

**Case Report**

# Delayed Sympathetic Ophthalmia Involving Posterior Segment a Dilemma: A Case Report

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**Abstract:** We report a case of 11 year old young girl referred with complaint of right sided photophobia and pain following faucet induced trauma to left eye 3 months ago, followed by loss of sight in left eye. Patient presented to us with preperthical left eye and anterior segment uveitis in right eye. Fundus picture revealed cream colour white nodules confirmed as Dalen Fuchs on fundus fluorescein angiography and presence of hyperelective lesions placed at level of retinal pigment epithelium with disruption of the inner and outer segment (IS/OS) junction on spectral domain optical coherence tomography. Ultrasonogram-B-scan confirmed closed funnel retinal detachment in traumatized left eye and increased choroidal thickness in sympathizing right eye. She underwent orbital computerized axial tomography scan to rule out intraocular foreign body. She was diagnosed as a case of delayed sympathetic ophthalmia. Subsequently she was put on intensive topical with oral steroids and immunosuppressive therapy constituted with oral azathioprine and methotrexate continued for one year and tapered on resolution of presenting signs. At final follow up sympathizing eye was quiescent and sympathetic eye was preperthical. Sympathetic ophthalmia needs to be distinguished from other ocular auto-immune disorder such as Vogt Koyanagi Harada disease and Acute Multifocal Pigment Placoid Epitheliopathy to which it bears striking resemblance. As these disorders have variable response to treatment with widely differing outcome one must keep that in view while managing them. It is important to remember as the treatment is prolonged recurrences and patient drop outs are commonly noted.

**Keywords:** APMPE, Sympathetic, Trauma, Uveitis, VKHD

## 1. Introduction

Sympathetic ophthalmia (SO) and sympathetic uveitis has been defined by "Duke Elder et al". as rare bilateral diffuse granulomatous uveitis that tends to occur few days to several decades after penetrating accidental or surgical trauma to an eye where the traumatised eye is referred to as exciting eye and the non-traumatised eye is referred to as sympathizing eye [1, 2]. It has been observed that there may be a time delay of few days to decades between the occurrence of trauma and SO with 80% of cases tend to occur within 3 months and 90% within 1 year [2, 3]. "Gass et al". in 1982 reported the

prevalence of SO at 0.06% after penetrating ocular trauma and 0.01% following pars plana vitrectomy (PPV) [4]. It has also been implicated with other intraocular procedures as cataract extraction, iridectomy, paracentesis, cyclodialysis, retinal detachment repair, keratectomy, PPV, evisceration, and laser cyclophotocoagulation [2, 5]. As per "Gomi et al". in 1997, SO was responsible for nearly 0.3% of total uveitis and its incidence rate at one year was close to 0.03/100000 population as reported by "Kilmartin et al" [6, 7]. As per "Galor et al". peak incidence of SO occurrence after accidental trauma is placed between 4-8 weeks with the presentation in sympathizing eye usually associated with pain, lacrimation,

photophobia, blurred vision [1, 2, 8, 9]. The sympathizing eye shows signs of granulomatous iridocyclitis with inflammatory cells and flare in anterior chamber. Findings suggestive of active inflammation in posterior segment include vitritis, hyperemia with optic disc edema, exudative retinal detachment and papillitis [1, 2, 3, 8, 9]. Multiple yellow-white lesions are seen in periphery, confluent at times representing the Dalen Fuchs nodules which are absent in 30-50% of cases [10]. "Reynard et al" described and classified the nodule on morphological basis. According to him the nodule is typically a hemispherical mound consisting of epitheloid cells and lymphocytes lying beneath retinal pigment epithelium (RPE) and is morphologically divided into three types of lesion. The first type consist of focal hyperplasia and aggregation of retinal pigment epithelial cells, the second type typically classified as Dalen Fuchs nodule consists of closely packed collection of epitheloid cells lying underneath the RPE and the third type involves RPE dome of Dalen Fuchs nodule which degenerates with time releasing the cells into subretinal space. There is a possibility of all three types of lesions presenting at same time [11]. These lesions may be seen in other masquerade syndromes needing differentiation on clinical history and findings [11]. Chronic stage of SO may show sunset glow fundus with RPE changes similar to that seen in Vogt Koyanagi Harada Disease (VKHD) [2, 12], which may present with additional features of meningismus, tinnitus, cerebrospinal fluid pleocytosis, alopecia, poliosis and vitiligo [2, 12].

## 2. Case Report

A young Indian girl of 10 years was referred to us with complaint of pain, photophobia, redness and visual decline in right eye of 9 days duration. She had sustained penetrating trauma to left eye following faucet injury 3 months ago where a left globe rupture with full thickness corneo-scleral tear from 6-9 o'clock hours leading to uveal prolapse, hyphema with near total loss of vision. A cranial imaging had ruled out presence of foreign body. Primary wound repair was advised which was refused on financial grounds by the father of patient. Her medical records gave history of having taken a tetanus toxoid intramuscular injection and thereafter started on topical dexamethasone (1% instilled 4 hourly) and gatifloxacin (1% instilled 2 hourly) with a mydriatic and cycloplegic (atropine 1% instilled 8 hourly). She was simultaneously started on oral antibiotics (Cefuroxime 500 mgm 12 hourly and Metronidazole 400 mgm 8 hourly for 7 days). Oral prednisolone 30 mgm as once single dose with H2 receptor blocker (pantaprazole) was initiated and tapered over 3 weeks. The medications were eventually tapered and stopped by patient after 6 weeks and she failed to maintain follow up thereafter. Symptomatically the pain had subsided and eye had apparently become quiet and pre-*p*-thical.

After 3 uneventful months the traumatised eye had become pre-*p*-thical, and the good right eye (RE) presented with pain, photophobia and visual decline of 9 days duration. She had consulted a local chemist and had been started on topical

medication (Moxifloxacin 1% instilled 4 hourly and Dexamethasone 1% instilled 6 hourly) with oral nonsteroidal anti-inflammatory drugs (NSAIDs) with minimal to no relief of symptoms. Worsening eye status had made it imperative to seek medical advice.

Eye examination revealed best corrected visual acuity (BCVA) of hand movements (HM) in left eye with slit lamp biomicroscopy showing pre-*p*-thical eye with corneo-scleral scar running from 6-9 o'clock, collapsed anterior chamber and loss of other structural details (Figure 1). Vision in right eye was 6/24 with anterior segment and fundus revealing granulomatous uveitis, mutton fat keratic precipitates (KP) which were large (>1mm in diameter) and greasy-white with 3+ cells and 3+ flare. There were few irregular faded and pigmented KPs. Pupil was small, fixed and non-reactive with > 180 degree posterior synechiae (3-4 and 7-8 o'clock meridians). The anterior lenticular surface showed multiple iris pigment deposits with presence of 2 + cells in retrolenticular space with hazy vitreous. Fundus showed a hyperemic disc with clear disc margins. Foveal reflex was lost and there was presence of small discrete multiple yellow creamy white nodules (Dalen Fuchs) at the level of retinal pigment epithelium involving posterior pole and retinal periphery (Figure 2 and Figure 3). Intraocular pressure (applanation tonometer) was 8 mmhg in right eye and non-recordable in left eye.

Fundus fluorescein angiography (FFA) demonstrated early phase staining with late phase leakage with hyperfluorescence from optic nerve head. It characteristically showed multiple discrete hypofluorescent dot lesions located in posterior pole and periphery in early phase with late phase staining, hyperfluorescence and pooling of dye (Figure 4 and Figure 5). Spectral domain optical coherence tomography (Optovue SD-OCT) showed minimal disintegration and elevation of RPE with multiple small hyporeflective lesion at the level of retinal pigment epithelium (RPE) (Figure 6). Repeat SD-OCT two weeks later showed increase in size of the hyporeflective lesion with associated disruption of photoreceptor inner segment and outer segment (IS/OS) junction (Figure 7).

Ultrasonography B-scan confirmed presence of vitritis with increase in choroidal thickness and uneven retinal surface as findings in right eye. Traumatized left eye showed closed funnel retinal detachment with altered globe contour (Figure 8).

Diagnosis of SO was made keeping in view the clinical history, findings and imaging results. Presence of Dalen Fuchs nodule confirmed it as a case of sympathetic ophthalmia (SO). We carried out a thorough neurological examination with the aim of distinguishing it from vogt koyanagi harada disease (VKHD) and acute multifocal pigment placoid epitheliopathy (APMPPE). There were no meningismus (malaise, headache, fever, nausea, abdominal pain, neck or back stiffness), there was no findings suggestive of tinnitus, alopecia, poliosis or vitiligo. There were no ocular findings of episleritis or scleritis, cornea appeared healthy and posterior segment was ruled out for retinal vasculitis, papillitis or venous occlusion suggestive of acute posterior multifocal placoid pigment epitheliopathy.

Laboratory investigation of hemogram (Complete blood count and Erythrocyte sedimentation rate) Beckman coulter ACT 5-DIFF AL showed hemoglobin at 14.1mgm/dl (Normal range 3 months-10 years: 11.2+2.3 mgm/dl), total leucocyte count 7500/uL (Normal range: 4000-11,000/ul), differential leukocyte count detected elevated neutrophils 61.7% (Normal range 40-60%), absolute leucocyte count was in range. Platelet count was 3.10 lakhs (Normal range: 1.50-4.50 lakhs), mean platelet volume was 9.10 fl (Normal range: 7.0-11.0 fl), erythrocyte sedimentation rate was elevated to 17 mm in 1 hour (Normal range: 0-15 mmhr) and HS-C reactive protein was negative at 1.9 units (Biological Referral Interval < 6mg/L). An x-ray chest was carried out which was normal in finding. Her body weight was 35 kilograms.

Treatment was started immediately. Topical intensive steroid regime was initiated with (Dexamethasone 1%) 1 hourly with a broad spectrum antibiotic (Moxifloxacin 1%) 6 times with a mydriatic and cycloplegic (Atropine 1%) 3 times and non-steroidal anti-inflammatory (Bromfenac 1%) 3 times daily. The medications were tapered keeping in view the severity of disease seen in anterior chamber, vitreous and choroid using imaging. Three consecutive doses of methylprednisolone 1gm/day (Pulse therapy) were given in 200 ml of 20% dextrose normal saline (DNS) over 2 hours followed by oral prednisolone 1-1.5mg/kg/day were slowly tapered over 6 months to a dose less than 10mgm/day. An H2 receptor blocker and an antiemetic (Rabiprazole-domperidone) were added for symptomatic relief with folic acid and calcium supplementation. Patient developed significant cushingoid facies due to steroid use and ocular hypertension which was successfully managed with anti-glaucoma medication (Brimonidine 1% and Timolol 0.5% twice daily).

Persistence of side effects and patients inability to tolerate oral steroids made it necessary to add early immunosuppression treatment. Our patient was young and one eye who started showing early outfall of steroids hence it became necessary to start immune-modulator therapy early in course of treatment. As per rheumatologist advice she was given an initial prescription of oral azathioprine (25 mgm twice daily) (1-3mgm/kg/bodywt) and a review was fixed for 7 days. A strict watch was kept on her complete blood count. She was tolerating azathioprine well and her dose had been elevated (50 mgm twice daily) after two weeks as no outfall or side effects were noticed.

On revisit at 14 days her visual acuity had improved to 6/18, anterior chamber reaction with vitreous cells and flare had reduced. Optic disc hyperemia persisted with continued presence of Dalen Fuchs nodule. We did notice a significant finding on SD-OCT which revealed a more well defined and prominent elevated dome shaped sub-retinal pigment epithelium located Dalen Fuchs nodules showing progression compared to first visit (Figure 7).

At 6 months follow up her vision had returned to 6/9 in sympathising right eye. The left inciting eye was quiet. Fundus picture showed RPE areas of depigmentation in periphery with normal appearing central fundus. She was on maintenance dose of oral azathioprine (50 mgm once daily)

and oral prednisolone (10 mgm once daily) with none features suggestive of intolerance. Her hemogram and liver function test (LFT) were normal.



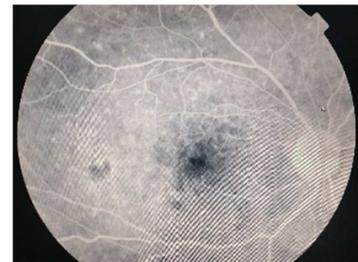
**Figure 1.** Shows a pre-ptical eye with organized haemorrhage in anterior chamber with loss of structural details.



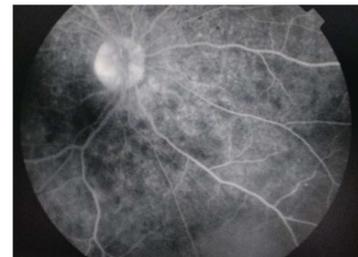
**Figure 2.** Colour photo of (RE) fundus shows multiple discrete creamy white to yellow oval lesions (Dalen-Fuchs nodule) at posterior pole and periphery measuring greater than 100 microns.



**Figure 3.** Colour photo of RE shows multiple yellow oval lesions in inferotemporal quadrant.



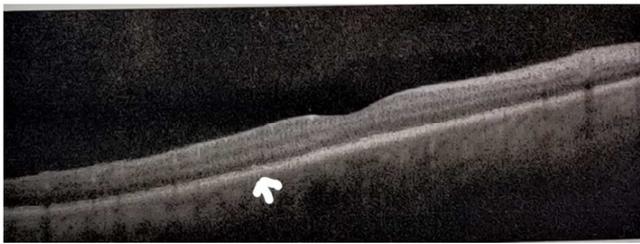
**Figure 4.** Flourescein angiography shows multiple discrete oval hyperflourescent lesions in posterior pole.



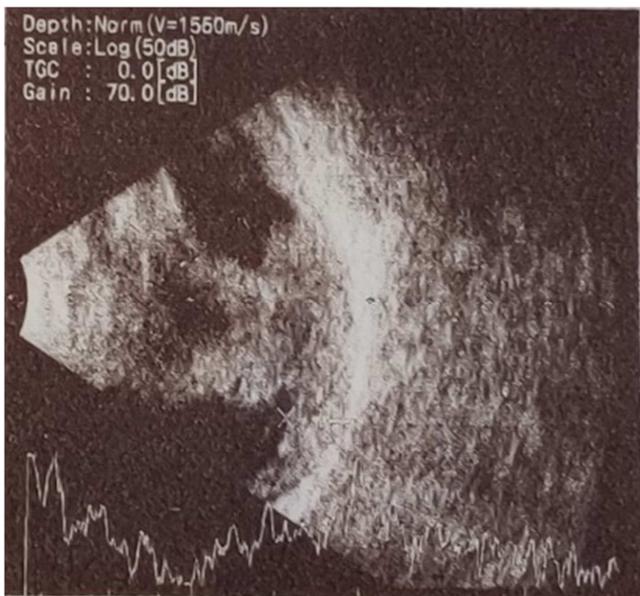
**Figure 5.** Fundus flourescein angiography shows multiple discrete oval hyperflourescent lesions in periphery.



**Figure 6.** SD-OCT (OPTOVUE) (Lower image) Progression of Dalen-Fuchs nodules: shows multiple oval hyperelective sub retinal pigment epithelium (RPE) lesion at the posterior pole (lower image short white arrow).



**Figure 7.** (upper image) shows a well defined enlarged sub RPE lesion (Dalen-Fuchs nodule, upper image long white solid arrow) showing progression of nodule at interval of two weeks.



**Figure 8.** USG B scan shows picture of total open funnel retinal detachment.

### 3. Discussion

SO is an autoimmune disorder bearing close resemblance to VKHD and APMPPE. These disorders act against antigens associated with melanocytes of the choroidal stroma. Antecedent surgical and trauma history would guide in differentiating SO from these disorders. SO commonly presents as bilateral granulomatous panuveitis bearing close resemblance histopathologically and clinically to VKHD with presence of Dalen Fuchs nodule.

SO occurred in our patient more than 3 months post trauma indicating a delayed autoimmune response to T-cell mediated

reaction to melanocytes in uveal tissue.

Lack of primary wound repair and existence of incarcerated uveal tissue would have served as inciting agent in sympathetic eye [1, 2]. Time of occurrence of inflammation stages disease into acute and chronic. Presentation in our patient was late compared to typical case of SO though late presentations have been documented to occur in 90% of patients within a year of penetrating or surgical trauma. The presence of old keratic precipitates on the endothelium indicates towards multiple episodes of mild intermittent uveitis in the sympathising eye [2, 3]. An absence of acute symptomatic disease would have served as a reason for late presentation and delay in seeking medical advice. Late occurrence of SO is not seen as frequently due to accessibility to early surgical repair with presence of good steroid coverage.

SO presentation was mild in our patient in contrast to commonly occurring fulminant uveitis in typical case. The early use of steroids could have contained the disease initially. SO may appear clinically as VKHD however the latter is preceded by meningismal signs and extraocular presentation of alopecia, poliosis, vitiligo and dysaacusis which were absent in our case [12]. All clinical features do not occur at initial presentation. Past medical treatment along with stage of disease would influence the clinical picture. USG B-scan efficiently aids in diagnosing early stage of disease in cloudy media due to dense posterior synechiae or cataract [13]. FFA picture bears striking resemblance to APMPPE and VKHD. "Correti et al". are of the belief that RPE overlying Dalen Fuchs nodule determines the nature of these lesions on angiography [14]. On OCT they appear as hyperelective lesions placed at level of RPE with disruption of the inner and outer segment (IS/OS) junction [15]. We were able to detect progression of Dalen Fuchs nodule by enhanced depth imaging over a time period of two weeks.

SO is a chronic disease with clinical course being characterised by remissions and recurrences. Corticosteroids are considered primary modality of therapy in such cases. Corticosteroids can be administered either as a systemic therapy in the form of pulse therapy with intravenous administration followed by oral administration or in the form of local intravitreal therapy as Flucinolone or Ozurdex implant [16]. Local intravitreal therapy benefits with nil systemic side effects and persistence of effectivity even after cessation of direct anti-inflammatory effect. Severe cases of SO are best controlled with pulse therapy initially and are effectively used where posterior segment visibility is poor. Oral steroids are tapered after seeing response to clinical therapy with assessment of anterior segment cellular activity and posterior segment inflammation with watch on choroidal thickness, subretinal fluid and optic disc status before tapering.

Immunomodulator therapy is introduced early in disease to reduce chances of recurrence and rebound after discontinuation of steroid therapy and for stabilizing disease. They may be used where steroids have to be discontinued due to their systemic side effects [17]. Azathioprine was used to good effect in our patient. It is advisable to taper

immunomodulator therapy with caution since recurrences are commonly known to occur [17]. Mycophenolate mofetil and methotrexate are equally effective. Evolving therapy which tend to work effectively in SO are biologic agents. Two agents used frequently are infliximab and adalimumab which suppress TNF-alpha a prominent key pro-inflammatory cytokine with elevated levels in SO [18].

## 4. Conclusion

Clinical history and imaging aid in diagnosing SO. We found classical picture of Dalen Fuchs nodule confirmed on SD-OCT. Delayed presentation of SO must be ruled out from VKHD and APMPPE as antecedent history of trauma may not be available. Treatment is prolonged and outcome not always desirable. Steroids with immune modulator therapy and biologic agents play crucial role in controlling initial disease and preventing recurrence. As SO require long treatment and follow up, high dropout and recurrences are commonly seen.

## Ethics Statement and Conflict of Interest

The author and co-authors hold no financial interest or conflict of interest with this publication.

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