, HIV, EBV, CMV, and tuberculosis were also negative.

The tube agglutination test confirmed brucellosis, with a positive titer of 1/160. The treatment involved administering systemic doxycycline (100 mg twice daily), rifampin (600 mg once daily), and ceftriaxone (2000 mg twice daily) for two weeks. Subsequently, doxycycline rifampin and trimethoprim sulfamethoxazole were continued for three months. Systemic prednisolone (1 mg/kg/day) was initiated during the ten days of systemic antibiotic therapy. The patient received treatment for a duration of three months. Steroid treatment was gradually tapered and ultimately discontinued over the 3-month treatment period.

By the third day of treatment, the patient's visual acuity improved from counting fingers at 30 cm to 20/125; however, vision was only perceivable from the inferior aspect. Roth spots resolved within three days, and within two weeks, optic disc edema significantly decreased, with an improvement in visual acuity to 20/100 (Figure 3). No recurrence of uveitis was noted during the 6-month follow-up period. (Figure- 4)

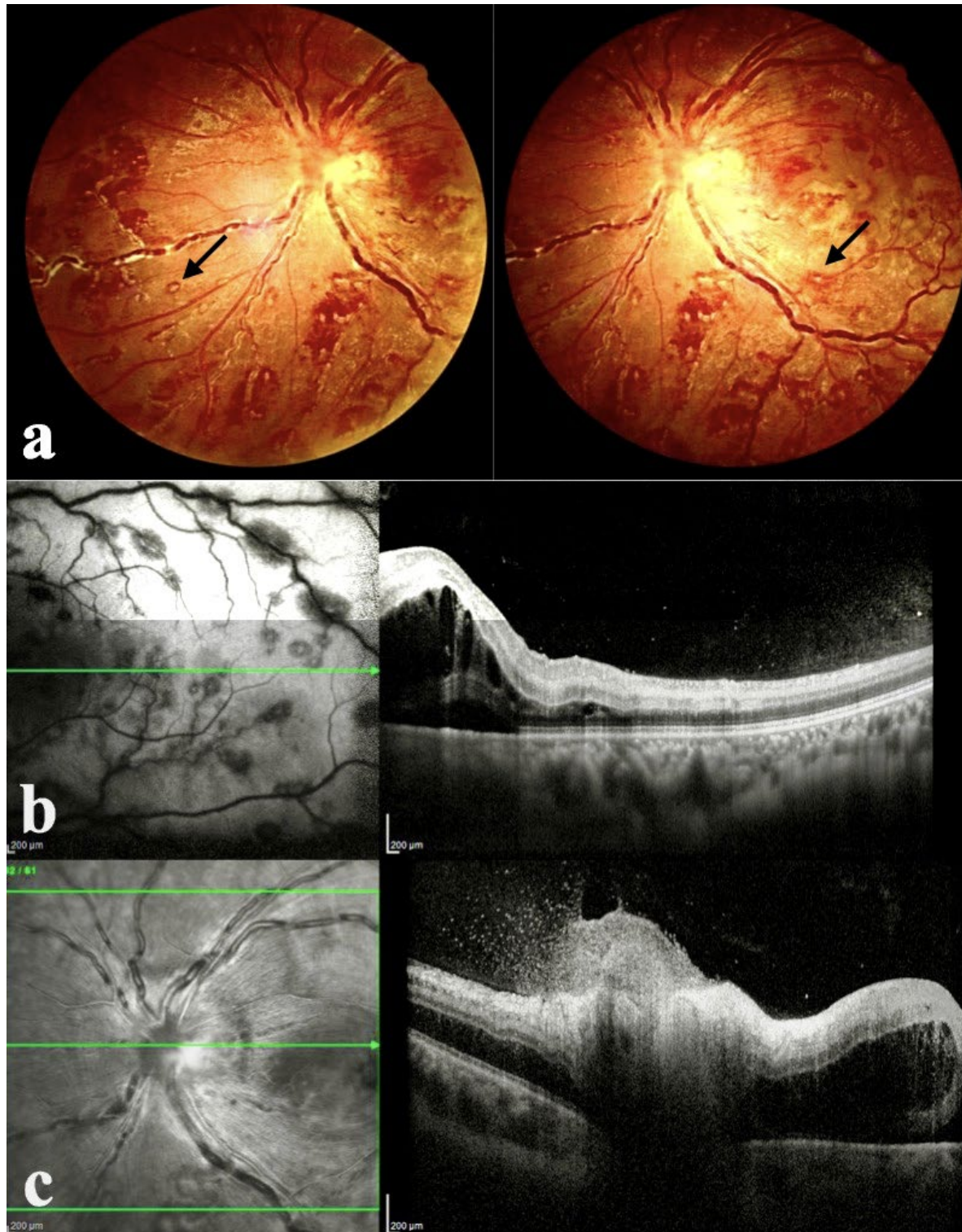


Figure 1. Initial patient examination showing extensive Roth spots in the posterior pole and on the nasal side of the optic disc, with black arrows indicating some of the Roth spots (a). The OCT images of the patient demonstrate the presence of intraretinal and subretinal fluid (b), optic disc edema, and inflammatory accumulation on the optic disc (c).

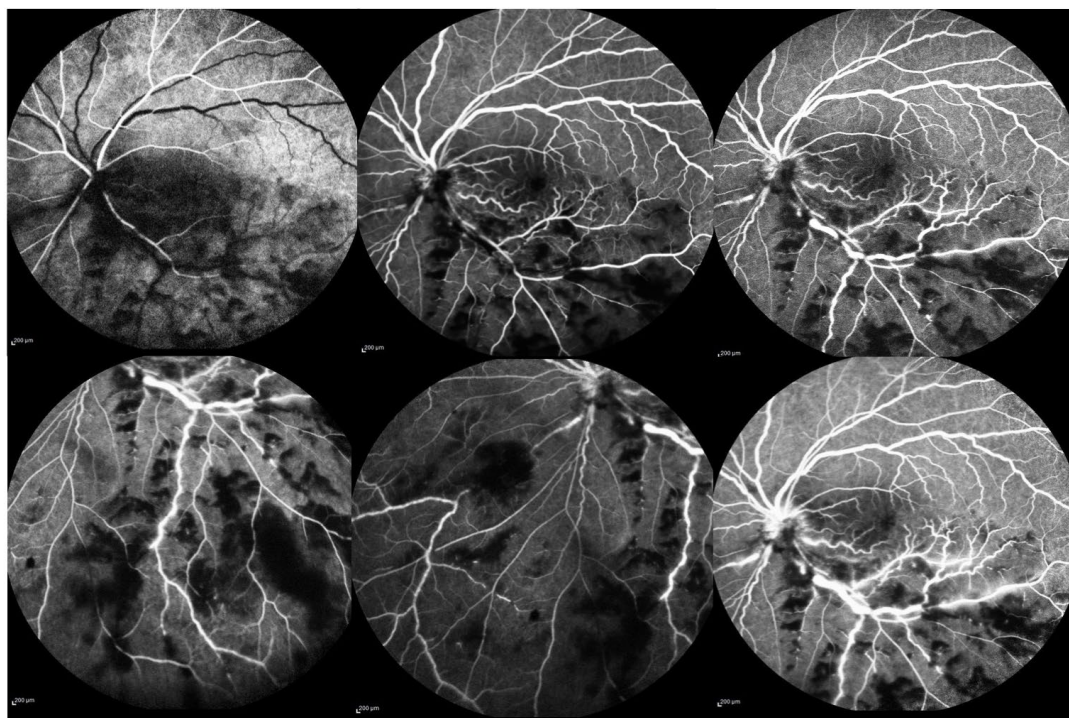


Figure 2. FFA images obtained during the initial examination revealed hemorrhage blockade, vasculitic involvement, and late leakage in the inferior temporal vein.

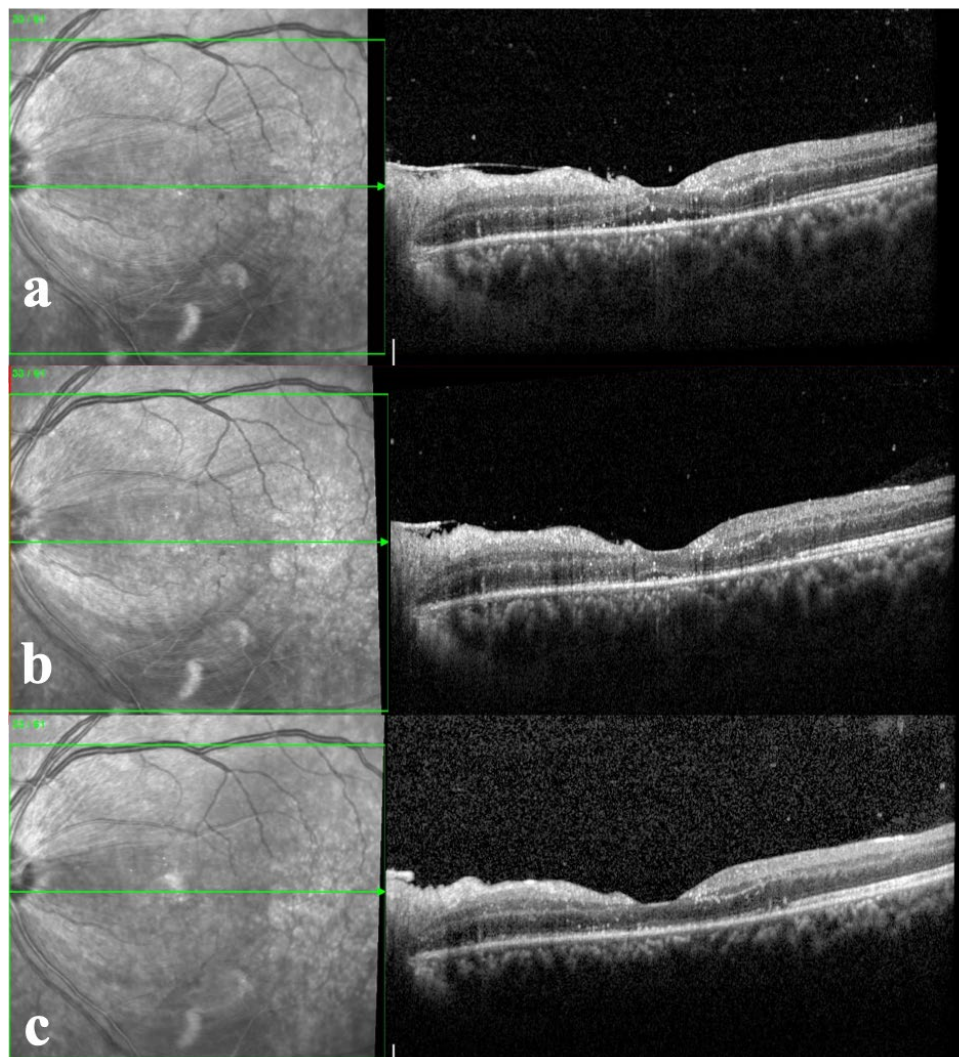


Figure 3. Following antibiotic and steroid treatment, OCT images indicate a reduction in subretinal and intraretinal fluid (a,b). By the 2nd week of treatment, a complete recession of the subretinal fluid and a decrease in inflammation were observed (c).

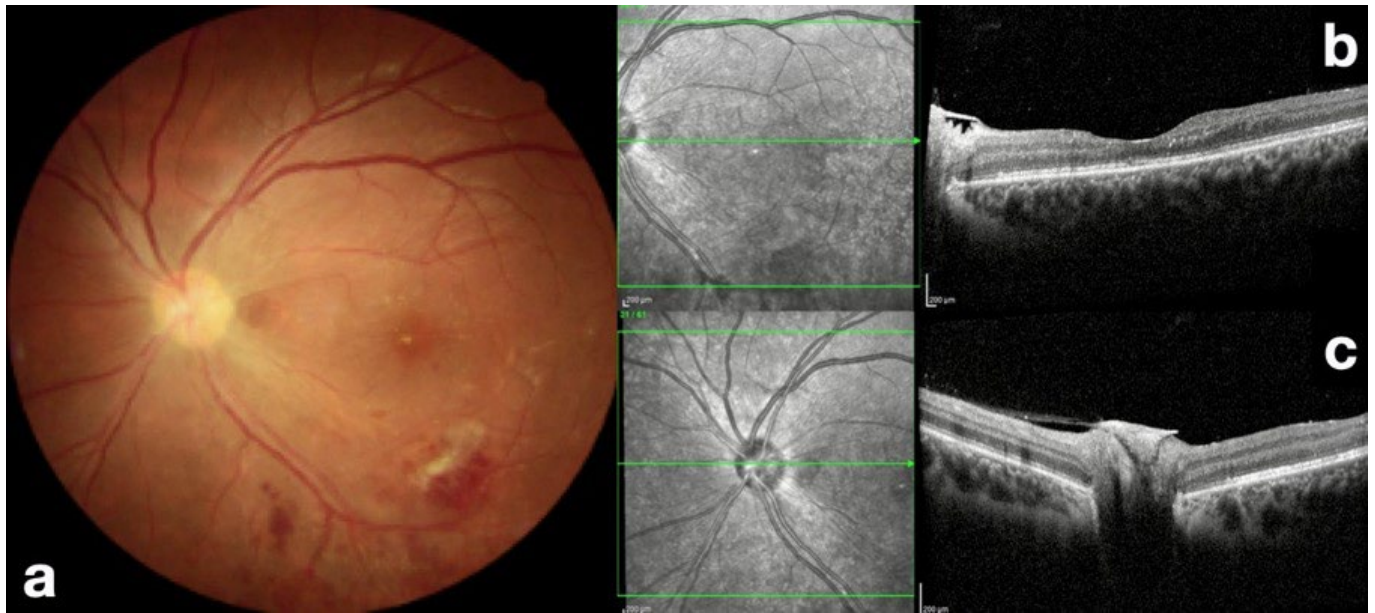


Figure 4. The fundus photo shows a significant disappearance of Roth spots (a). Macula-OCT reveals improvement in the External Limiting Membrane (ELM) and Ellipsoid Zone (EZ) (b). On optic disc OCT, inflammation receded and was replaced by a fibrotic band that did not create macular traction (c).

DISCUSSION

Brucellosis usually starts as an acute illness with fever, and if left untreated, can develop into a systemic disease with ongoing symptoms such as recurring fever, fatigue, arthritis, lethargy, and general discomfort, as well as occasional enlargement of the liver and spleen (2). Transmission in endemic countries commonly occurs through the consumption of unpasteurized infected dairy products, whereas in developing nations, it is often associated with occupational exposure. Occupations at high risk include animal breeders, butchers, veterinarians, and laboratory workers (6). Our patient was actively involved in animal husbandry and reported consuming cheese obtained from the goats that he raised. In our case, there was no prior diagnosis or treatment of brucellosis. The patient presented with ocular involvement, without significant fever. Rheumatological investigations were conducted based on vasculitic-like involvement. However, apart from the positive *Brucella* Tube Agglutination (Wright) test, no other positive findings were observed. We initiated treatment considering that the ocular findings were related to brucellosis ocular involvement. Our case presents an exceptional demonstration of optic neuropathy, Roth spots, and retinal vasculitis in brucellosis patients.

The incidence of neurobrucellosis ranges from 0.5-25% and can cause meningitis, meningoencephalitis, meningovascular involvement and peripheral neuropathy. In neurobrucellosis, damage is due to direct bacterial impact and cytokine and endotoxin damage caused by inflammation. Hence, brucellosis can cause damage not only in the brain and peripheral nervous system but also in the optic nerve, often manifesting as optic nerve edema (7). In cases of optic nerve edema associated with *Brucella* infection, one possible pathogenesis is vasculitis is a characteristic manifestation of brucellosis (8). *Brucella* infection induces an immune-mediated response in the central nervous system, leading to vasculopathy, which is strongly linked to diseases affecting the optic nerve (4). Optic disc edema can develop as a secondary condition due to inflammation caused by demyelination behind the optic nerve bulb (4). This is a result of axoplasmic flow obstruction in unmyelinated axons of the optic nerve head. Optic nerve head infiltration and swelling due to *Brucella* infection have been reported previously in some reports (8,9). A possible pathogenesis of this condition is associated with vasculitis. In our case, fundus examination revealed decreased clarity of the optic nerve head borders, optic nerve head infiltration, and concentrated vitreous

inflammation over optic nerve head. In the late period, this inflammation resulted in fibrosis that did not cause traction.

Cavallaro et al. previously reported a case of a 14-year-old male with brucellosis who showed bilateral optic disc edema and was treated with antimicrobial therapy alone, without the need for corticosteroids or anti-inflammatory therapy, resulting in complete visual recovery (9). Abd Elrazak et al. reported a case of *Brucella* optic neuritis that was effectively treated with a combination of anti-*Brucella* therapy and corticosteroids, leading to full recovery of visual acuity (10). In our case, the existing subretinal fluid was considered inflammatory and a faster response to steroid treatment was anticipated. A reduction in subretinal fluid was observed upon addition of 1 mg/kg steroids after completing the appropriate duration of antimicrobial therapy. The antimicrobial treatment administered to the patient consisted of rifampicin 1x600 mg, doxycycline 2x100 mg, and ceftriaxone 2x2 grams. After two weeks, the patient was switched to doxycycline 2x100 mg, trimethoprim and sulfamethoxazole 2x1, rifampicin 1x600 mg for 12 weeks. The patient received treatment for a duration of three months.

Roth spots are defined as white-centered retinal hemorrhages and are most commonly associated with various systemic diseases, notably bacterial endocarditis (11). They can also be manifestations of *Brucella* endocarditis. *Brucella* can lead to various complications, yet cardiovascular involvement is rare, occurring in less than 2% of cases (12). In clinical practice, this involvement typically presents as endocarditis. Endocarditis frequently affects the aortic valve, is often diagnosed late, and results in significant morbidity and mortality. In patients diagnosed with *Brucella* who present with Roth spots on fundus examination, a high index of suspicion and thorough clinical history are essential to avoid overlooking the complication of infective endocarditis. However, since Roth spots are nonspecific ocular signs, they can also be observed in systemic infections, cardiac pathologies, dental infections, intravenous drug use, immune deficiencies, and other chronic conditions (such as hypertension, anemia, and known hematological disorders). Roth spots may also accompany various hematological disorders such as thrombocytopenia, anemia, leukemia, and septicemia; therefore, a thorough evaluation of patients for

common hematological symptoms (such as weight loss, fatigue, abnormal bleeding) and laboratory parameters is recommended (11). In our patient, we performed a comprehensive diagnostic laboratory work-up, including peripheral blood smear, which excluded hematological disorders. Consequently, the Roth spots were attributed to *Brucella* infection and occlusive vasculitis. Numerous hypotheses have been proposed to elucidate the pathogenesis of Roth spots, with the most widely accepted being retinal capillary rupture and intraretinal hemorrhage (11). Retinal capillary rupture arises from endothelial cell dysfunction, leading to extravasation of red blood cells, vessel rupture, activation of the coagulation cascade, and the formation of a platelet-fibrin plug at the site of endothelial damage. Histopathological studies demonstrate that Roth spots are predominantly composed of platelet-fibrin thrombi. During the initial examination of the present case, Roth spots were observed along with vasculitis. Interestingly, no signs of endocarditis were initially detected or at subsequent follow-ups. Over time, we observed regression of the Roth spots with systemic antibiotic therapy and steroid treatment. Various reports in the literature discuss *Brucella* involvement in the optic nerve; however, cases of retinal vasculitis accompanied by Roth spots without signs of endocarditis have not been reported. In this case, we believe that the Roth spots developed secondary to occlusive retinal vasculitis, as suggested by the baseline imaging findings.

In summary, brucellosis can lead to various systemic and ocular complications such as vasculitis, optic neuritis, and retinal hemorrhage. No specific diagnostic features clearly indicate ocular involvement due to brucellosis. *Brucella* infection is rare in non-endemic regions, and accurate diagnosis may be challenging. Clinicians should take into account the ocular pathology associated with brucellosis during the diagnostic process. Early pharmacological intervention for ocular lesions associated with *Brucella* infection can play a crucial role in preserving and restoring vision.

Statements & Declarations

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Competing Interests

The authors declare that they have no conflicts of interest.

Consent to participate

The patient provided informed consent for publication of his disease and ocular findings.

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