

Diffuse Unilateral Subacute Neuroretinitis

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Abstract

Review Article

Diffuse unilateral subacute neuroretinitis is caused by a mobile worm in subretinal space. Acute phase of the disease is characterized by vitritis, papillitis, vision loss if macula is involved and pain. Live worm can be seen on careful examination, tracks of worm and a crop greyish- white lesion in the area of worm is the characteristic finding. In late phase severe vision loss is seen due to optic atrophy, retinal pigment epithelial mottling and narrowing of retinal arteries.

Keywords: Neuroretinitis, DUSN, Subretinal worm.

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DEFINITION

DUSN is a clinical syndrome characterized by early visual loss, vitreitis, papillitis, retinal vasculitis and recurrent crops of evanescent grey-white outer retinal lesions and later by progressive visual loss, optic atrophy, retinal vessel narrowing and diffuse RPE degeneration occurring in one eye of otherwise healthy patients.

DUSN is always unilateral as name suggest. Till date only 1 case with similar presentation and subretinal worms in both eyes has been reported (1999 Brazil) [1].

HISTORY OF THE DISEASE

Between 1963 and 1973, thirteen patients were described at Bascom Palmer with a clinical syndrome consisting of decreased vision, inflammatory cells in the vitreous cavity, optic atrophy, vascular attenuation, diffuse and focal retinal pigment epithelial atrophy and abnormalities of the electroretinographic responses. This was referred to as the 'unilateral wipe-out' syndrome [2].

In 1975 the earlier stages of the clinical syndrome were recognized as mild optic disc edema, vitreitis, extensive pigment epithelial changes, yellow-white lesions affecting the deep retina. J Donald M Gass gave the term diffuse unilateral subacute neuroretinitis in 1978. He described the clinical features and postulated that the toxic damage to optic nerve and retina is by a migrating subretinal worm [2]

EPIDEMIOLOGICAL DISTRIBUTION

DUSN is prevalent in south-eastern USA, Caribbean area and Latin America [3]. Cases have been reported from India, China, Germany, England and Canada also.

In India cases have been reported from Coimbatore, Madurai and New Delhi. Most of the patients were from Kerala or had history of travel to Kerala [4].

CLINICAL FEATURES

There are two stages of presentation early and late. Clinical features vary according to the stage of presentation. In most of the cases the visual loss is insidious, so the late stage presentation is more common.

In early presentation patients present with acute loss of vision. Along with diminution of vision they have mild to moderate vitreitis, mild optic disc edema, and recurrent crops of evanescent, multifocal, grey- white or yellow lesion at the level of outer retina. On clinical examination there is relative afferent pupillary defect is seen. The active lesions are typically clustered in one segment of fundus. In the vicinity of active lesions, presence of worm should be sought. These active lesions generally disappear in 1 to 2 weeks.

Less than 1% lesions are of sufficient strength to cause focal chorioretinal scar. Other less common

early presentations are: ocular discomfort, congestion, iridocyclitis, retinal perivenous exudation, sheathing, hemorrhages, serous exudation and subretinal neovascularization. Marked loss of vision and early presentation is due to involvement of macular area and toxic dysfunction of outer retina and optic nerve [5].

In late presentation, if the diagnosis is missed and worm is not destroyed or patient doesn't report early, there will be progressive optic atrophy, narrowing of retinal arteries and patchy atrophy of retinal pigment epithelium (RPE).

DIAGNOSTIC EVALUATION

Identification of subretinal worm is the gold standard diagnostic modality. Careful indirect ophthalmoscopic examination can help in detecting the worm directly in subretinal space. But most of the time it is difficult to identify the worm. Fundus fluorescein angiography (FFA), Indocyanine green angiography (ICG), Electroretinography (ERG), Optical coherence tomography (OCT) and GdX all have been tried and described in literature.

In FFA-Lesions in the early stage of the disease, appear hypo fluorescent during the early stages of angiography and they stain during the later stages. Leakage of dye is found from optic disc. In late stage there is widespread abnormal hyperfluorescence suggestive of diffuse loss of RPE.

In ICG there is widespread punctate hypo fluorescence that doesn't correspond directly to active lesions. Reports of staining of worm with hyperfluorescent area on ICG are available in literature.

In ERG there is subnormal response in affected eye and b wave is affected more than a wave. OCT shows thinning of RPE and loss of retinal nerve fiber layer in late stage of the disease [6]. GdX reveals loss of RNFL. All the above mentioned tests are useless as far as diagnostic value is concerned.

CSLO video photography with blue light enhances the contrast between worm and retina and may detect the moving hyper reflective worm. OCT angiography has also been recently found useful in diagnosing DUSN [7].

Serology and blood test may help in identification of species of causative worm. Test for Antibody titer assay is available for Baylis Ascaris and Toxocara but not for Ancylostoma. ELISA and Western blot can be done for serological detection.

PATHOGENESIS

Histopathologically eye shows-nongranulomatous vitreitis, retinitis, retinal and optic nerve perivasculitis, extensive degeneration of

peripheral retina, mild degeneration of central retina, mild optic atrophy, degenerative changes in RPE and low-grade patchy choroiditis

ETIOLOGY

Two types of worm have been described as the causative agent of DUSN. Smaller one of 400 μ -1000 μ and a larger one of 1400 μ -2000 μ length. Many organisms have been implicated including *Ancylostoma caninum*, *Toxocara*, *Baylisascaris procyonis*, and filarial worms. But the precise identity of worm and portal of entry are still a mystery.

De Souza and Nakashima removed a live worm in 1996 and claimed it to be *Toxocara caninum* morphologically but not proved histopathologically [8]. But claim was rejected due to lack of consistent serologic evidence and infective second stage larva is smaller than the small worm. Moreover, *T. canis* has worldwide distribution while DUSN has limited and clinical feature of other ocular toxocara doesn't match with DUSN.

According to the epidemiological distribution, size of worm, distribution of alternate host, history of exposure to them and serological correlation the smaller worm is *A. caninum* and the larger worm is *B. procyonis* [9] (most accepted claim).

DIFFERENTIAL DIAGNOSIS

Early stage

- Active retinal lesion –*Toxoplasmosis, Cytomegaloviral disease, Fungal or bacterial retinal abscess, APMPE, MEWDS, Serpiginous choroiditis, Behcet's disease, Pseudo-POHS*
- Perivasculitis -*Sarcoidosis*
- Optic disc swelling –*Acute neuroretinitis, Papilloedema*
- Vitreitis -*Pars planitis*

Late stage

Retinal pigment epithelial atrophy–Presumed ocular histoplasmosis, Unilateral Retinitis Pigmentosa, Secondary to traumatic chorioretinopathy, ophthalmic artery occlusion

Optic atrophy-Secondary to optic neuritis, Compressive lesion, Ischemic optic neuropathy

TREATMENT

Destruction of live worm by retinal laser is the gold standard treatment when the worm is identified [10]. Argon or double frequency Nd: YAG laser can be used. Laser should immediately be done whenever the worm is identified.

Worm is photophobic, so it starts moving when laser is focused. Forward moving end is head and

a single shot of laser if targeted clearly can kill the worm. Otherwise many laser spots can be given safely if worm is outside macula. Sub foveal worm can be lured out of fovea by aiming laser beam and can be killed.

If worm can't be found, scatter laser treatment can be done in the area of active lesion. Sometimes inactive worm starts moving when low intensity burns (50mW) are given in the area of active lesions, which subsequently identified and killed.

Settings of laser for treatment is Power-150-200mW, Spot size 200-300 μ m and duration 150-200mS. Some of authors have advocated use of corticosteroid with laser to avoid reaction of toxin released by dying worm.

Treatment becomes difficult when worm is not identified. Oral Albendazole (thiabendazole in US), has been found effective. Albendazole is a broad-spectrum benzimidazole anthelmintic. Single-dose (400 mg) is believed to achieve cure rates of 90% against *Enterobius*, *Ascaris*, hookworm, cutaneous larva migrans, and giardiasis [11].

It acts by binding to parasite -tubulin, inhibiting its polymerization and impairing glucose uptake. Dose tried for DUSN is 400mg OD or BD, PO for 2-4 days. Largest case series recommends 400mg OD for 30 days [12]. In this case series steroid was not given with albendazole. But steroid is started before albendazole in treatment of orbital or neurocysticercosis.

Scatter laser treatment in the area of active lesion disrupts the blood retinal barrier (BRB) and facilitates the entry of drug in subretinal space. Patients with diffuse active lesion and vitreitis responds well as BRB is already disturbed.

Thiabendazole has been used in US in dose of 2gm PO for 2-4 days with good efficacy. Diethyl carbamazepine and ivermectin has also been used along with albendazole. But there is no case report available claiming efficacy without albendazole, of these two drugs.

Surgical treatment

Two cases have been reported in which worms were removed surgically [8]. One in 1996 from Sao Paulo, Brazil and another in 1999 from US. Three port vitrectomy with parallel retinotomy besides the worm was done. The worm was removed either by 20 gauge plastic suction cannula or fine forceps. Removed samples could not be subjected to histopathological examination due to early decay of material.

But surgical removal is difficult because it can be done only when nematode is seen and, in that case, it

can be easily destroyed by laser. Pre-operatively identified worm may move to some other area and may not be found during surgery leading to failure to remove. Worm is photophobic, so it starts moving with light of vitrectomy and removal becomes difficult. Live worm is highly adherent to retina and may brake during removal leading to failure in complete removal.

CONCLUSIONS

- DUSN is a unilateral disease presenting as vitreitis, papillitis, diffuse outer retinitis (early) and optic atrophy, vascular narrowing and patchy RPE atrophy (late).
- Strong suspicion and meticulous examination for worm may be rewarding in cases with similar presentation.
- Two types worm of can be found- smaller one 400-1000 μ and larger one 1400-2000 μ .
- Many worms have been suggested as the causative agent as *Ancylostoma*, *baylisacaris*, *toxocara*, *filaria* etc. but none has been proven.
- Laser induced destruction of worm is the treatment of choice when worm is seen.
- Albendazole is the drug of choice when worm is not seen.
- Identifying the case in early stage and proper treatment may prevent permanent loss of vision.

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