

ATYPICAL BARTONELLA HENSELAE NEURORETINITIS IN AN IMMUNOCOMPETENT PATIENT

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ABSTRACT

We report a case of a 57-year-old immunocompetent male, admitted to our Department due to the loss of visual acuity to the right eye, occurred during the two weeks before the hospitalization, and hyperglycaemia. Our patient suffered from metabolic syndrome, characterized by visceral obesity, impaired glucose tolerance, arterial hypertension, complicated by proteinuria, and moderate grade hypertensive retinopathy. Surprisingly, and despite its many comorbidities, the final diagnosis was neuroretinitis by *Bartonella henselae*, without any other symptoms/signs of cat-scratch disease. The patient denied any kind of contact with cats. He was cured by specific antibiotic therapy, restoring status 'quo ante'.

Key words: Cat-Scratch Disease; *Bartonella henselae*; Neuroretinitis.

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Introduction

Cat-scratch Disease (CSD) is a benign lymphoreticulosis characterized by "local" forms, affecting the skin and the loco-regional lymph nodes. This infection is usually benign and self-limiting, but, sometimes, can evolve in systemic granulomatous forms, which acquire a particular severity in immunocompromised hosts^(1,2). The etiologic agent is a pleomorphic gram-negative bacillus, *B. henselae*, inoculated through the bite or the scratch of an infected cat, thus configuring a zoonotic infection^(3,4).

CSD is spread worldwide (accounting about 24,000 cases a year just in the United States, mostly children) and occurs more frequently during the cold seasons, probably due to a closer contact with pets (main reservoir of the pathogen)^(5,6). Its typical onset is characterized by the appearance of a primary cutaneous lesion (macule, papule, or vesicle) in the site of inoculation (cat scratch or bite), followed by a local painful and/or suppurative (10% of cases) lymphadenopathy, occasionally associated to

systemic symptoms (fever, discomfort, etc.). In immunocompetent patients it usually resolves spontaneously in a few weeks^(7,8). Systemic involvement with atypical organ presentations, or haematogenous disseminated infection, is quite rare, except for immunocompromised hosts. Among the possible manifestations it is possible to observe neurological involvement (encephalitis, facial paralysis, transverse myelitis, etc.), ophthalmologic complications, hepatosplenic granuloma, osteomyelitis, endocarditis, prolonged fever and some other; in these cases, diagnostic suspicion and immediate antibiotic therapy are essential⁽⁹⁻¹²⁾.

This case report focuses on unusual unilateral neuroretinitis associated to *B. henselae* infection in an immunocompetent patient, with no other symptoms/signs related to CSD, with an optimal response to antibiotic treatment.

Case report

A 57-year-old male smoker (40 cigarettes/day) patient, suffering from metabolic syndrome, with visceral obesity, reduced tolerance to carbohy-

drates, arterial hypertension of moderate to severe grade, complicated by proteinuria (600 mg/day) and moderate grade hypertensive retinopathy, was admitted to our Department of Internal Medicine complaining a rapid decreased of visual acuity and scotomas in the right eye occurred during the two weeks before the hospitalization, and hyperglycaemia (about 250 mg/dl), without any other symptoms/signs of organ alert. His general condition was satisfactory, and the patient was afebrile. Blood pressure was 120/80 mmHg, and physical examination of the main organs did not showed any noteworthy abnormality. Eyes external examination was unremarkable, whereas his pupils revealed a right relative afferent pupillary defect. Slit-lamp exam showed nothing relevant except for rare cell in the anterior chamber and vitreous in both eyes. Intraocular pressures were normal. Hereafter, the patient underwent dilated funduscopy examination that revealed the presence of retinal hard exudates and macular edema of the lower half of the optic disc. Visual acuity of the right eye proved to be greatly reduced (6/20 with correction). All these findings were considered compatible with the previous diagnosis of moderate grade hypertensive retinopathy, even if such a rapid visual acuity reduction seemed unusual - the previous visual acuity examination (20/20 with correction) being carried out just few months before. On the basis of our personal experience, specific serological test (i.e. indirect fluorescent antibody test, IFAT) for *B. henselae* was performed, and despite low probabilities the presence of high title serum specific IgG and IgM (1/256, r.v. <1/64, and 1/40, r.v. <1/20, respectively). Retrospectively enquired, the patient denied any kind of contact, even occasional, with cats. This laboratory finding has therefore led to a deeper and more careful search of any sign indicative of the CSD, but neither skin lesions, nor superficial adenopathies (cervical, axillary or inguinal) could be noted. Meanwhile, the patient underwent optical coherence tomography (Figure 1), which showed slight macular edema in the right eye, and fluorescein angiography, highlighting a diffuse leakage from the optic nerve head and the retinal vessels. Visual field examination with static perimetry proved a right paracentral scotoma. Additional laboratory tests, including complete blood count, liver and renal function tests, as well as urinalysis, were all within normal limits. Standard chest X-ray, in posterior-anterior and lateral projections, and abdomen ultrasonography

proved no noteworthy abnormality. Patient underwent also to a brain magnetic resonance which suggested right-sided retinitis and possible inflammation or swelling of the right optic nerve head; this finding was consistent with neuroretinitis. Angiotensin-converting enzyme level, tuberculin skin test, and other serologic specimen (HIV, Lyme disease, syphilis, toxoplasmosis, and toxocariasis) were negative too. Once the diagnosis was established, therapy with ciprofloxacin 500 mg *plus* prednisone 5 mg *per os* (po), *bis in die*, was started, but after 10 days, due to the onset of nausea, abdominal pain, and diarrhoea, it was replaced by azithromycin 250 mg po every 24 hours for 6 days. Eight months after, the patient had a right eye visual acuity of 14/20 with correction. Dilated funduscopy examination, with fundus autofluorescence imaging (Figure 2), and optical coherence tomography (Figure 3) showed a gradual disappearance of the macular edema, despite the persistence of a slight edema of the upper portion of papilla, and peripapillary retinal hard exudates. IgG antibody titers to *B. henselae* increased (1/1600), whereas IgM became negative.

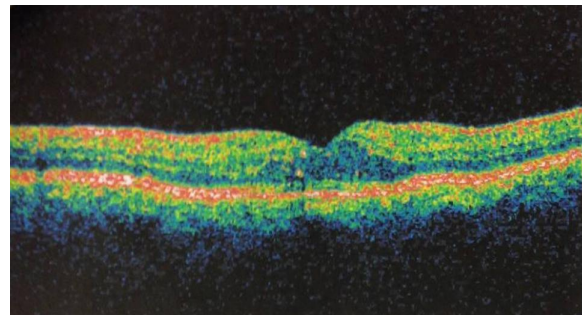


Figure 1: Optical coherence tomography showing macular edema.

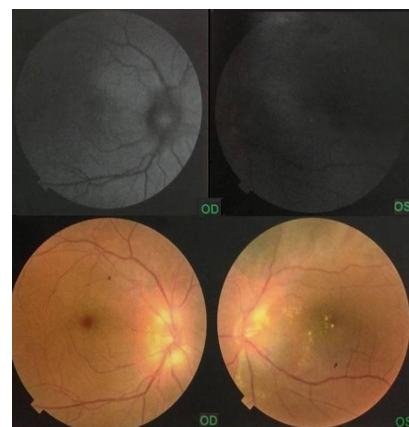


Figure 2: Dilated funduscopy examination showing slight edema of the upper portion of papilla, and peripapillary retinal hard exudates and resorption.

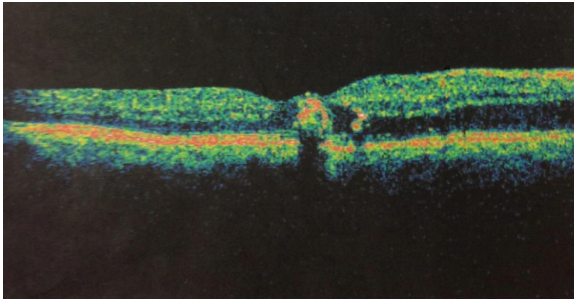


Figure 3: optical coherence tomography in the follow-up showing reduction of macula edema and retinal hard exudates.

Discussion

The typical presentation of *B. henselae* infection in immunocompetent hosts is usually a self-limited and paucisymptomatic disease. As already stated, it usually manifests with local painful lymphadenopathy, preceded by erythematous papule and/or pustule at the site of inoculation (typically cat scratch or bite). General symptoms (such as fever) are often absent or mild, and sometimes no history of contact with cats could be revealed, as in the case of our patient. An examination of the international literature reports rare cases of haematogenous spread or atypical organs involvement, as encephalitis, transverse myelitis, meningitis, facial paralysis, peripheral neuropathy, lung nodules, granulomatous hepatitis, hepatosplenic infection, osteomyelitis, endocarditis, and ocular involvement. All these are more frequent in immunocompromised patients and rare (<5%) in immunocompetent ones⁽⁸⁻¹²⁾.

The most common non-lymphatic organ involvement in CSD is represented by ocular one, occurring in 5-10% of all cases. Henri Parinaud first described it, reporting the cases of 3 patients with chronic fever, regional lymphadenopathy, and follicular conjunctivitis. This form of *B. henselae* infection with ocular involvement, known as Parinaud's oculoglandular syndrome, is the most common and occurs in 5% of cases⁽¹³⁻¹⁵⁾. Neuroretinitis is an atypical occurrence, seen in 1-2% of systemic CSD. Other ocular manifestations such as Parinaud's oculoglandular syndrome, vitreous haemorrhage, focal choroiditis, intermediate uveitis, panuveitis, massive exudative maculopathy, diffuse retinal haemorrhages, vascular occlusive episodes, necrotizing retinitis, and serous retinal detachment, are reported in about one quarter of neuroretinitis cases. CSD neuroretinitis usually appears few weeks after the onset of typical febrile

prodromal illness (lymphadenopathy, headache) and/or appearance of the cutaneous lesions in the site of a cat scratch or bite. Isolated vision loss, like in our case, is an extremely rare occurrence. The main symptom is the abrupt unilateral loss of visual acuity, as in our case, although cases with bilateral affection have been described. A predictable sign of an ocular manifestation of CSD is optic disc swelling associated to delayed (at least 2-4 weeks post-infection) stellate maculopathy (i.e. macular exudates which form a star-like pattern). In most cases *restitutio ad integrum* of visual acuity occurs after 6-12 months. Periodic ophthalmologic examinations are required. Even if two-third of all neuroretinitis are due to *B. henselae* infection, however other etiologies should be discarded, such as retinopathy by arterial hypertension and/or diabetes mellitus, HIV infection, Lyme disease, syphilis, leptospirosis, tuberculosis, toxoplasmosis, pseudotumor cerebri, multiple sclerosis and acute disseminated encephalomyelitis (although macular star exudates are not observed in demyelinating diseases)⁽¹⁶⁻¹⁸⁾.

Diagnostic suspicion of *B. henselae* infection in atypical presentations is difficult, especially in those cases without skin lesions and/or lymphadenopathy. Diagnosis is mainly serological, through enzyme immunoassays or indirect immunofluorescence, with a high sensibility and specificity, which makes microbiological methods (direct identification and/or isolation) unnecessary. DNA sequencing and polymerase chain reaction (PCR) from gland tissue samples and visceral granulomas require invasive and expensive procedures, and are usually reserved for questionable diagnosis cases or for research studies. In our case, diagnosis was established through indirect immunofluorescence demonstration of increased IgM antibody titer to *B. henselae* although a significant increase in IgG antibodies titer was also observed, enough to consider the infection in an acute phase⁽¹⁹⁻²¹⁾.

No antibiotic treatment is required for the most of CSD cases, excluding patients with general symptoms or big and/or painful lymphadenopathies. In these cases it must be administered azithromycin 500 mg po once, then 250 mg/day for other 4 days. Suppurate nodes needle aspiration relieves pain. In complicated CSD and in immunocompromised patients the recommended treatment consists of doxycycline 100 mg twice a day, with or without rifampin 300 mg twice a day. Other suggested antibiotics are ciprofloxacin or

trimethoprim-sulfamethoxazole (cotrimoxazole). In patients with CSD complicated by neuroretinitis an antibiotic therapy is also recommended, despite its evolution is usually benign. As a matter of fact, the possibility, even if extremely unlikely, of ophthalmic irreversible structural lesions suggests the prescription of combined antibiotic therapy: doxycycline plus rifampicin in patients older than eight, or azithromycin or cotrimoxazole plus rifampicin for patients below that age of four to six weeks. Other suggested antibiotics are clarithromycin, ciprofloxacin and gentamicin. To date, no specific agreement has been obtained about the role of corticosteroids, so their use remains controversial. In our case, antibiotic prescription was based upon clinical and epidemiological suspicion, subsequently confirmed by IFAT, and steroids were prescribed, despite their questionable usefulness, after the findings of the multifocal-visual evoked potentials recording. Quick and complete recovery of ophthalmic symptoms experienced by this patient, in contrast to other cases reported by the literature, could be in relation to the prompt beginning of treatment^(22,23).

In conclusion, CSD with associated neuroretinitis is quite rare condition, especially in immunocompetent patients. It should be suspected in any patient presenting with an abrupt loss of visual acuity, with the finding of optic disc swelling and macular star exudates, even in absence of history of contact with cats, and other specific CSD symptoms/sign. It remains to determine, given the absence of an immunodepression state, if the bacterium succeeded to provoke the retinal infection and the neuroretinitis thanks to a previous retinal damage, such as the one caused by intolerance to carbohydrates or arterial hypertension, or both. To date, it has been highlighted the presence of retinal damage in patients suffering from full-blown diabetes mellitus type 2, however, also intolerance to carbohydrates could create a predisposition to such an event. Such condition, from an anatomical and pathogenic point of view, could contribute to the genesis of a *locus minoris resistentiae* which, in association with the already present arterial hypertension, would have favoured the *B. henselae* infection in this site, with onset of macular edema and related symptoms^(24,25). Another predisposing condition to infection may have been the metabolic syndrome itself and its influence on the homeostasis and the proper functioning of the immune system^(26,27).

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