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Case Report

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Diffuse unilateral subacute neuroretinitis in children: Report of three cases

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ABSTRACT

Rationale: Diffuse unilateral subacute neuroretinitis is a form of posterior uveitis and has a few clinical presentations according to the onset of presentation.

Patients' concern: A girl (5-year-old) and 2 boys (both 12-year-old) were included in this report. Upon presentation, the visual acuity ranges from 6/12 to 6/60. All three cases had different symptoms (case 1: floaters; case 2: eye redness and pain; case 3: central scotoma). All of them had variable posterior uveitis features (case 1: vitritis and focal retinitis; case 2: subretinal larva track; case 3: choroiditis).

Diagnosis: Diffuse unilateral subacute neuroretinitis.

Intervention: All 3 patients were treated with oral albendazole.

Outcome: All patients showed remarkable resolution of inflammatory reactions of the eye and also improvement of vision.

Lesson: High index of suspicion should be made for children and young adults who are previously healthy but presented with suddenly onset of reduced vision with clinical features of posterior uveitis of variable degree. Clinical features together with a full blood picture can help to diagnose the problem when other parameters are negative.

KEYWORDS: Diffuse unilateral subacute neuroretinitis; Worms' infestations; Nematodes

1. Introduction

Diffuse unilateral subacute neuroretinitis (DUSN) is an ocular infectious disease that is progressive, debilitating, and can cause profound visual loss. DUSN was first reported by Gass *et al*. in 1978, and it was initially termed as "unilateral wipe-out syndrome"[1]. At that time, it was thought that *Toxocara canis* causes the syndrome, but later Gass *et al*. found out that other species of nematode may also cause DUSN[2]. Other nematodes include *Ancylostoma caninum*, *Storngyloides stercoralis*, *Ascaris lumbricoides* which are smaller nematodes. *Baylisascaris procyonis* is an example of larger one[3]. In the United States, nematodes have been isolated ranging from 400-2000 μm in length[3].

The nematodes can cause inflammatory and degenerative processes in the retinal pigment epithelium and outer retina alike. Inflammatory cell aggregations for example by eosinophils and macrophages may lead to retinal layer damage and subsequent loss of ganglion cells[4]. Toxic excretions from the larva may also cause a negative effect on the retinal layers[4]. The worm being infested may wander for months to years before they travel hematogenous to the eyes. Rare studies reported multiple worms lingering in the same eye in DUSN cases. If happens, it will make the treatment challenging[5].

Children and young adults are a vulnerable group that predisposes to many diseases. Children under 5-year-old especially when they cannot tell their eye symptoms are worrisome as DUSN is a progressive disease and can lead to a debilitating visual outcome.

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If it occurs among children, the examination might be difficult as children are more anxious as compared to young adults. We report 3 cases of DUSN with variable clinical features of posterior uveitis.

2. Case report

This study was approved by the Ethical Committee of Hospital Universiti Sains Malaysia, Kelantan. Informed consent was obtained from the patients' relatives before reporting this case report.

This report was a retrospective case study based on medical records review in which the cases were treated as DUSN from 2019 to June 2020.

2.1. Case 1

A 12-year-old Malay boy presented with the recurrent attack of posterior uveitis over the left eye. At the first presentation, he presented with floaters for 3 weeks. It was associated with a slightly blurry vision. However, there was no eye pain, eye redness, or eye discharge. He denied any history of ocular trauma or fever, but close contact with cats at home and has a history of scratches by cats.

His right eye visual acuity was 6/7.5 with normal anterior and posterior segments examination. His left eye visual acuity was 6/12 and no improvement with the pinhole. Left eye examination showed the presence of fine keratic precipitates on the cornea, moderate to severe anterior chamber cells, multiple areas of posterior synechiae, and moderate anterior vitritis. Fundus examination showed moderate vitritis especially inferiorly obscuring fundus view. There was no retinitis, choroiditis or vasculitis. The optic disc was pink with a well-defined margin and normal cup-disc ratio. Systemically he had multiple small painless cervical lymphadenopathies. Respiratory and cardiovascular systems were normal with no organomegaly.

Blood investigations were taken to screen for infective causes and connective tissue disease. Cytomegalovirus (CMV) immunoglobulin (Ig) G was positive with a titer of 444.8, but CMV IgM was negative. Repeated CMV serology two weeks later reported that there was no significant rise in CMV IgG titer (only 461.1). Toxoplasma and herpes simplex virus serology were negative. Connective tissue screening was also negative and C-reactive protein was within the normal limit. Mantoux test, chest X-ray, and low erythrocyte sedimentation rate were not suggestive of tuberculous infection.

Based on the history of close contact with a cat, the patient was initially treated as a cat scratched disease with oral azithromycin 250 mg two times per day. There was no improvement in vision and ocular inflammation after two weeks of treatment. Given positive titer for CMV, then azithromycin was changed to a trial of oral acyclovir 400 mg 5 times per day for 6 weeks. After 6 weeks of completion of antiviral, although there was partial resolution of anterior segment inflammation, there was no resolution of vitritis. Then, the second cycle of oral azithromycin 250 mg daily was restarted for 6 weeks together with oral prednisolone at the dosage of 1 mg/kg per day. The oral steroid was tapered down 5 mg weekly to be completed for 6 weeks. There was the resolution of anterior chamber inflammation and vitritis with residual vitreous clumps inferiorly upon completion of medication.

The left eye was quiescent for about 5 months until he presented again with two weeks history of the left eye seeing floaters and redness. The left eye showed injected conjunctiva, moderate anterior chamber cells, and mild vitritis inferiorly. There was focal retinitis at the inferotemporal arcade. There was no vasculitis or choroiditis. The infective screening was repeated, and the results were negative. However, a full blood picture (FBP) showed eosinophilia suggestive of parasitic infestation. Repeated eye examination showed that there was the absence of a worm. Stool examination for ova and cyst was screened, but the result was negative.

Based on clinical presentation and the presence of eosinophilia, the patient was diagnosed as DUSN. He was started on oral albendazole 400 mg daily for 5 d. Concurrently, oral prednisolone 1 mg/kg per day was initiated and tapering off 5 mg weekly to be completed for four weeks. At one month after completion of oral albendazole, his eye condition showed remarkable improvement. His left eye visual acuity was improved to 6/9 with quiescent anterior chamber cells and resolved vitritis and retinitis over the posterior segment. There were no recurrent floaters or eye redness with good vision at one-year follow-up.

2.2. Case 2

A 5-year-old healthy girl presented with a 2 d history of right eye redness. It was associated with eye pain, but there was no eye discharge. She denied any preceding ocular trauma or insect bites. She had a history of visiting a farm and following that she developed low-grade fever with a cough, which was resolved spontaneously.

On examination, her right eye visual acuity was 6/60, and of no improvement with the pinhole. Her left eye visual acuity was 6/6. There was no relative afferent pupillary defect. Right eye anterior segment examination showed injected conjunctiva and the presence of severe anterior chamber cells with a 1.2 mm level of hypopyon. However, the cornea was clear with no keratic precipitates or iris nodules. Fundus view was obscured due to severe anterior segment inflammation. A B-scan of the posterior segment showed a clear vitritis with no loculations, and the retina was flat. Left eye examination was normal for both anterior and posterior segments.

Blood investigations for infective causes including toxoplasma and syphilis serology were negative. Mantoux's test result was not suggestive of tuberculosis infection. Screening for connective tissue disease was also negative. However, FBP showed eosinophilia.

The patient was started on topical steroids, antibiotics, and cycloplegic agents initially for the right eye while waiting for the blood investigations result. After 3 d on topical medication, there was a reduction of anterior segment inflammation, and the fundus view became more visible. Fundus examination showed the presence of hypopigmented lesion inferiorly below the inferotemporal arcade. The hypopigmented lesion was spiral in shape with fluffy edges suggestive of larva track. However, there was no worm seen and the

absence of vitritis, retinitis, or choroiditis. The optic disc was pink with a well-defined margin.

Based on the clinical finding of larva track on fundus examination and the presence of eosinophilia, the child was diagnosed as right eye DUSN. She was started on syrup albendazole 400 mg daily for 5 d. Topical antibiotics and cycloplegic agents were discontinued, meanwhile, the frequency of topical steroids was tapered down. Screening stool for oval and cyst was done, but the result was negative.

One month after completion of syrup albendazole, her right visual acuity was improved from 6/60 to 6/18. There was complete resolution of anterior segment inflammation and hypopyon. Fundus examination showed spiral shape hypopigmented lesions with fluffy edges becoming well-defined edges with mottling of the macula. Given the improvement of vision and resolution of ocular inflammation, the topical steroid was discontinued and the child is still under regular follow-up.

2.3. Case 3

A 12-year-old boy presented with 2 weeks history of central scotoma over the right eye. It was not associated with eye redness or eye discharge. The symptom was acute in onset and no preceding ocular trauma was reported. This was his first-ever episode, and he was well before that. He had no fever and no upper respiratory tract infection. He has underlying bronchial asthma and allergy rhinitis.

His right eye visual acuity was 6/45 and 6/6 in the left eye. A relative afferent pupillary defect was absent. Right eye examination revealed a normal anterior chamber with the absence of the anterior chamber cell. Fundus examination showed multifocal orange/yellow choroiditis at the posterior pole (Figure 1). However, there was no vitritis, vasculitis, or retinitis. The optic disc was pink and not swollen. Left eye examination showed normal anterior and posterior segments examination.

Given ocular toxoplasmosis is very common in children, oral azithromycin 250 mg two times per day was started while waiting for blood investigation results. Blood investigations for infective causes for CMV, syphilis, and toxoplasma infection were negative. Erythrocyte sedimentation rate, Mantoux test, and chest X-ray were normal. FBP showed eosinophilia suggestive of parasitic infections.

One week after starting on oral azithromycin, regular fundus examination showed the presence of new multiple choroiditis over the superotemporal arcade, which was a spiral shape in distribution (Figure 2). However, there was no worm seen. Based on new fundus examination finding and the presence of eosinophilia, a clinical diagnosis of DUSN was made. The patient was then started on tablet albendazole 400 mg two times per day for 5 d. Oral azithromycin was continued to be completed for 2 weeks. Stool examination for ova and cyst was screened, however, it was negative.

His right eye vision was improved to 6/12 one week after albendazole administration. Fundus examination showed progressive resolution of multiple choroiditis with no new lesion. The child is still under follow-up for further observation and review.

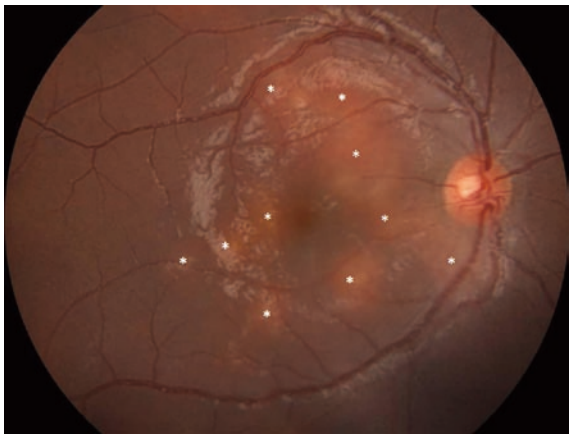

Figure 1. Right eye fundus photograph of a 12-year-old boy diagnosed as diffuse unilateral subacute neuroretinitis showing multiple choroiditis (*) at the posterior pole before treatment.

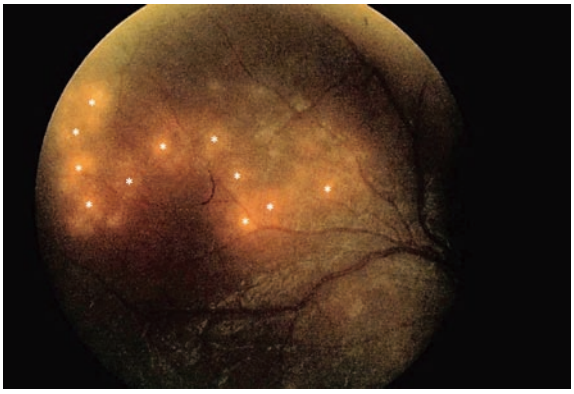

Figure 2. Right eye fundus photograph of a 12-year-old boy diagnosed as diffuse unilateral subacute neuroretinitis showing spiral shape distribution of multiple choroiditis lesions (*) at superotemporal arcade one week after treatment.

3. Discussion

DUSN onsets in two clinical phases, either early or late presentation. Early manifestations include mild to moderate vitritis, papillitis, and evanescent multifocal yellow-white lesions at the level of the outer retina and choroid as the worm moves. The late presentation includes optic nerve atrophy, narrowing of the retinal artery, and focal or diffuse retinal pigment epithelium degeneration.

All the 3 cases are presented in the early phase. None of the cases revealed any intraocular worms making the diagnosis challenging. For case number 2, fundus examinations showed the presence of subretinal larva track supported with eosinophilia by FBP suggestive of the diagnosis of DUSN. One retrospective clinical study reported that there were 121 patients with DUSN. Nearly 40% (48 patients) had live worms visible either in the early or late stage of disease[6].

When the worm can visualize, laser photocoagulation is the first choice of treatment as the laser can kill the worm and reduce the inflammatory process. It should be performed as fast as possible due to the worm can migrate elsewhere and causing more damage[7].

In our case series, case number 1 exhibits a clinical dilemma as the child gave a history of scratched by a cat and presented with clinical presentation of posterior uveitis predominantly vitritis. He was initially treated with cat scratch disease, CMV retinitis, and a trial of steroids. Although the eye was quiescent for few months there were still persistent vitreous clumps inferiorly. He had another relapse of posterior uveitis with features of vitritis and focal retinitis. There were no visible worms noted. However, FBP showed eosinophilia that supports the diagnosis of DUSN. Furthermore, treatment with oral albendazole showed remarkable resolution of inflammation and improvement of vision.

Case number 2 initially was treated with topical steroid while waiting for blood results. Eventually, when the anterior chamber inflammation reduced and hypopyon resolved, the fundus view was clearer, and was able to visualize the presence of subretinal larva track. Together with the FBP result which showed eosinophilia, a diagnosis of DUSN was made.

Case number 3 presented with multiple choroiditis lesions at the posterior pole and was treated as ocular toxoplasmosis while waiting for blood investigation results. However, with the new choroiditis lesions that have a peculiar spiral in shape and the ancillary test FBP which showed eosinophilia, it was suggestive of DUSN. There was an improvement of vision after completed oral albendazole.

There is no specific laboratory test available to diagnose DUSN. Even stool examination for ova and cyst is of little value. The stool screening was negative for our patients. No further test needed if intraocular worms were visible. For our patients, the FBP test with eosinophilia points toward parasitic or helminth infection that caused ocular inflammation. Ocular investigations like fluorescein angiography and indocyanine green angiography showed non-specific findings besides localizing the retinal leakage area and also choroidal involvement[3]. Electroretinogram can be used to identify the function of the retina and differentiate between DUSN from tapetoretinal degenerations. A-wave and b-wave can be reduced in the course of the disease and can show full recovery of normal findings. Although not specific, it can be a tool to monitor progression and response to treatment[3,8].

As mentioned earlier, photocoagulation is the main treatment of choice to halt the motility of the worms. When worms cannot be seen, oral antihelminthic drugs play a role. Not all patients respond well to oral antihelminthic drugs. It depends on the severity of ocular inflammation and severe inflamed eye may require longer durations to reduce the rate of recurrence[4,8]. Oral steroids have also been proposed base on the pathogenesis that DUSN causes inflammation. In our case series, an oral steroid was administered in case number 1 due to the presence of vitritis. One case report demonstrates the potential usage of intravitreal triamcinolone to reduce inflammation especially severe vitritis obscuring the retina[7].

4. Conclusions

Uveitis is always a challenging ocular condition. Although the prevalence of uveitis among children is lower than adults, correct diagnosis and proper treatment are essential because children suffer more due to vision loss in the long run. For DUSN per se, close monitoring to watch the response of treatment is important besides picking up any clinical signs that point towards this helminth infection.

Conflict of interest statement

The authors report no conflict of interest.

Authors' contributions

N.M.N.N. and A.S.A. are responsible for data collection and manuscript preparation. K.I. and E.Z. are responsible for manuscript editing and review.

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