Int Ophthalmol (2010) 30:553–558
DOI 10.1007/s10792-010-9389-5

ORIGINAL PAPER

Cat-scratch disease: ocular manifestations and visual outcome

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Received: 27 January 2010 / Accepted: 18 July 2010 / Published online: 30 July 2010
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Abstract To describe the intra-ocular manifestations of cat-scratch disease (CSD) found at two uveitis reference centers in Brazil. Retrospective case series study. Review of clinical records of patients diagnosed with CSD in the Uveitis Department of São Geraldo Hospital and the Ophthalmology Department of the Instituto de Pesquisa Clínica Evandro Chagas—FIOCRUZ, from 2001 to 2008. In the 8-year period, 24 patients with the diagnosis of CSD were identified. Twelve patients were male and 12 female. The mean age was 27.04 years (range 7–56). Sixteen patients (66.6%) presented with a history of a cat scratch and all patients reported cat exposure. Visual acuity ranged from counting fingers to 1.0 in the affected eye. Thirteen patients presented with bilateral disease. Sixteen (66.6%) patients complained of systemic symptoms, including fever, lymphadenopathy, liver and spleen enlargement and rash. All patients presented with serum antibodies (IgG) to *Bartonella henselae*. Thirty-seven eyes were affected. The most common findings were small areas of retinal infiltrates which occurred in 11 eyes (29.7%) and angiomatous lesions which occurred in nine eyes (24.3%). Neuroretinitis occurred in only six eyes (16.2%). The most common findings of CSD in our study were retinal infiltrates and angiomatous lesions. CSD patients may present with significant visual loss. Patients may benefit from systemic treatment with antibiotics.

Keywords Cat-scratch disease · Neuroretinitis · Retinitis

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Introduction

Cat-scratch disease (CSD) is a systemic disease caused by the Gram-negative rod *Bartonella henselae*. Ocular manifestation of CSD was primarily reported as a chronic ulcerative conjunctivitis, associated with lymphadenopathy, called Parinaud ocular glandular syndrome. In 1970 Sweeny and Drance described the first case of neuroretinitis associated with CSD [1], with several studies of intra-ocular manifestations of CSD being published since. Intra-ocular changes secondary to *B. henselae* infection include neuroretinitis, subretinal lesions, retinitis, intermediate uveitis, inflammatory masses, and angiomatous lesions [2].

The aim of this study is to report the ocular manifestations and visual outcomes of CSD found at two Brazilian uveitis reference centers.

Patients and methods

The authors reviewed the clinical records of patients diagnosed with CSD at the Uveitis Department of São Geraldo Hospital, Federal University of Minas Gerais and at the Ophthalmology Department of the Instituto de Pesquisa Clínica Evandro Chagas—FIOCRUZ, over a period of 8 years.

Patients were eligible for the study if they presented with intra-ocular changes and serologic evidence of *B. henselae* infection (IgG). Serological analysis was performed by indirect immunofluorescence assay, cut off 1:64, using a commercial kit (*Bartonella henselae* IFA IgG; Bion, Illinois, USA).

All patients underwent complete ophthalmologic examination (visual acuity—Snellen chart, biomicroscopy, tonometry, fundoscopy), fundus photography, fluorescein angiography (FA) and indocyanine green angiography (ICG) where necessary. Patients with positive serology for the human immunodeficiency virus (HIV) were not excluded (Table 1).

This study was approved by the institution's ethics committee.

Results

Twenty-four patients, 12 male and 12 female, presented with ocular changes as a result of CSD. The group had a mean age of 27.04 years, ranging from 7 to 56. Sixteen patients (66.6%) reported a cat scratch and all patients had a history of cat exposure. Systemic findings included fever (eight patients), lymphadenopathy (seven patients), liver and spleen enlargement (one patient), headache (two patients), rash (one patient), and aseptic meningitis (one patient). Thirteen patients (54.1%) presented with a bilateral disease and eleven (45.9%) unilateral (37 eyes). Visual acuities ranged from counting fingers to 20/20 in the affected eyes. Of the 37 affected eyes, 21 (56.8%) presented with visual acuity (VA) worse than 20/200 and 16 (43.2%) better than 20/200. Six eyes (16.2%) presented with mild anterior segment inflammation.

All patients presented IgG-positive for *B. henselae* and seven patients presented IgM-positive. Twenty of the 24 patients (83.3%) were treated with systemic doxycycline, three patients (12.5%) with oral ciprofloxacin and one patient (4.2%) with oral doxycycline and oral steroids. Of the 37 affected eyes, five eyes (13.5%) presented with VA worse than 20/200 after treatment and 32 (86.5%) presented with VA better than 20/200. Of the 24 patients, four (16.6%) were HIV-positive, two of whom showed ocular disease relapse following discontinuation of systemic therapy. One patient was treated for 1 month with ciprofloxacin and the second for 3 months with doxycycline. Both patients were treated after relapses where the CD4+ count reached 250 cells/mm.

Of the 37 affected eyes, six (16.2%) presented with neuroretinitis. Small areas of retinitis occurred in 11 eyes (29.7%) and subretinal lesions occurred in five eyes (13.5%) (Fig. 1). Angiomatous lesions occurred in nine eyes (24.3%) and peripapillary angiomatous lesions occurred in two eyes (5.4%) (Fig. 2a, b). Disc edema was seen in five eyes (13.5%), and two eyes (5.4%) showed optic disc inflammatory mass.

Discussion

Since 1970 when Sweeney and Drance first reported a case of CSD and neuroretinitis, this ocular manifestation has been considered by most authors to be the most common finding in cases of *B. henselae* infection.

Ormerod et al. reviewed 25 published cases of confirmed CSD associated with posterior segment inflammatory disease and found that neuroretinitis associated with macular star was the most common ocular manifestation. In this study the authors describe two cases of multiple retinal arteriolar occlusions, revealing that many other features besides neuroretinitis may occur in CSD [3]. In our study we found that six of 37 affected eyes presented with neuroretinitis. Ormerod and colleagues also described a small number of non-progressive small white intraretinal infiltrates in their two cases. Of the six eyes with neuroretinitis in our study, all eyes presented with associated small areas of retinitis/retinal

Table 1 Demographics of 24 patients with ocular manifestation of cat-scratch disease

Gender	Age (years)	Serology	Cat exposure	Cat scratch	Bilateral or unilateral	Ocular changes	Initial visual acuity	Systemic findings	Treatment	Final visual acuity	HIV status
M	16	IgM/IgG	Yes	Yes	B	Disc edema/serous detachment/retinal infiltrates	CF 30 cm/20/20	Fever/ lymphadenopathy	Doxy	20/20 BE	HIV−
F	9	IgG	Yes	No	U	Neuroretinitis	20/100/20/20	Fever/ lymphadenopathy	Cipro	20/40/20/20	HIV−
M	30	IgG	Yes	No	B	Angiomatous lesions/retinal infiltrates	20/20/CF 20 cm	None	Cipro	20/20/CF 20 cm	HIV+
F	22	IgM/IgG	Yes	Yes	B	Subretinal lesions RE/disc edema/subretinal lesions LE	20/20 BE	Cold 2 weeks	Doxy	20/20 BE	HIV−
F	26	IgG	Yes	Yes	U	Angiomatous lesions	20/30/CF 20 cm	None	Doxy	20/30/20/80	HIV−
F	56	IgM/IgG	Yes	No	B	Disc edema/vitritis	20/60/CF 20 cm	Headache	Doxy	20/30/20/160	HIV−
M	53	IgG	Yes	No	U	Angiomatous lesions RE	CF 50 cm/20/50	None	Doxy	HM/20/25	HIV+
F	7	IgM/IgG	Yes	Yes	B	Neuroretinitis/subretinal lesions	20/20/20/200	Fever/rash/ liver/Spleen	Doxy	20/20 BE	HIV−
M	12	IgM/IgG	Yes	Yes	U	Inflammatory optic disc mass	CF 30 cm/20/20	None	Doxy	20/160/20/20	HIV−
M	18	IgG	Yes	Yes	B	Retinal infiltrates RE/ peripapillary angiomatous lesion LE	20/20/20/800	None	Doxy	20/20/20/120	HIV−
M	27	IgG	Yes	No	U	Retinitis	20/20/20/800	None	Doxy	20/20 BE	HIV−
M	27	IgG	Yes	No	B	Angiomatous lesions BE	20/100 BE	Fever	Doxy	20/20 BE	HIV+
M	24	IgG	Yes	No	B	Angiomatous lesions BE	20/200/20/150	Fever	Doxy	20/80/20/100	HIV+
F	29	IgM/IgG	Yes	Yes	U	Subretinal lesions	20/200/20/20	None	Doxy	20/200/20/20	HIV−
F	14	IgM/IgG	Yes	Yes	U	Angiomatous lesions/ granulomatous lesions	20/20/20/800	Fever/ lymphadenopathy	Doxy	20/20/20/800	HIV−
F	20	IgG	Yes	Yes	B	Neuroretinitis/retinal infiltrates LE	CF 40 cm/20/100	Fever	Cipro	20/20 BE	HIV−
M	40	IgG	Yes	Yes	U	Neuroretinitis	20/70/20/20	Aseptic meningitis	Doxy	20/20 BE	HIV−
F	38	IgG	Yes	Yes	B	Retinal infiltrates BE/macular star LE	20/40/CF 4M	Lymphadenopathy	Doxy	20/20 BE	HIV−
F	42	IgG	Yes	Yes	U	Retinitis	20/100/20/20	Lymphadenopathy	Doxy	20/20 BE	HIV−

Table 1 continued

Gender	Age (years)	Serology	Cat exposure	Cat scratch	Bilateral or unilateral	Ocular changes	Initial visual acuity	Systemic findings	Treatment	Final visual acuity	HIV status
F	25	IgG	Yes	Yes	B	Disc edema RE/retinal infiltrates BE	20/20 BE	Fever/ lymphadenopathy	Doxy	20/20 BE	HIV−
M	18	IgG	Yes	Yes	U	Disc edema RE/retinal hemorrhages	20/30/20/20	Lymphadenopathy	Doxy+Pred	20/20 BE	HIV−
F	25	IgG	Yes	No	U	Neuroretinitis	20/20/CF 4M	None	Doxy	20/20/20/30	HIV−
M	45	IgG	Yes	Yes	B	Neuroretinitis/retinal infiltrates LE	20/100/20/70	Fever	Doxy	20/20 BE	HIV−
M	26	IgG	Yes	Yes	B	Optic disc granuloma RE/ retinal infiltrates LE	LP/20/20	Fever	Doxy	20/200/20/20	HIV−

B, bilateral; BE, both eyes; Cipro, ciprofloxacin; Doxy, doxycyclin; LE, left eye; Pred, prednisolone; RE, right eye; U, unilateral

Fig. 1 Fundus photography showing small whitish retinal infiltrates associated with complete macular star

Fig. 2 **a** Fundus photography showing an angiomatous lesion in the optic disk. **b** Fluorescein angiography showing hyperfluorencence of the optic disk corresponding to the angiomatous lesion

infiltrates. This association may be an important clinical feature to help ophthalmologists in the diagnosis of intra-ocular CSD.

Solley et al. published a study of 24 patients (35 eyes) with ocular manifestation of *Bartonella* infection and they found that isolated foci of retinitis or choroiditis were the most common ocular manifestations of CSD. Of the 35 eyes, the retinal or choroidal white lesions were seen in 29 (83%), and 16 (46%) presented with disc edema [4]. In our study we found 16 eyes (43.2%) with small areas of retinitis or subretinal lesions similar to those described by Solley et al. In our study these lesions were the most common finding in CSD.

Less importance has been given to vascular changes in CSD. Our group published two studies showing the abnormal vascular network in CSD associated with HIV infection [5, 6]. Matsuo et al. studied four consecutive patients with CSD and considered granuloma with an abnormal vascular network arising specifically at the optic disc as the hallmark of ocular manifestations of CSD [7]. The relationship between *Bartonella* infection and vasoproliferation has been shown since the isolation of *Bartonella* species in bacillary angiomatosis [8]. Dehio discussed two distinct mechanisms for *Bartonella*-induced vascular proliferation: triggering proliferation and inhibiting apoptosis, and stimulating the production of vascular endothelial growth factor (VEGF) by infected macrophages. VEGF and interleukin-1B, a potentiator of VEGF, are released from macrophage-infected cells in response to *B. henselae* infection [9]. In 2004 Kirb established an in vitro model of *Bartonella*-induced angiogenesis [10]. These studies show that vascular proliferation is one of the most important events in *Bartonella* infection, and our study has shown that these events can occur in the eye.

In the group studied by Solley et al. the authors treated 11 patients out of 24 with oral or intravenous antibiotics, associated or not with steroids, and did not treat 13 patients. The authors reported that there were no differences in final VAs in the two groups. Although there are no prospective studies showing differences between treated and untreated patients, CSD has been considered a self-limited disease. In Japan, Kodama et al. studied 14 patients with CSD: 13 were treated with antibiotics and steroids because of optic nerve involvement; the authors suggested treatment with antibiotics and steroids since a good outcome was achieved and no relapse occurred in their group [11]. Reed et al. described seven cases of consecutive patients treated with oral doxycycline and rifampin. The authors suggested that prompt treatment may shorten the course of the disease [12]. In our study all patients were treated with systemic antibiotics. Of 37 affected eyes, 32 (86.5%) showed a final VA better than 20/200 and only five were worse than 20/200. Two patients showed intra-ocular relapses after the discontinuation of the antibiotics. Although most of the affected eyes evolved with good VA, in some cases this did not occur despite oral treatment. The role of steroids in the treatment of CSD remains unclear; in our study only one patient was treated with oral antibiotics and steroids due to significant macular edema. In this patient the steroids did not seem to affect the patient's recovery.

In conclusion the spectrum of CSD ocular manifestations is very large. Subretinal lesions and small foci of retinitis associated with an abnormal vascular network seem to be the most common ocular finding. Treatment with systemic antibiotics should be considered since significant visual impairment and relapses can occur.

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