Case Report

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Presumed diffuse unilateral subacute neuroretinitis and cat-scratch disease: Dual infection in a single patient

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Abstract:

A healthy 35-year-old Malay woman presented with left eye pain for 1 week, and ocular examination showed evidence of panuveitis. She had granulomatous type of anterior uveitis with secondary high intraocular pressure (IOP). Fundus showed optic disc swelling, mild vitritis, and multiple subretinal lesions, which later formed a migratory track. A diagnosis of presumed diffuse unilateral subacute neuroretinitis was made. At the same time, the serology test for *Bartonella henselae* was positive. The patient was treated with antiglaucoma medicine and topical steroids. An antihelminthic was initially used, and later, an antibiotic for cat-scratch disease was added. In addition, focal laser photocoagulation was performed. After 3 months, her visual acuity improved together with a reduction in inflammation and well-controlled IOP.

Keywords:

Cat-scratch disease, diffuse unilateral subacute neuroretinitis, migratory lesion, panuveitis

Introduction

Diffuse unilateral subacute neuroretinitis (DUSN) is a rare cause of unilateral posterior uveitis. The term "DUSN" was coined by Gass *et al*. in 1978 to replace the previous terminology of "unilateral retinal wipe-out syndrome."[1] In 1983, Gass and Braunstein concluded that DUSN is caused by nematode species when he observed 18 cases of nematodes in DUSN patients within the endemic area.[2] The hallmark of diagnosis is a visible motile worm observed in serial fundus photographs. Other clues can be multiple deep retinal or subretinal lesions that can represent worm migration.[3] Treatment with systemic antihelminthics is an option that has been used with focal laser photocoagulation.[4]

Bartonella henselae is a facultative pleomorphic Gram-negative bacterium and is the causative pathogen of cat-scratch disease (CSD). As the name suggests, CSD usually occurs following exposure to an infected flea or a scratch or bite from a cat. Patients may present with Parinaud's oculoglandular syndrome, neuroretinitis, or uveitis. Diagnosis is usually made clinically and supported by a serology test. Treatment with doxycycline can hasten the visual recovery and clear bacteremia.[5] In our case, this patient presents as panuveitis.

Case Report

A 35-year-old woman presented with a history of left eye (LE) pain, redness, and reduced vision for 1 week. Otherwise, she denied any medical illness or exposure to tuberculosis. She denied having any pets at home and had no close contact with stray cats.

She was petite, afebrile, and had normotensive blood pressure. There was no

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skin lesion or lymphadenopathy. Visual acuity (VA) for the right eye (RE) was 6/6 and VA for the LE was 5/60, with a pinhole of 6/60. Anterior segment examination of the LE showed injected conjunctiva and mutton-fat keratic precipitates with anterior chamber cells of 4+. The intraocular pressure (IOP) was 38 mmHg. The left fundus examination revealed mild vitritis with a swollen, hyperemic optic disc and a localized whitish subretinal lesion near the macula [Figure 1a]. Her RE examination was unremarkable.

The patient was placed on antiglaucoma medications, namely guttae timolol, guttae brimonidine, and oral acetazolamide. As for the inflammation, guttae dexamethasone was started together with guttae tropicamide.

After 2 days of treatment, the LE VA improved to 6/12 pinhole, and there was a reduction in inflammation and IOP. However, upon left fundus examination, it was found that the subretinal lesion formed a migratory track toward the superotemporal arcade [Figure 1b]. On the third follow-up, left fundus examination showed subsequent migratory lesion (white arrow) toward the peripheral retina [Figure 1c].

Spectral-domain ocular coherence tomography (SD-OCT) showed generalized thickening of the macula with a hyperreflective layer on the surface of the papillomacular bundle, correlating with fibrosis seen clinically [Figure 2a]. Apart from that, hyperreflective dots were seen at the posterior vitreous phase, suggestive of vitritis. There was focal hyperreflectivity with minimal disruption of outer retinal layers [Figure 2b]. Fundus fluorescein angiography (FFA) was performed and revealed a hot disc with angiographic cystoid macular edema, vasculitis, and peripheral capillary fall out [Figure 3].

The patient was treated for presumed DUSN. Focal laser photocoagulation was applied to the migratory lesion, and sectoral FFA-guided laser photocoagulation was performed on the peripheral capillary nonperfusion area. The patient was started on oral albendazole 400 mg once daily for 6 weeks with an anti-inflammatory dosage of oral steroid. During follow-up 1 week later, there was a new subretinal lesion; thus, further focal laser treatment was performed [Figure 1d].

Her full blood count showed a slightly raised total white count of 11.1 × 10^9/L with predominant neutrophil 83% and normal level of eosinophil. Tuberculosis and syphilis screening were negative. However, her serology titers for *B. henselae* were elevated, with immunoglobulin G titer of 1:128. Stool sample for worm detection and identification was not taken.

In view of this, she was started on oral doxycycline 100 mg twice a day (BD) for 6 weeks. The steroid treatment was gradually tapered off. She had completed treatment for both DUSN and CSD. At month 3 of follow-up, her LE VA improved to 6/9, and the IOP was controlled at 20 mmHg with two topical antiglaucoma medications. Fundus showed epiretinal membrane with resolved intraretinal fluid [Figure 4].

Discussion

Our patient was diagnosed and treated for presumed DUSN based on clinical presentation while CSD was supported by positive investigation results. It is not

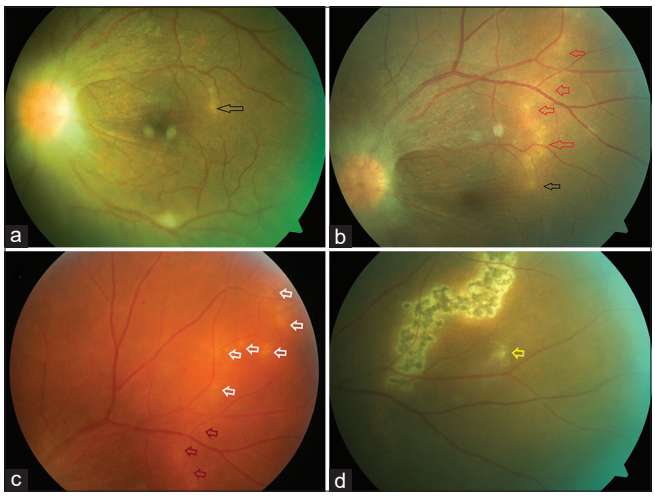

Figure 1: (a) Left eye fundus photo showing initial subretinal lesion (black arrow). (b) Left eye fundus photo showing initial subretinal lesion (black arrow) with new lesions (red arrow) on the second visit suggesting migratory tract. (c) Left fundus photo with subsequent migratory lesion (white arrow) on the third follow-up. (d) Left fundus photo showing new lesion (yellow arrow) with laser scar seen

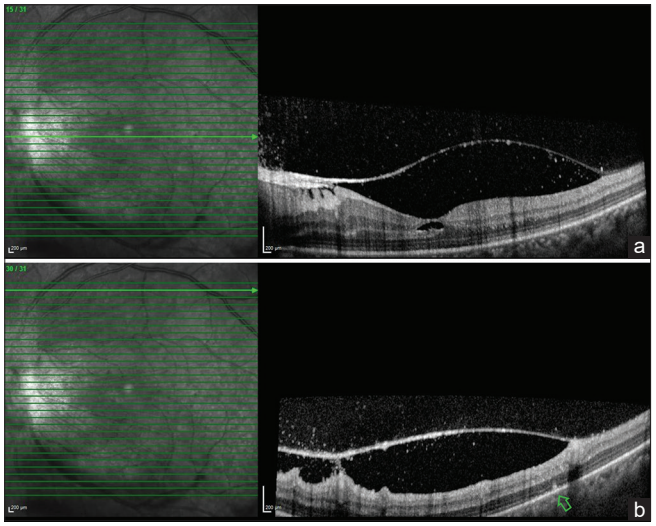

Figure 2: (a) Left eye spectral-domain ocular coherence tomography showing generalized thickening of the macula with vitritis. (b) Spectral-domain ocular coherence tomography showing focal hyperreflectivity with minimal disruption of outer retinal layers (green arrow)

a common scenario to have dual infection in a single patient.

DUSN may affect apparently healthy individuals.[1] DUSN is often found in children and young adults. Local authors reported high prevalence of soil-transmitted helminth (STH), which ranges from 52% to 76%.[6-8] Thereby, the diagnosis of DUSN was made based on typical clinical presentation with epidemicity of STH. Earlier studies proposed that humans acquire the parasite through an oral route by ingesting contaminated soil with larvae.[9] Other authors have suggested that the ingestion of undercooked soil from underground plants is among the modes of larva entry.[10] It was postulated that in the intestine, worms may hatch and then travel via the blood stream to the eye.[9]

Following that, the nematode exerts toxic damage to the retina and optic nerve, caused by the migration of a worm in the subretinal space over a period of many months or years. The cellular sign of inflammation was evident on histopathological examination by intranuclear and intracytoplasmic inclusions in some retinal ganglion cells.[1]

DUSN is divided into two stages. In the initial stage, patients usually present with paracentral or central scotoma with ocular discomfort. Clinically, there will be posterior uveitis, characterized by papillitis, vitritis, and a cluster of evanescent gray–white outer retinal lesions. These are thought to be due to a toxic inflammatory reaction of the host in response to the larva product.[1,2]

The nematode exists in varying sizes, with the smaller nematode measuring 400–700 nm, including *Toxocara canis*, *Ancylostoma caninum*, *Strongyloides stercoralis*, and *Ascaris lumbricoides*, while the larger nematode measures 1500–2000 nm, namely *Baylisascaris procyonis*.[11] Hence, not all nematodes are visible clinically. A large study in Brazil showed that only 39.44% presented with a visible nematode. The majority, 91.7%, of DUSN presented as subretinal tracks, while 80.2% presented with a small white spot.[12] At this stage, the visual prognosis is usually good.[12] Similarly, our patient initially presented with a small white spot, but the subsequent review showed evidence of migratory track, suggestive of DUSN. However, none from this study presented with severe granulomatous anterior uveitis, as seen in our patient.

The later stage is characterized by optic atrophy, diffuse pigment epithelial degeneration, and retinal artery narrowing with abnormal electroretinogram. DUSN is known to mimic many diseases in both active and late stages, which makes this disease a challenge for diagnosis. In cases of late diagnosis, patients could become permanently blind.[13] Complications of DUSN include development of subretinal mass and choroidal neovascularization.[1] Furthermore, prolonged inflammation and the use of steroids could contribute to the development of secondary open-angle glaucoma, as seen in our patient.

A local author found that the DNA of *B. henselae* was identified in 11.5% of fleas in Malaysia.[14] This suggests that even without a scratch or bite, *B. henselae* infection can be contracted. A recent study showed that CSD has

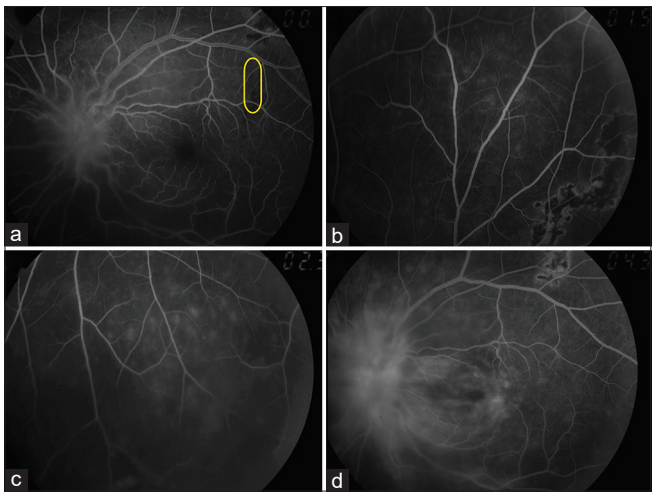

Figure 3: (a) Mid-venous phase showing leakage at optic disc and hypofluorescence spot at initial track (yellow circle). (b) Evidence of small-vessel vasculitis. Area of hypofluorescence corresponding with focal laser photocoagulation at migratory track. (c) Evidence of capillary fall out at peripheral fundus. (d) Late frame showing hot disc with angiographic cystoid macula edema

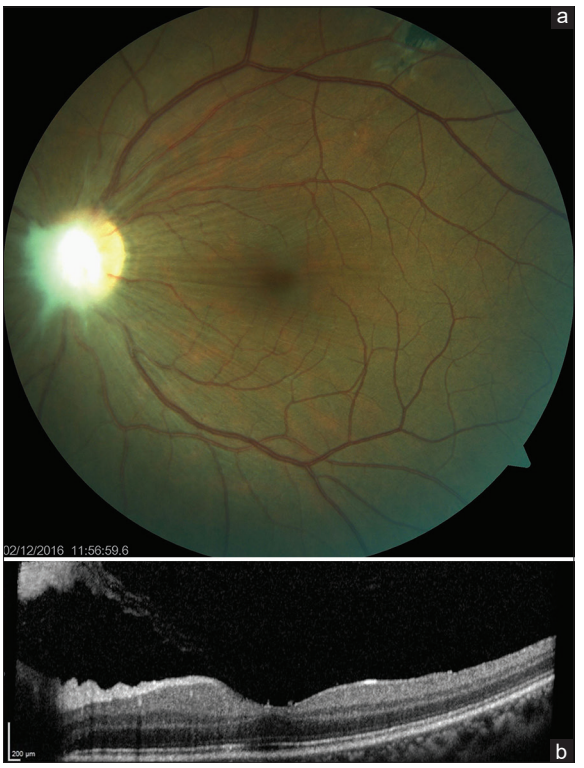

Figure 4: (a) Left eye fundus photo showing minimal gliosis at optic disc with epiretinal membrane. (b) Left eye spectral-domain ocular coherence tomography showing epiretinal membrane with resolved intraretinal fluid

a myriad of clinical manifestations, including uveitis in addition to neuroretinitis.[5] CSD may also manifest as optic neuropathy, retinochoroiditis, branch retinal arteriolar occlusion, and endophthalmitis.[15] Other authors have reported that CSD develops into macular hole and choroidal neovascularization, which could lead to permanent vision loss.[16,17] Diffuse atrophy of all 10 retinal layers is seen on SD-OCT in DUSN at late stages. The Orefice's sign was also observed.[18]

DUSN and CSD are among the important differential diagnoses in white dot syndromes because, unlike others, DUSN and CSD have definitive treatments.[19] Among healthy individuals, DUSN could be the cause of an unexplained unilateral vision loss.[10] As in our case, the diagnosis of DUSN is entirely clinical, while serological testing of CSD aids in the diagnosis of ocular bartonellosis.

In cases where the live worm can be identified and located away from the macula, the treatment for DUSN involves the use of a focal laser.[2] In cases where DUSN is suspected, but worm is not visualized, antihelminthics are recommended.[20] Another indication for antihelminthic includes pediatric age group.[21]

Subretinal tracks may suggest remnants of worm migration, which may be mistaken for the presence of an actual subretinal worm, leading to pointless photocoagulation.[12] This may explain what happened to our patient, who underwent focal laser photocoagulation twice. In addition, she was also treated with intensive topical steroids, antihelminthics, and an anti-inflammatory dosage of oral steroids.

Treatment for *B. henselae* is antibiotics. The choices include macrolide and tetracycline. Macrolide has a high concentration within phagocytes, which makes it more potent for intracellular organisms like *B. henselae*.[22] Another option is tetracycline, such as doxycycline, which acts similarly by augmenting the oxygen-free radical burst used by the polymorphonuclear cells to kill phagocytized organisms.[23]

A similar case of dual-pathogen infection has been reported. In comparison to our case, the previous patient presented with migratory track along with vitritis, swollen optic disc, and macular star.[24] In both cases, patient presented at initial stage and responded well to treatment.

Conclusion

Dual infection of DUSN and CSD may have occurred concurrently in a patient who presented with panuveitis. Early treatment may provide a better outcome.

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Conflicts of interest
The authors declare that there are no conflicts of interests of this paper.

Human subject
Consent was obtained from patient for images and other clinical information to be reported in this journal.

Declaration of patient consent
Authors certified that they have obtained appropriate patient consent form. In the consent form patient has given consent for clinical information and other images to be reported in the journal. Patient also understands that name and initial will not be published and due effort will be made to conceal identity but anonymity cannot be guaranteed.

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