Original Article

A Case Series of Cat-Scratch Disease with Ocular Manifestations: Clinical Findings and Treatment Approach

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Abstract

Objectives: To present the clinical and demographic characteristics, imaging findings, diagnosis and treatment approach in cases of cat scratch disease (CSD) with ocular involvement.

Materials and Methods: The records of 19 patients followed-up and treated between 2010 and 2020, including detailed ophthalmological examinations, imaging findings, and treatment approach, were evaluated retrospectively.

Results: Twenty-three eyes of 19 patients, 7 female (37%) and 12 male (63%), were included in the study. The mean age was 34.1±13.3 (range: 11-56) years, and the mean follow-up duration was 12.6±18.0 (range: 1-81) months. Unilateral involvement was observed in 15 cases (79%). Cat contact was reported in 14 cases (74%). In 6 cases (32%), flu-like symptoms were present before the ocular complaints. The mean visual acuity (VA) at presentation was 0.42±0.36 (range: 0.001-1.0). Anterior uveitis was observed in 3 eyes (13%). Posterior segment findings included neuroretinitis in 14 (61%), superficial retinal infiltrate(s) in 8 (35%), papillitis in 3 (13%), branch retinal artery occlusion in 2 (8%), and cilioretinal artery occlusion in 1 (4%) of the eyes. All cases were positive for *Bartonella henselae* immunglobulin (Ig)M and/or IgG. Systemic antibiotic therapy was administered to all patients. Intravenous pulse or oral corticosteroids were given, especially in cases with optic disc involvement. The mean final VA was 0.80±0.25 (range: 0.01-1.0).

Conclusion: CSD may present with different ocular involvement patterns. Apart from the classical neuroretinitis and macular star appearance, patients may present with isolated optic disc edema, branch retinal artery occlusion, and retinal infiltrations. In such patients, cat contact history and *Bartonella* serology should be evaluated to differentiate CSD.

Keywords: Cat scratch disease, neuroretinitis, imaging, treatment, prognosis, branch retinal artery occlusion

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Introduction

Cat scratch disease (CSD) is a systemic disease first described by Parinaud in 1889 and caused by the gram-negative bacillus *Bartonella henselae*.[1,2] The main reservoir is the cat, and the cat flea is thought to be a vector.[3,4] CSD is transmitted by cats through scratching or biting. Approximately 90% of patients have a history of cat contact.[4] Children and adolescents, veterinarians, and cat owners are at increased risk.[2,3,5] human immunodeficiency virus (HIV) positivity is also a risk factor for *Bartonella* infection.[2,6] The incidence of CSD was reported to be 9.3/100,000 in the United States.[7] In two studies conducted in Türkiye, seropositivity rates were 3.3% and 6% among healthy individuals. This rate was reported as 12.5% in veterinarians and 26.5% in cat owners.[8,9]

Lymphoid involvement is most commonly observed in CSD.[10] The disease, also known as Parinaud's oculoglandular syndrome, presents with other symptoms such as granulomatous conjunctivitis, preauricular lymphadenopathy, and fever.[10] It has a self-limited course in immunocompetent people under the age of 20 years. Papules and pustules form at the inoculation site after 3-10 days. Systemic symptoms develop after local infection and regress spontaneously within a few weeks. In immunocompromised individuals, disseminated infection may cause serious clinical manifestations such as endocarditis, encephalitis, meningitis, pneumonia, and osteomyelitis.[10,11,12]

Ocular involvement occurs in 5-10% of CSD patients.[13] Ocular involvement can manifest as granulomatous conjunctivitis and preauricular lymphadenopathy, as in Parinaud's oculoglandular syndrome, but can also present with different clinical manifestations, such as neuroretinitis, anterior uveitis, intermediate uveitis, focal/multifocal chorioretinitis, choroidal mass, retinal infiltrate, branch retinal vein or artery occlusion, serous retinal detachment, or acute endophthalmitis.[12,14] CSD is the most common known cause of neuroretinitis.[15,16] *B.*

henselae seropositivity is detected in two-thirds of neuroretinitis patients.[15,16] Although *B. henselae* is the most common cause, neuroretinitis is detected in only 1-2% of infected individuals.[13]

In addition to the role of history (cat contact) and clinical findings in the diagnosis of ocular CSD, serology and imaging such as fundus fluorescein angiography (FFA) and optical coherence tomography (OCT) are also important for a definitive diagnosis. In this study, we aimed to evaluate the clinical and demographic characteristics, imaging findings, diagnosis, and treatment approach of 19 patients with ocular involvement of CSD.

Materials and Methods

The clinical and demographic characteristics of 19 patients who were followed up and treated for CSD in the uvea units of Ulucanlar Eye Training and Research Hospital and Beyoğlu Eye Training and Research Hospital between 2010 and 2020 were evaluated retrospectively. The study was conducted in accordance with the principles of the Declaration of Helsinki. All patients' demographic information, detailed ocular and systemic disease history, detailed ophthalmological examinations at admission and during follow-up (consisting of best corrected visual acuity [BCVA] by Snellen chart, intraocular pressure [IOP] measurement, anterior segment and dilated fundus examination), OCT (Heidelberg Engineering, Hedielberg, Germany) and FFA (Visucam 500, Carl Zeiss Meditec AG, Jena, Germany) imaging findings, and treatment approaches were evaluated. Patients also underwent routine analysis of complete blood count/biochemistry, acute phase reactants (erythrocyte sedimentation rate, C-reactive protein), *B. henselae* immunglobulin (Ig)M/IgG serology, syphilis serology, hepatitis markers, and HIV enzyme-linked immunosorbent assay (ELISA), as well as additional laboratory tests if deemed necessary based on history and examination findings.

Results

The study included 23 eyes of 19 patients, 7 women (37%) and 12 men (63%). The patients' mean age was 34.1±13.3 years (range: 11-56 years) and the mean follow-up time was 12.6±18.0 months (range: 1-81 months). In terms of systemic comorbidity, 2 patients (10.5%) had diabetes mellitus. Involvement was unilateral in 15 patients (78.9%) and bilateral in 4 patients (21.1%). HIV positivity was detected in 2 patients with bilateral involvement (10.5%). History of cat contact was present in 14 patients (73.6%) but not in the other 5 patients (26.4%) (Table 1). The presenting complaint was decreased visual acuity in all cases, and 6 patients (31.6%) had systemic symptoms associated with CSD such as recent or ongoing malaise, flu-like symptoms, fever, or diarrhea.

The patients' mean BCVA at admission was 0.42±0.36 (range: 0.001-1.0); BCVA was ≤0.1 in 8 eyes (34.7%), 0.2-0.5 in 7 eyes (30.4%), and ≥0.6 in 8 eyes (34.7%). The mean IOP was 15.2±1.83 mmHg (range: 14-19 mmHg). Relative afferent pupillary defect (RAPD) was observed in 7 patients (36.8%) but not in the other 12 patients (63.1%), including the 4 patients with bilateral involvement. Three eyes (13.0%) exhibited anterior chamber reaction and 1 eye (4.3%) had granulomatous keratic precipitation, while anterior segment findings were normal in the other eyes. Vitritis with or without vitreous haze was detected in 11 eyes (47.8%). Posterior segment findings included neuroretinitis (Figure 1) in 14 eyes (60.8%), superficial retinal infiltrate (Figure 2) in 8 eyes (34.7%), papillitis (Figures 3 and 4) in 3 eyes (13.0%), branch retinal artery occlusion (Figure 5) in 2 eyes (8.1%), and cilioretinal artery occlusion in 1 eye (4.3%). The patients' clinical findings are summarized in Table 1.

Serological tests for *B. henselae* revealed both IgM and IgG positivity in 8 patients (42.1%), only IgG positivity in 9 patients (47.4%), and only IgM positivity in 2 patients (10.5%). The patients' laboratory results and systemic and ocular imaging findings are summarized in Table 2.

All patients received either single or combined oral antibiotics (ciprofloxacin [Cipro 500 mg, Biofarma Pharmaceuticals, Türkiye], rifampicin [Rifcap 300 mg, Koçak Pharmaceuticals, Türkiye], azithromycin [Azitro 500 mg, Deva Pharmaceuticals, Türkiye], trimethoprim-sulfamethoxazole [Bactrim Forte 800/160 mg, Deva Pharmaceuticals, Türkiye], doxycycline [Tetradox 100 mg, Teva Pharmaceuticals, Türkiye]). The mean treatment duration was 8.8±5.4 weeks (range: 4-24 weeks). Patients with anterior segment inflammation were treated with topical corticosteroid (prednisolone acetate; Pred Forte 1%, Allergan Pharmaceuticals, Ireland) and cycloplegic (cyclopentolate hydrochloride; Sikloplejin 1%, Abdi İbrahim Pharmaceuticals, Türkiye) eye drops. Seventeen patients (89.5%) were also given systemic corticosteroid therapy (methylprednisolone; Prednol tablet 16 mg, Gensenta, Türkiye) while receiving antibiotic therapy. Of these, 4 patients (21.0%) with severe optic disc edema were switched to maintenance oral corticosteroid therapy after 3 days of intravenous pulse methylprednisolone (1 g/day), Prednol-L 250 mg, Mustafa Nevzat İlaç, Türkiye while the other 13 patients (68.4%) received oral corticosteroid therapy (0.5-1 mg/kg/day). Oral corticosteroid therapy was tapered and discontinued according to the patient's clinical condition. Two patients (11.1%) (Patients 6 and 9) were not treated with corticosteroids. Patient 9 received highly active antiretroviral therapy (zidovudine [Retrovir, 250 mg, GlaxoSmithKline Pharmaceuticals, Poland]; lamivudine [Zeffix 100 mg, Pharmactive İlaç, Türkiye]; efavirenz [Stocrin 600 mg, MSD Pharmaceuticals, China]) for HIV positivity.

Regression of clinical findings was observed in all patients after treatment, and BCVA improved in all patients except one (Patient 10). The patients' mean BCVA at last follow-up was 0.80±0.25 (range: 0.01-1.0), with BCVA ≤0.1 in 1 eye (4.3%), 0.2-0.5 in 2 eyes (8.7%), and ≥0.6 in 20 eyes (87.0%). Because vision was impaired due to cilioretinal artery occlusion in Patient 10, there was no increase in BCVA after treatment. The treatment approach, follow-up periods, and final BCVA of the patients are summarized in Table 3.

Table 1. Demographic characteristics and clinical findings

Patient	Age (years)/ sex	Cat contact	Side	VA	RAPD	Anterior segment	Vitreous	Fundus
1	50/F	Yes	Right	0.3	Slight +	Quiescent	1+ vitritis, 0.5+ haze	OD edema, hemorrhagic retinitis focus at inferior margin of OD, macular star
2	56/F	Yes	Left	HM	+	Granulomatous KP, 1+ cells	2+ vitritis, 2+ haze	OD edema, large hemorrhagic retinitis focus inferotemporal of OD
3	37/M	Yes	Bilateral	0.7/0.7	-	Quiescent	Quiescent	Bilateral OD edema, superficial retinal infiltrate in the right foveal region
4	24/M	Suspected	Right	0.4	+	Quiescent	Quiescent	OD edema, small area of hemorrhage in the fovea
5	19/M	Yes	Right	0.1	+	Quiescent	1+ vitritis	OD edema, macular star
6	40/M	Yes	Right	0.5	-	Quiescent	Quiescent	superficial infiltrate at OD margin, temporal peripheral artery occlusion
7	38/F	Yes	Left	0.01	Slight +	Quiescent	1+ vitritis, 0.5+ haze	Edema at OD margins, peripapillary and macular exudate, areas of retinal vasculitis and hemorrhage
8	47/M	No	Right	0.3	-	4+ cells	1+ vitritis	OD edema, infiltration, retinal hemorrhages in the posterior pole
9	29/M	No	Bilateral	1.0/1.0	-	Quiescent	Quiescent	White spots in the bilateral midperiphery, Right inferotemporal artery occlusion and retinal hemorrhage
10	32/M	No	Bilateral	0.01/0.6	-	Quiescent	Quiescent	Bilateral OD edema, right macular edema, exudates, Left macular exudate
11	11/M	Yes	Right	0.01	+	Quiescent	1+ vitritis	OD edema, macular star
12	21/M	Yes	Right	0.16	+	Quiescent	1+ vitritis	OD edema, macular star
13	49/F	Suspected	Right	0.3	-	Quiescent	Quiescent	OD edema, macular star
14	49/F	Yes	Right	0.02	+	Quiescent	1+ vitritis	OD edema, macular star
15	20/M	Yes	Left	0.01	-	Quiescent	Quiescent	OD edema, macular star
16	39/F	Suspected	Right	0.3	-	Quiescent	1+ vitritis	Retinitis focus 1/3 of OD diameter superonasal of the fovea
17	21/M	Yes	Right	0.5	-	Quiescent	Quiescent	OD edema, macular star
18	45/F	Yes	Bilateral	0.7/1 .0	-	1+ cells	Right quiescent, Left 1+ vitritis	Right retinitis focus, soft exudates, and hemorrhages Left retinitis focus, OD edema, macular star
19	20/M	Yes	Right	1.0	-	Quiescent	1+ vitritis, 1+ haze	Papillitis, retinitis focus superior to the OD

F: Female, M: Male, HM: Hand movements, VA: Visual acuity, RAPD: Relative afferent pupillary defect, KP: Keratic precipitate, OD: Optic disc

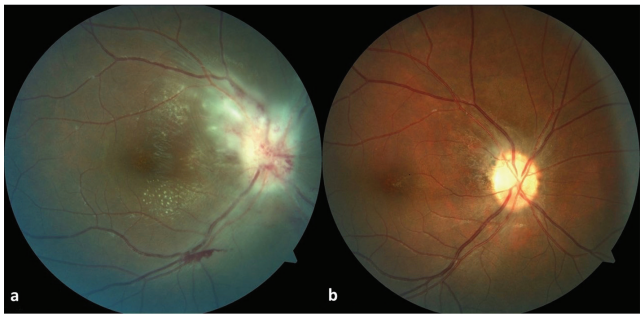

Figure 1. Case 5, patient with neuroretinitis in the right eye. Color fundus photograph shows optic disc edema, peripapillary areas of superficial retinal hemorrhage, and macular exudates with macular star sign (a). Fundus photograph 6 months after treatment shows disc pallor and peripapillary and macular pigment changes (b)

Discussion

This study presents the epidemiological features, different clinical findings, and results of different treatment regimens in CSD with ocular involvement. CSD is a systemic disease with global distribution caused by the gram-negative bacillus *B. henselae*.[2] Although usually passed to humans through cat contact, it is also transmitted by the parasites of cats.[3,4] In a study conducted in the USA, seropositivity was detected in 10-40% of domestic cats.[4] A history of cat contact has been reported in more than 90% of CSD cases.[13] In our series, 74% of the patients had a history of cat contact.

CSD is known in the literature as a disease that generally affects the under-20 population, independent of gender and race.[2,3] However, Oray et al.[17] reported in a Turkish study that

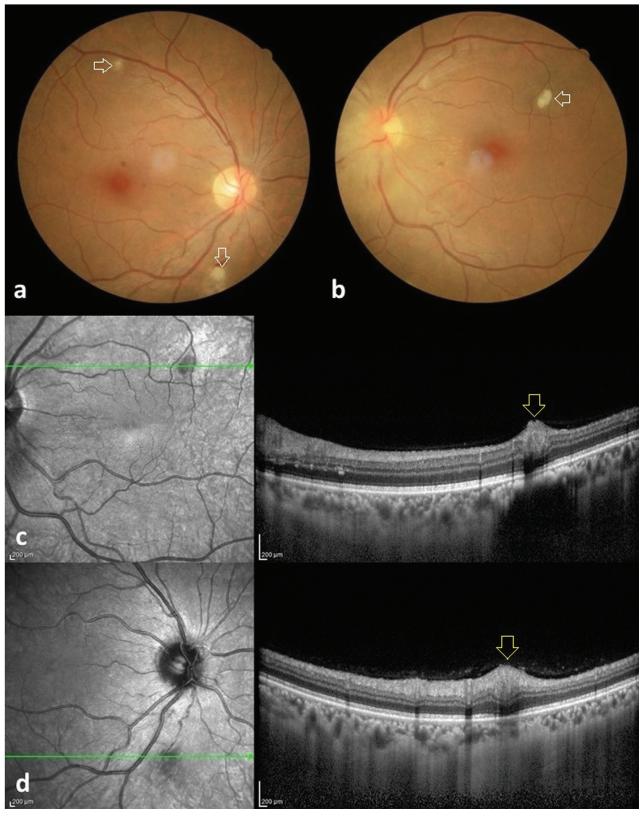

Figure 2. Case 18, patient with bilateral superficial retinal infiltrate and neuroretinitis in the left eye. Right eye fundus photograph shows superficial retinal infiltrates (white arrow) (a). Left eye fundus photograph shows disc edema, exudate and superficial retinal hemorrhages in the macula, and a superficial retinal infiltrate focus in the midperiphery (b). Optical coherence tomography sections through the infiltrates show superficial hyperreflective retinitis foci (yellow arrow) (c-d)

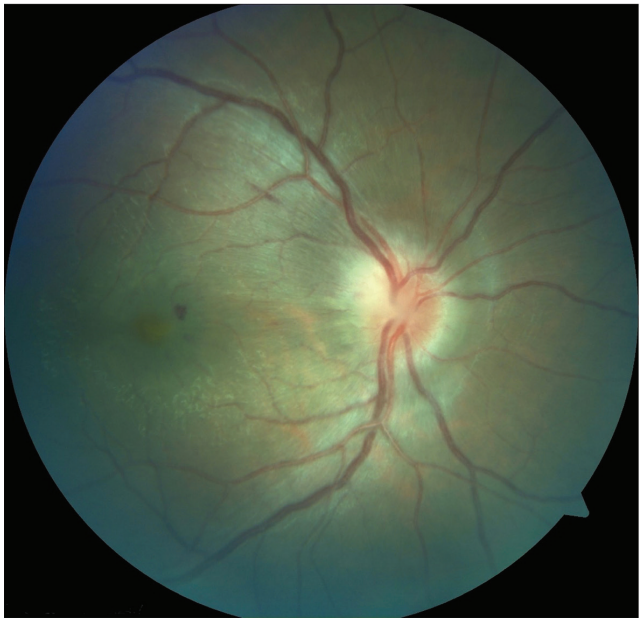

Figure 3. Case 4, patient with isolated papillitis in the right eye. Color fundus photograph shows optic disc edema and hyperemia

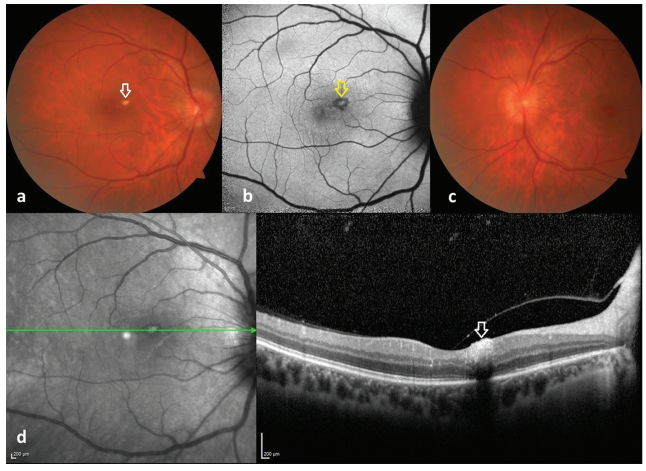

Figure 4. Case 3, HIV-positive patient with bilateral involvement. Right eye color fundus photograph shows papillitis and superficial retinal infiltrate focus in the macula (white arrow) (a). In the right eye fundus autofluorescence image, the superficial retinitis focus is observed as a lesion with inner isofluorescence and peripheral hypoautofluorescence (yellow arrow) (b). Left eye fundus photograph shows isolated papillitis (c). Right eye optical coherence tomography shows a superficially located hyperreflective retinitis focus (white arrow) adjacent to the fovea (d)

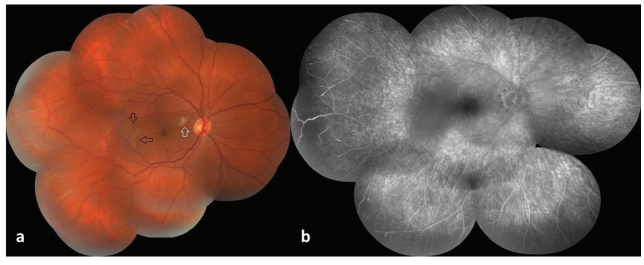

Figure 5. Case 6, patient with branch retinal artery occlusion and superficial retinal infiltration in the right eye. Color fundus photograph revealed a superficial retinitis focus temporal to the optic disc (white arrow) and branch retinal artery occlusion in the temporal macula (black arrows) (a). Fundus fluorescein angiography shows an area of nonperfusion temporal to the macula (b)

adults accounted for 50% of the patients in their series of CSD with ocular involvement. Curi et al.[18] reported that 71% of CSD patients with ocular involvement were over the age of 18. Similar to these studies, 95% of the patients in our series were adults, and we had only one patient in the pediatric age group.

The most common form of ocular involvement in CSD patients is neuroretinitis.[12,13,19] Neuroretinitis is characterized by sudden, painless loss of vision on one side. Although generally unilateral, bilateral cases have been reported in the literature.[20,21] In a study conducted by Chi et al.[22] with 62 eyes of 53 patients, neuroretinitis was observed in 28 eyes (45%) and 9 patients (17%) had bilateral involvement. We also observed that neuroretinitis was the most common ocular manifestation (61%) (Figure 1a). Unilateral involvement was observed in 79% and bilateral involvement was detected in 21% of the patients. HIV positivity was detected in two patients with bilateral involvement (Figure 4).

Table 2. Laboratory and imaging findings of the patients

Patient	Ocular involvement	Laboratory *Bartonella henselae*	Ocular imaging	Other imaging
1	Right neuroretinitis	IgG+	FFA: OD hyperfluorescence, hypofluorescence in hemorrhagic areas, macular leakage	
2	Left neuroretinitis	IgG+	FFA: OD and macular leakage OCT: Serous macular detachment	Brain MRI: normal (with diagnosis of optic neuritis)
3	Bilateral papillitis Right superficial retinal infiltrate	IgM+ anti-HIV+	FFA: Bilateral OD hyperfluorescence, right eye hypofluorescence in the infiltrate area OCT: Infiltrate involving inner retinal layers on the right FAF: lesion with isofluorescent interior and hypoautofluorescent margins (superficial infiltrate)	
4	Right papillitis	IgG+		
5	Right neuroretinitis	IgM+		
6	Right superficial retinal infiltrate, branch artery occlusion	IgG+	FFA: Infiltrate with inner hypofluorescence and peripheral hyperfluorescence at OD margin, peripheral arterial occlusion OCT: PAMM appearance corresponding to area of artery occlusion in right macula	
7	Right neuroretinitis and retinal vasculitis	IgM+/IgG+	FFA: OD hyperfluorescence, hypofluorescence of hemorrhagic areas, infiltrate with inner hypofluorescence and peripheral hyperfluorescence, arteriole filling defect OCT: Foveal exudate	Brain MRI: normal
8	Right neuroretinitis	IgG+	FFA: OD hyperfluorescence, hypofluorescence in hemorrhagic areas OCT: Serous macular detachment, cystoid macular edema	
9	Bilateral retinitis, right branch artery occlusion	IgM+/IgG+ anti-HIV+	FFA: Bilateral OD hyperfluorescence, hypofluorescence in areas corresponding to lesions OCT: Superficial retinal hyperreflective lesions	
10	Bilateral neuroretinitis, right cilioretinal artery occlusion	IgG+	FFA: Bilateral OD hyperfluorescence, right cilioretinal artery occlusion OCT: Right serous macular detachment, bilateral macular edema	
11	Right neuroretinitis	IgM+/IgG+	FFA: Right OD leakage OCT: Subretinal fluid	Right arm MRI: pathological lymph nodes in the epicondyle and axilla
12	Right neuroretinitis	IgM+/IgG+	FFA: Right OD leakage	
13	Right neuroretinitis	IgM+/IgG+	FFA: Right OD leakage	Brain MRI: normal Orbital MRI: normal
14	Right neuroretinitis	IgM+/IgG+	FFA: Right OD leakage OCT: Right subretinal fluid and hyperreflective dots	Brain MRI: normal Orbital MRI: normal
15	Left neuroretinitis	IgM+/IgG+	FFA: Left OD leakage	
16	Right superficial retinal infiltrate	IgG+	FFA: Early hypo-, late hyperfluorescent juxtavascular hyperfluorescent focus/retinitis superonasal to the right fovea	
17	Right neuroretinitis	IgG+		
18	Bilateral superficial retinal infiltrate, left neuroretinitis	IgM+/IgG+	FFA: Right retinitis-related hyperfluorescence, Left OD leakage, retinitis-related hyperfluorescence, peripheral vascular leakage OCT: Left serous macular detachment and hyperreflective dots	
19	Right papillitis, superficial retinal infiltrate	IgG+	FFA: Right OD leakage, retinitis area with inner hypofluorescence and peripheral hyperfluorescence	

Ig: Immunglobulin, FFA: Fundus fluorescein angiography, OCT: Optical coherence tomography, FAF: Fundus autofluorescence, PAMM: Paracentral acute middle maculopathy, MRI: Magnetic resonance imaging

Table 3. Treatment approach and follow-up results of the patients

Patient	Treatment	Follow-up (months)	Post-treatment VA
1	Doxycycline 2x100 mg (1 month), Oral methylprednisolone 32 mg (6 weeks)	1	0.5
2	Azithromycin 500 mg (21 days), TMP-SMX 2x1 2 months, 1x1 2 months (total 4 months) IV pulse methylprednisolone (3 days), oral 64 mg with tapering (3 months)	4	0.8
3	Doxycycline 2x100 mg (1 month), Ciprofloxacin 2x500 mg (2 weeks), Oral methylprednisolone 32 mg (6 weeks)	6	0.9/0.9
4	Doxycycline 2x100 mg (1 month) Oral methylprednisolone 64 mg (6 weeks)	2	0.9
5	Azithromycin 1,000 mg (10 days) TMP-SMX 2x1 (3 months) IV pulse methylprednisolone (3 days), oral 64 mg with tapering (3 months)	7	0.8
6	Doxycycline 2x100 mg (1 month)	1	0.7
7	Doxycycline 2x100 mg (1 month) IV pulse methylprednisolone (3 days), oral 64 mg with tapering (3 months)	2	0.6
8	Azithromycin 1,000 mg (10 days) TMP-SMX 2x1 (3 months) Oral methylprednisolone 64 mg (6 months)	18	1.0
9	HAART+ Doxycycline 200 mg (1 month)	1	1.0/1.0
10	Azithromycin 1,000 mg (10 days) TMP-SMX 2x1 (3 months) IV pulse methylprednisolone (3 days), oral 64 mg with tapering (3 months)	81	0.01/0.8
11	Doxycycline 2x100 mg Azithromycin 500 mg (2 weeks) TMP-SMX 2x1 (5 weeks) Oral prednisolone 16 mg (6 weeks)	21	0.7
12	Rifampicin 1x300 mg Doxycycline 2x100 mg Oral prednisolone 48 mg with tapering (3 months)	18	0.9
13	Doxycycline 2x100 mg Azithromycin 500 mg Oral prednisolone (6 weeks)	6	1.0
14	Rifampicin 1x300 mg Doxycycline 2x100 mg Oral prednisolone (6 weeks)	8	0.6
15	Rifampicin 1x300 mg Ciprofloxacin 2x500 mg Oral prednisolone (3 months)	14	0.4
16	Doxycycline 2x100 mg TMP-SMX 2x1 Oral prednisolone (6 weeks)	3	0.9
17	Doxycycline 2x100 mg TMP-SMX 2x1 Oral prednisolone (6 weeks)	12	1.0
18	Doxycycline 2x100 mg Azithromycin 500 mg (2 weeks) Oral prednisolone 16 mg (6 weeks) Followed by rifampicin and ciprofloxacin	20	1.0/1.0
19	Doxycycline 2x100 mg TMP-SMX 2x1 Oral prednisolone 48 mg (6 weeks)	6	1.0

TMP-SMX: Trimethoprim-sulfamethoxazole, HAART: Highly active antiretroviral therapy, IV: Intravenous, VA: Visual acuity

Optic disc involvement is an important sign of CSD neuroretinitis. Optic disc edema with optic disc leakage on FFA is observed and may be accompanied by peripapillary subretinal fluid. Macular star appears an average of 1-4 weeks after disc edema.[21] Star formation can be peripheral or partial, and usually involves the nasal macula.[21] Disc edema and macular star may persist for 6-12 months.[23,24] Ocular CSD can present with isolated optic disc involvement, without macular involvement. As macular star formation occurs after 1-4 weeks, patients may present with only optic disc edema.[21] CSD should be considered in the differential diagnosis of unilateral optic disc edema, especially in young adult patients. In our study, isolated optic disc involvement (papillitis) was observed in one case (Patient 4; Figure 3), unilateral papillitis and superficial retinitis were observed in one case (Patient 19), and bilateral isolated papillitis with superficial focal retinitis in one eye was observed in one case (Patient 3; Figure 4).

Chi et al.[22] detected RAPD in 40 (90%) of 44 unilateral cases. In our study, RAPD was positive in only 7 (46%) of 15 patients with unilateral involvement.

In CSD, ocular involvement can also manifest as multifocal retinitis or focal chorioretinitis, without optic disc edema or macular star.[18,19] Serous retinal detachment may occur in the peripapillary and macular regions.[21] Ocular CSD can also present with retinal infiltrates. These infiltrates appear as soft exudates involving the superficial retinal layers, with internal hypofluorescence and peripheral hyperfluorescence on FAF.[25] In the case series of 37 eyes reported by Curi et al.,[18] focal retinitis was reported as the most common ocular involvement, at a rate of 30% (11 eyes). Solley et al.[19] reported in a different study of 35 eyes that retinitis and choroiditis were the most common (83%) ocular manifestations of CSD. In our study, retinal infiltrate was detected in 8 eyes (35%) and was the most common form of ocular involvement after neuroretinitis (Figure 4a, Figure 5a).

Other causes of infectious and non-infectious neuroretinitis should be investigated in the differential diagnosis of CSD-related neuroretinitis. These include malignant hypertension, central retinal vein occlusion, anterior ischemic optic neuropathy, diabetes, pseudotumor cerebri, sarcoidosis, Behçet's disease, tuberculosis, syphilis, *Toxocara*, and Lyme disease.

B. henselae infection predisposes to thrombosis because of its tropism for vascular endothelium and erythrocytes.[26,27] Clinicians should be vigilant for retinal vessel occlusion, especially in patients with retinitis and retinal infiltrates. Branch retinal artery occlusion has been reported in many case series.[28,29,30,31] Habot-Wilner et al.[32] reported branch retinal artery occlusion in 4%, branch retinal vein occlusion in 3%, and branch retinal artery and vein occlusion in 1% of eyes in their retrospective case series including 107 eyes. In our study, retinal artery occlusion was observed in 13% of the cases, including branch retinal artery occlusion in 2 patients (Figure 5) and cilioretinal artery occlusion in 1 case, whereas branch retinal vein occlusion was not observed in any case. The site of arterial occlusion is one of the main factors determining pre- and post-treatment visual acuity. In our study, visual acuity decreased to less than 0.1 in a patient with central vision loss due to cilioretinal artery occlusion, and no increase in vision was observed after treatment.

CSD is diagnosed based on clinical (systemic and/or ophthalmologic) symptoms and findings; serologic tests support the diagnosis. A high *B. henselae* IgM titer is an indicator of acute infection, and values typically return to normal within 3 months. *B. henselae* IgG level gradually increases and remains positive for up to 2 years. Positive *B. henselae* IgM or high *B. henselae* IgG titer is sufficient to diagnose CSD.[32,33] In our study, *B. henselae* IgM and/or IgG positivity was detected in all cases.

When diagnosing CSD, ocular imaging findings support the diagnosis. Isolated optic disc leakage without macular leakage on FFA is an important finding in cases of CSD with primary papillitis.[34] OCT is another important imaging method that demonstrates macular edema and exudative retinal detachment in CSD.[35] It can also show edema and thickening around the optic disc.[35] In addition, OCT sections through lesions play the most important role in visualizing superficial retinitis foci (Figure 2c,d). Although clinical findings offer the most important clues in the diagnosis of CSD, serology and imaging are indispensable aids in differential diagnosis and supporting the diagnosis.

Ocular CSD is a self-limited infection in individuals without immunodeficiency. Therefore, randomized controlled trials of treatments are not possible, and there is no definitive treatment guideline.[25] Systemic antibiotic therapy is recommended for patients with immunodeficiency, severe systemic disease, and vision-threatening ocular involvement (e.g., neuroretinitis, papillitis, retinitis).[21] Doxycycline, tetracycline, and erythromycin are first-line antibiotics in systemic therapy, while ciprofloxacin, rifampin, and trimethoprim-sulfamethoxazole can also be used as alternatives.[36] Combinations of these antibiotics were frequently used in our study (Table 3). Doxycycline and azithromycin and trimethoprim-sulfamethoxazole are the most commonly used systemic antibiotics. There are publications in the literature indicating that the use of oral or intravenous steroids in combination with systemic antibiotic therapy positively affects visual outcomes.[33] In their retrospective case series, Habot-Wilner et al.[32] emphasized that combined antibiotic and corticosteroid treatment yielded better final visual acuity compared to antibiotic treatment alone, especially in patients with optic disc involvement and low initial visual acuity. All patients in our study received corticosteroid treatment except for one without optic disc involvement and two with HIV infection (Patients 6 and 9).

Our study is the largest case series evaluating the clinical features, imaging findings, and treatment approach of CSD with ocular involvement reported in our country.

Conclusion

CSD can manifest not only with neuroretinitis but also with various clinical presentations such as papillitis, retinitis, branch retinal artery occlusion, and retinal infiltrations. CSD should be considered in patients with superficial retinal infiltrate and retinal artery occlusion, especially young patients. History of cat

contact should be questioned in patients with clinical suspicion of CSD, but the absence of this history does not exclude the diagnosis, and patients with a consistent clinical presentation should be assessed for *Bartonella* serology.

Ethics

Ethics Committee Approval: Ankara Training and Research Hospital (number: E-93471371-514.01.99/date: 09.12.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: P.Ç.Ö., B.B., Ç.A., Ö.B., Concept: A.A., P.Ç.Ö., K.Ö.Y., Design: A.A., P.Ç.Ö., K.Ö.Y., Data Collection or Processing: A.A., P.Ç.Ö., B.B., K.Ö.Y., Ç.A., Ö.B., Analysis or Interpretation: A.A., P.Ç.Ö., B.B., K.Ö.Y., Ç.A., Ö.B., Literature Search: A.A., P.Ç.Ö., B.B., Writing: A.A., P.Ç.Ö., B.B.

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