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Case Series

Pre-retinal Inflammatory Precipitates (PIP) in Three Cases of Acute Retinal Necrosis Caused by Herpes Zoster Virus

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Abstract

Aim: To describe unusual Pre-retinal Inflammatory Precipitates which are noted at the Optical Coherent Topography in three cases of Acute Retinal Necrosis (ARN).

Methods: Retrospective case series.

Results: Pre-retinal Inflammatory Precipitates (PIPs) were identified using the Spectralis Heidelberg optical coherence tomography (OCT) in three cases of Acute Retinal Necrosis in which vitreous tap confirmed the presence of Herpes Zoster Virus by polymerase chain reaction (PCR). Patients were successfully treated with intra-vitreal Foscarnet injections and oral Valacyclovir.

Conclusion: The unusual sign of Pre-retinal Inflammatory Precipitates can be found on OCT scan in some cases of Acute Retinal Necrosis caused by Herpes Zoster Virus and may prove to be helpful in making a correct diagnosis and monitoring the disease activity.

Keywords: *Pre-Retinal Inflammatory Precipitates; Acute Retinal Necrosis; Optical Coherence Tomography; Herpes Zoster; Foscarnet*

Background

Acute retinal necrosis is an inflammatory condition affecting the posterior pole of the eye causing vitritis and retinitis. Varicella-zoster virus is well documented as the leading cause of acute retinal necrosis and it is recognised that early diagnosis and treatment is key to achieving a good visual result. Complications include retinal detachment, anterior ischaemic optic neuropathy and central retinal artery occlusion.

We describe three cases of ARN in which additional clinical information was available as a result of imaging with Heidelberg OCT, multicolour imaging and Optos wide field photography.

Case Reports

All three cases had positive polymerase chain reaction (PCR) for Herpes Zoster Virus. They all received Intra-vitreal Foscarnet (2.4 mg/0.1 ml) injection twice a week and oral valacyclovir 1g tds.

Case 1

A fifty years old man presented with one day of painless blurred vision and floaters affecting the left eye only. Visual acuity (VA) was RE 6/7.5 and LE 6/38. The left eye had 2+ cells in the anterior chamber with posterior synechiae, dense vitritis and there was a suspicion of

a peripheral white retinal lesion although the view was very poor. Normal fundus camera revealed no useful details (Figure 1a) however Spectralis optical coherence tomography (OCT) showed pre-retinal inflammatory precipitates (PIPs) on the retinal surface at the fovea (Figure 1b). Further imaging with Heidelberg multicolour imaging showed extensive PIPs across the retina following the main retinal vessels as well as Kyrieleis plaques (Figure 1c and 1d). At six months follow up acuity had improved to LE 6/6.

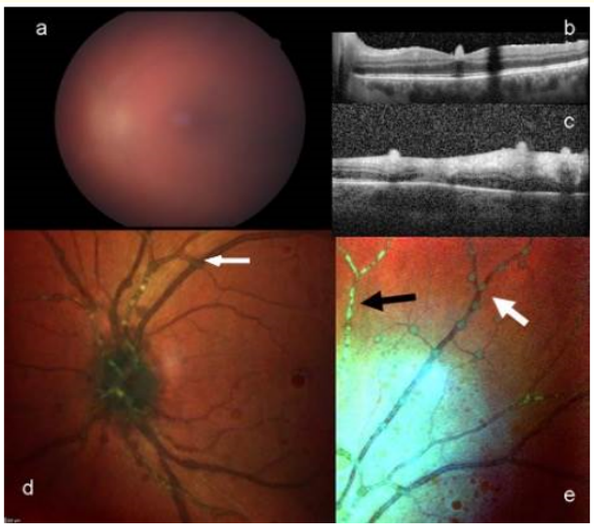

Figure 1: *(a) Dense vitritis and a white retinal lesion through the poor view with a conventional fundus camera.(b) Spectralis optical coherence tomography (OCT) showing Pre-retinal Inflammatory Precipitates (PIPs) on the retinal surface at fovea. (c) Spectralis OCT showing PIPs overlying retinal blood vessels (d and e) Heidelberg multifocal imaging showing extensive PIPs across the retina (white arrows) following main retinal vessels as well as Kyrieleis Plaques (black arrow).*

Case 2

An eighty nine years old gentleman had chemotherapy for Follicular Non-Hodgkin's Lymphoma. He developed left sided Herpes Zoster Ophthalmicus and oral candidiasis. He was treated with intravenous then oral Acyclovir and oral Fluconazole for 10 days. Two months later, he represented with hand movement vision in left eye due to ARN (Figure 2a) and was treated with intravitreal foscarnet and valaciclovir. OCT demonstrated PIPs (Figure 2b) as well as inflammatory condensations on the posterior surface of the vitreous which had

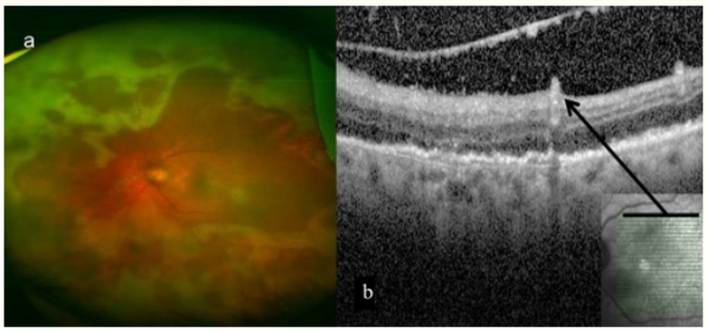

Figure 2: *(a) Left Acute Retinal Necrosis (ARN) at Optos wide field imaging. (b) Pre-retinal Inflammatory Precipitates (PIPs) and inflammatory condensations on the posterior surface of vitreous which has separated from retina.*

separated from the retina. Vision did not improve with treatment.

Case 3

A sixty-six years old male presented with a two weeks history of painless blurred vision and floaters in his right eye ten weeks after routine cataract surgery. On examination the visual acuity was counting finger RE and 6/6 LE. The right eye had 2+ cells in the anterior chamber, keratic precipitates and vitritis. Fundoscopy revealed white patches in the temporal retina (Figure 3a) and Kyrieleis plaques (Figure 3b). After initial improvement of vision to 6/60 on treatment the patient prematurely stopped taking the oral valacyclovir after two weeks. A week later he represented with a new area of retinal necrosis within the macula and count fingers vision. The dramatic visual loss was felt to be due mainly to a new foveal PIP (Figure 3d) and increased vitritis. Multiple other PIPs were also picked up using Optos widefield imaging (Figure 3a-3c). Treatment was restarted and 8 weeks later vision had improved to RE 6/9.5 with complete resolution of the pre-foveal deposit and gradual regression of the retinal necrosis with persistence of the Kyrieleis plaques (Figure 4).

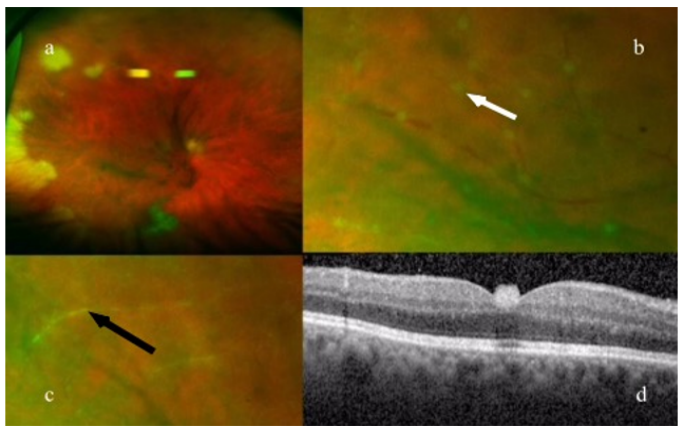

Figure 3: *(a) Optos wide field imaging showing white patches on the temporal retina. (b) Optos wide field imaging showing multiple Pre-retinal Inflammatory Precipitates (white arrow). (c) Optos wide field imaging showing Kyrieleis Plaques. (d) Spectralis optical coherence tomography (OCT) showing Foveal PIP.*

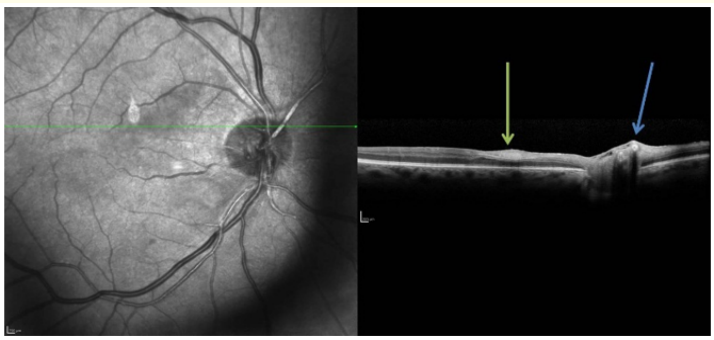

Figure 4: *Spectralis optical coherence tomography showing regressing patch of retinal necrosis (yellow arrow) and a Kyrieleis plaque surrounding a blood vessel at the optic disc (blue arrow).*

Discussion

A recent review of ARN explored the factors contributing to visual loss listing retinal detachment, optic nerve or macular involvement by ischaemic vasculopathy, and less frequently to macular hole formation, macular pucker or hypotony but did not mention pre-retinal inflammatory precipitates which we believe can be a cause of significant reversible visual loss in this group of patients [1].

There is scant reference to pre-foveal condensations in the literature. One case report, published before the availability of OCT, did document gray-white spherical deposits on the retinal vessels and vitreo-retinal interface of the fovea. These were discovered in one patient with acute retinal necrosis secondary to varicella-zoster virus and one with pre-proliferative diabetic retinopathy [2]. Both these patients were asymptomatic carriers of human T-lymphocyte virus 1 (HTLV-1) and interestingly, gray- white granular deposits had been previously been described with patients suffering from HTLV-1 associated uveitis (HAU) raising the possibility of a link between HTLV-1 and the formation of gray- white granular deposits on the retina [3]. It is likely that pre-foveal condensations would have been detected on OCT in these patients if OCT had been available. In our series case 2 and case 3 were tested for HTLV-1 but were both negative.

Pre-foveal condensation on OCT has been reported previously by Paulus., *et al* [4]. They described two cases of chronic ocular inflammation with inflammatory vitreous opacities attached to the fovea at the vitreo-foveal interface as a 'pre-foveal white vitreous condensation'. One patient was a child with intermediate uveitis, the other a 65 year old woman with bilateral recurrent intraocular lymphoma. On pathological and cytological evaluation these condensations were unremarkable except for inflammatory cells. It is likely that the condensations represent clusters of inflammatory cells. In our cases the precipitates were present on the retina even when the vitreous had separated so we prefer the term "Pre-retinal Inflammatory Precipitate". It is possible that these blobs represent migration of white cells through the retinal blood vessels into the vitreous space but the accumulation of material at the fovea where there are no retinal blood vessels suggests that it is more likely that they are precipitating there in a similar manner to keratic precipitates on the corneal endothelium. It may be that precipitating cells can stick more easily to the retinal vessels than the retina between vessels and this is why they have a predilection for clumping along vessels. A case with similar finding was reported as a rare association of perivascular Granulomatous Lesions in a Patient with Acute Retinal Necrosis (ARN) [5]. In our cases, we identified perivascular as well as fovea accumulation. The foveal accumulation in our cases shows that they are not simply a stage in the formation of Kyrieleis plaques.

Pre-foveal vitreous deposits are not a common sign despite the frequent occurrence of vitreous cells in uveitis. We postulate that it is the specific subtype of white cells involved in killing virus in the eye which makes them clump in this unusual way but not enough cases have been reported to assess how useful this OCT sign will be clinically. Despite Alessandro Invernizzi., *et al.* stated that hyper-reflective round deposited along the posterior hyaloid were noted in eyes with toxoplasmosis and hyper-reflective vertical strips within the outer nuclear layer were suggestive if viral etiologies, Pre-retinal inflammatory precipitates (PIPs) were not specifically discussed in other causes of vitritis [6]. Certainly it is a very unusual OCT sign not yet reported in commoner causes of vitritis such as sarcoidosis.

It was particularly interesting that in the case 3, the pre-foveal vitreous condensation resolved with initial treatment but then reappeared as the ARN relapsed and progressed. All three cases also developed extensive Kyrieleis plaques, a sign more commonly associated with toxoplasmosis but increasingly reported with ARN in recent years [7]. The OCT imaging of the Kyrieleis plaques showing that the plaque fully encloses the circumference of the artery has, to the best of our knowledge, never been published before.

In cases where there is a very dense vitritis it can sometimes be difficult to differentiate viral ARN from toxoplasmosis but a hexagonal pattern of corneal keratic precipitates may be seen in herpes virus ARN again demonstrating an atypical pattern of inflammatory cell deposition. It remains to be seen if this pre-foveal condensation is in any way helpful in differentiating these, and other, causes of dense vitritis. What was very striking in all three of our cases was the enormous benefit of having confocal (SLO) based imaging. In case 1 the retinal view was poor yet reasonable images could be produced with the multi-colour confocal SLO camera giving a good deal of additional information. In case 3 the Optos camera also revealed extensive changes not easily recorded by any other imaging system allowing easy identification of new areas of retinitis.

Conclusion

Pre-retinal inflammatory precipitates can be a useful OCT sign in cases of Acute Retinal Necrosis caused by Herpes Zoster Virus. We believe routine use of laser-based multimodality imaging such as Spectralis Multicolor Scanning laser imaging, wide field Optos and the use of Spectralis OCT can usefully complement clinical information in ARN cases.

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