Case report

Tick-borne infection revealing human immunodeficiency virus (HIV) positivity in a young adult

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ABSTRACT

Purpose: To describe a patient whose retinal findings suggestive of tick-borne disease but evaluations led to early diagnosis and treatment of human immunodeficiency virus (HIV) infection.

Observation: A young patient presented with bilateral uveitis, branch retinal artery occlusion and retinal findings suggestive of infective/inflammatory etiology. Laboratory evaluations revealed that the patient was positive for co-infection with \textit{Rickettsia conorii} and \textit{Bartonella henselae}. On further investigation, the patient tested positive for HIV infection. The patient was treated with doxycycline as well as highly active anti-retroviral therapy (HAART) to control both opportunistic infections as well as HIV infection.

Conclusion and Importance: Patients with HIV infection are at risk for multiple, simultaneous opportunistic co-infections, including those with tick-borne diseases.

1. Introduction

Tick-borne diseases are a heterogeneous group of disorders with a significant burden worldwide. Despite their prevalence, tick-borne diseases widely remain under-detected due to intrinsic challenges of making diagnosis which require high level of clinical suspicion. It also requires the ability to interpret supportive laboratory data accurately in the setting of confounding factors such as false-positive and false-negative results and exclude other co-infections.\textsuperscript{1}

HIV infection is a very common cause of increased opportunistic infections as well as co-infections due to immunosuppression. Delay in the diagnosis can lead to delay in the treatment influencing both morbidity as well as mortality.\textsuperscript{2}

Herein, we describe a case of bilateral uveitis due to \textit{Rickettsia conorii} and \textit{Bartonella henselae} co-infection. On further investigation, an underlying HIV infection was also diagnosed. Although, immunocompromised state is known to predispose to co-infections; concurrent \textit{Bartonella henselae}, \textit{Rickettsia conorii} and HIV infection has not been reported in the literature.

2. Case

A 29-year-old male patient was referred to our Ophthalmology Department with acute painless visual field loss in the superonasal side in the right eye, two days prior to his admission. Three weeks before presentation, the patient had fever, night sweats, and diarrhea. These symptoms lasted 3–4 days and started ten days after a camping trip in rural area. He denied any dermatological findings or lymphadenopathy.

He had a history of unprotected sexual encounter six months prior to presentation but denied any tick bite or contact with pets.

On examination, best corrected Snellen visual acuity (BCVA) was 20/20 in both eyes (OU). Anterior segment examination was normal, OU. There was no inflammation seen in the anterior segment or vitreous. Fundus examination revealed retinal white spots (sized 25–250 μm in diameter) scattered along the retinal vascular arcuates, from posterior pole to midperiphery in both eyes (Fig. 1A and B). In the right eye, the inferotemporal retinal artery was thinned and a focal area of white retinal lesion with adjacent retinal hemorrhage was evident at the very beginning of the vessels adjacent to the optic disk. A wedge-shaped retinal whitening along the part of retina supplied by the inferotemporal arterial branch was also prominent (Fig. 1A). The patient...
Fig. 1. Multimodal imaging of the patient at initial visit. The montage image of color fundus photographs of right eye (A) and left eye (B) show retinal white spots (sized 25–250 μ in diameter) scattered mostly along the retinal vascular arcuates, from posterior pole to midperiphery. In the right eye (A), the inferotemporal retinal artery appears thinned and a focal area of white retinal lesion with adjacent retinal hemorrhage is evident at the very beginning of the vessels adjacent to the optic disk. A wedge-shaped retinal whitening along the part of retina supplied by the inferotemporal arterial branch is also prominent. Fluorescein angiography (FA) of early (C) and late (D) phases of the right eye showing delay in dye transit through the inferotemporal branch retinal artery (BRA) with masking of background fluorescence along the area of retinal whitening and retrograde filling. Fluorescein angiography of the left eye at early (E) and late (F) phases appears normal except the areas corresponding to retinal white lesions. In both eyes, those retinal lesions appeared as hypofluorescent dots during the early phase (C, E) with slight staining of the outer borders in late phase (D, F). Optical coherence tomography (OCT) horizontal scans through the retinal lesions, which revealed slight hyperreflectivity at very superficial layers of retina in both eyes. Deeper retinal layers and choroid seem to preserved (Fig. 1 C–F). Enhanced depth imaging–OCT (EDI–OCT) was also performed through the retinal lesions, which revealed slight hyperreflectivity at very superficial layers of retina in both eyes. Deeper retinal layers and choroid seem to be preserved (Fig. 1 C–F). Based on the retinal, systemic findings and medical history, an infectious/inflammatory etiology was suspected, and further laboratory testing was ordered. *Rickettsia conorii* and *Bartonella henselae* antibodies were positive by indirect immunofluorescence antibody with antibody titers supporting recent infection from both microbial agents (*Rickettsia conorii* IgM titer: 1/160-IgG titer: 1/320, *Bartonella henselae* IgM titer: 1/100-IgG titer:1/320). At the same time, laboratory tests for human immunodeficiency virus (HIV) antibodies were positive on ELISA testing. Subsequently, presence of HIV antibodies were also confirmed by western blot test. CD4 count was 358 cell/mm3, and his viral load was 10,000 copies/ml, thereby putting him under the definition of HIV infection. Additional tests carried out to investigate other infective agents like HBV, HCV, CMV, EBV, acute toxoplasmosis, syphilis, Lyme disease, Legionella, leptospirosis, toxocariasis and brucellosis were negative. Immunological panel was also negative. Doxycycline 200 mg/day was then started for the tick-borne coinfection and highly active antiretroviral therapy (HAART; emtricitabine 200mg/day, tenofovir disoproxil 245 mg/day, and efavirenz 600mg/day) was started for the tick-borne coinfection. A month later, nearly all of the retinal white lesions and the retinal whitening at the inferotemporal arcuate resolved (Fig. 2 A–D). However, the patient’s scotoma did not fully recover and continued to show as an arcuate defect in visual field examination of the right eye. (Fig. 3).

3. Discussion

We have described a patient who had co-infection with *Rickettsia conorii* and *Bartonella henselae* presenting with both systemic as well as ocular manifestations that ultimately led to the diagnosis of HIV infection. In our patient, systemic manifestations were rather obscure, and the diagnosis was eventually made by a uveitis specialist. The patient had fever and diarrhea but denied skin rash or the characteristic “tache noire” eruption at the site of the bite.

The key ocular findings in our patient were inner retinal white lesions distributed along the vascular arcuates and branch retinal artery occlusion. These features can be observed both in HIV retinopathy as well as in tick-borne ocular diseases.1–4 The differential diagnoses of superficial retinal white dots can be quite challenging, as they also include clinical differential for “cotton wool spots”.

Noninfectious HIV retinopathy refers to cotton-wool spots (CWS), retinal hemorrhages, and microvascular abnormalities that do not progress, enlarge, or cause permanent structural damage. In HIV retinopathy, the retinal lesions (CWS) are mostly confined to the posterior
pole near the optic disc, whereas in inflammation, the lesions tend to be more diffuse and involve the periphery. Retinal infiltrates in patients with acute Rickettsia conorii infection can also present in the form of white retinal lesions. These infiltrates primarily involve the inner retina and are variable in number and size. These are mostly located adjacent to retinal vessels in the posterior fundus, although they can involve peripheral retina. Fluorescein angiography, in patients with acute Rickettsia conorii infection, shows early hypofluorescence and late staining of large acute retinal lesions and isofluorescence or moderate hypofluorescence of small active retinal lesions. FFA, in general, can be useful to differentiate retinal infarcts (CWS) from retinitis as the latter tend to be iso- or hyperfluorescent during the late phases of FFA whereas the infarcts remain hypofluorescent at the center with a surrounding hyperfluorescence ring. The lesions of our patient in that aspect were more compatible with retinal infarct than retinitis. Histopathologic study of retinal cotton-wool spots in AIDS patients has demonstrated that these lesions have pathologic features identical to those seen in cotton-wool spots of other causes. Attempts to isolate organisms from these superficial retinal lesions to explain their cause in HIV retinopathy and tick-borne disease have been unsuccessful.

Branch retinal artery occlusion have been reported as a rare component in HIV patients without infectious retinitis. With increasing awareness of tick-borne diseases, BRAO is now being reported to be more frequent with Bartonella and Rickettsial infection than previously reported. Bartonella henselae, an intracellular bacterium, known to cause cat scratch disease (CSD), was also reported as a major cause of BRAO especially in young adults. The ocular signs of CSD arise from the resulting endothelial damage leading to occlusive vasculitis and angiomatosus vasoproliferative lesions. In the current case, whether Rickettsia conorii or Bartonella infection led to the ocular findings is arguable. Both bacteria can cause occlusive vasculitis. Also, the typical presentation of neuroretinitis commonly seen with Bartonella infection and CSD was not present in this patient, suggesting that the manifestations of CSD may be protein, depending on whether the Bartonella infection is alone or part of a co-infection.

The index case is also unique because of the co-infection with both Bartonella henselae as well as Rickettsia conorii. Double and triple infections of ticks with viruses and bacteria are not unusual. It has been reported that one tick species can transmit a variety of pathogens, and several kinds of tick-borne diseases which often co-exist with the same natural foci. Rhipicephalus sanguineous is a well-known vector of Rickettsia conorii in Mediterranean spotted fever (MSF) whereas transmission of Bartonella henselae with tick vector is controversial. Whether current patient acquired these two infections from the same or two different vectors, is speculative. On further review, we also did not find any cross reactivity between Bartonella and Rickettsia conorii antibodies in the literature which can cause false positive serology.

It is possible that the HIV infection has facilitated the co-infections, although by definition, the patients did not have acquired immunodeficiency syndrome (AIDS). Most of these patients usually present with non-specific systemic features which makes diagnosing them rather difficult, thereby delaying the treatment. Furthermore, as reported by Segura et al., sometimes systemic features and cutaneous findings of these infections overlap. Primary HIV infection can also mimic MSF in clinical presentation. Ocular findings may be differentiating; therefore, it is always important for the ophthalmologists to have a high clinical suspicion. Prompt diagnosis not only helps in improving the ocular findings but also the overall mortality and morbidity. Tick borne diseases such as Rickettsia conorii infections may cause edema in vital organs leading to a mortality rate of 3% in immunocompetent patients. In the literature, only a single case of MSF is described in an immunocompromised patient after liver transplantation causing death of the patient.

Low CD4 count is strongly related to the increased prevalence of ocular lesions as well as ocular symptoms. Non-infective HIV retinopathy is also much more common with low CD4 counts. Patients with CD4 count ≥200/µL have low prevalence of ocular disease. In our patient, the CD4 counts was not strikingly low and most likely did not play a major role in the prognosis of the patient. It is crucial to generate awareness of these co-infections for early recognition and timely antibiotic administration. Early actions can greatly reduce the symptomatic period and associated severe complications. Clinicians should suspect tickborne co-infections in returning travelers and vacationers with clinical and immunological evidence of multiple infecting agents, especially in cases of unusual presentation.
Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Patient consent

Consent to publish this case report has been obtained from the patient(s) in writing.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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Appendix A. Supplementary data

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