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CASE REPORT

Vitreous Haemorrhage: A Consequence of Herpes Simplex Acute Retinal Necrosis

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ABSTRAK

Nekrosis retina akut adalah penyakit yang jarang sekali berlaku, tetapi jika terjadi, ia mengakibatkan kebutaan dan biasanya melibatkan orang dewasa. Walau bagaimanapun, dalam laporan ini, kami ingin mengutarakan pengenalpastian, rawatan dan hasil rawatan penyakit ini yang dialami seorang gadis sihat yang berumur 13 tahun. Pesakit ini datang untuk konsultasi dengan aduan kabur penglihatan pada mata kanan yang juga merah dan sakit. Pemeriksaan mata menunjukkan optik disk bengkak dan retina pucat. Kelihatan juga tompok-tompok keradangan retina dan pendarahan di pertengahan pinggiran saraf mata, di samping retina lekang. Keradangan yang melarat dengan begitu pantas dalam masa empat hari dan pembentukan katarak menyukarkan lagi diagnosa dan proses rawatan. Walaupun demikian, rawatan anti virus tetap dimulakan dengan serta-merta sementara menunggu keputusan ujian 'polymerase chain reaction' ke atas cecair vitreous, di mana virus Herpes Simplex-1 telah dikenalpasti. Keradangan bertambah pulih, tetapi komplikasi pendarahan vitreous berlaku. Berikutan itu, laser pada retina telah diberi. Oleh itu, adalah penting untuk ditegaskan bahawa nekrosis retina akut pada dasarnya adalah diagnosa klinikal dan perlu dikenalpasti seawal yang mungkin, lebih-lebih lagi jika melibatkan kanak-kanak supaya rawatan yang sewajarnya dapat diberi dengan segera. Komplikasi yang timbul juga perlu ditangani dengan sewajarnya secepat mungkin untuk meningkatkan peluang memelihara penglihatan yang baik.

Kata kunci: imunokompeten, nekrosis retina akut, virus Herpes Simplex-1

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ABSTRACT

Acute retinal necrosis (ARN) is a rare, blinding disease that typically affects adults. However, in this case report, we highlight the diagnosis, management and outcome of herpes simplex acute retinal necrosis in a 13-year-old healthy girl, who presented with painful right eye, redness and blurring of vision for one week. Examination of the right eye showed features of granulomatous panuveitis. Optic disc was swollen and retina appeared pale. There were multiple patches of retinitis and haemorrhages at mid-periphery of the fundus with inferior serous detachment observed. Rapidly progressive inflammation in just four days along with secondary cataract that obscured fundus view, imposed greater challenge to the diagnosis and management. Intravenous acyclovir 300mg, 3 times a day was initiated promptly while vitreous fluid was sent for polymerase chain reaction, which identified Herpes Simplex Virus-1. Inflammation improved, but she developed vitreous haemorrhage secondary to proliferative retinopathy, which required panretinal photocoagulation. ARN is therefore, principally a clinical diagnosis and high index of suspicion is crucial particularly, in children for prompt diagnosis and treatment. Complications should also be addressed timely to improve the chances of preserving vision.

Keywords: acute retinal necrosis, herpes Simplex Virus-1, immunocompetent

INTRODUCTION

Acute retinal necrosis (ARN) is a viral syndrome that characteristically occurs in otherwise healthy young adults, aged 20-50 years (Lewis et al. 1989; Lauren et al. 2017; Andrew et al. 2017). It was first reported in 1971 (Urayama & Sasaki 1971). Incidence in the UK is 1 in 1.6 to 2.0 million populations per year and the commonest cause is Varicella-zoster Virus (VZV), accounting for 50-80% of all cases (Muthiah et al. 2007), followed by Herpes simplex virus type 1 (HSV-1), Herpes simplex virus type 2 (HSV-2) and rarely Cytomegalovirus (CMV) (Lauren et al. 2017). ARN caused by HSV-1 was first reported in 1988 and may occur following reactivation of latent viral infection or even as a primary infection (Lewis et al. 1989). HSV is the commonest cause of ARN in children (Silva et al. 2013). We report an unusual case of Herpes Simplex acute retinal necrosis following viral keratitis in a young, healthy girl which was complicated by vitreous haemorrhage.

CASE REPORT

A 13-year-old healthy girl presented with painful right eye, redness and blurring of vision for one week preceded by a brief history of eye redness following alleged foreign body (sand) entry into the right eye which resolved spontaneously within

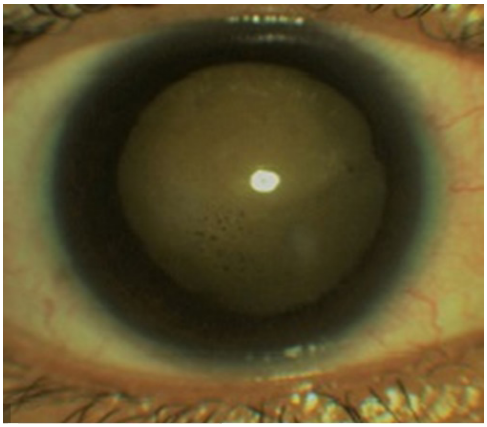

Figure 1: Anterior segment photograph of the right eye showing multiple sub-epithelial corneal opacities with keratic precipitates on endothelium

a week. She denied history of ocular trauma, recent viral-like illness or fever, tuberculosis contact, jungle trekking, contact with pets or high risk behaviours. Her vision at presentation was 1/60 in the right eye and 6/6 in the left.

Examination of the right eye revealed injected conjunctiva, presence of multiple sub-epithelial

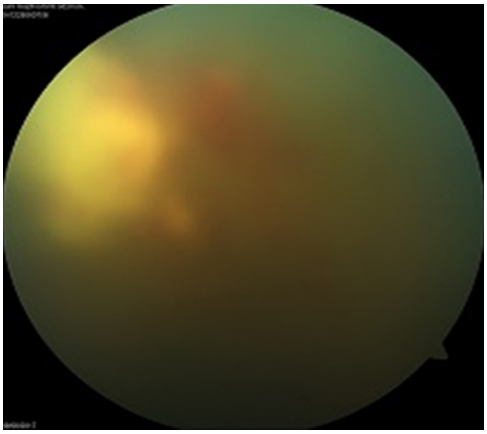

Figure 2B: Fundus photography at presentation showing largest retinitis, measuring 3 disc diameter at superotemporal quadrant with surrounding mid-periphery retinal hemorrhages.

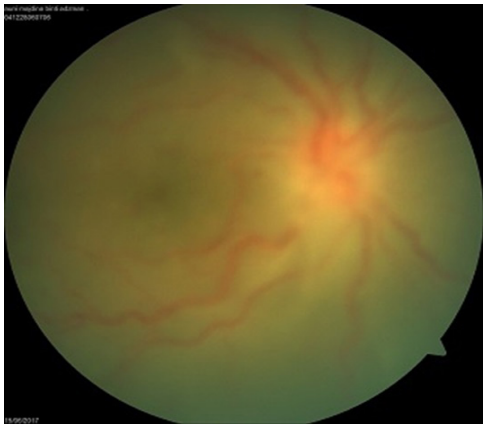

Figure 2A: Fundus photography at presentation showing right swollen optic disc and dilated, tortuous vessels.

corneal opacities and thickened corneal nerves (Figure 1). The corneal sensation was also reduced. Right pupil was mid-dilated, with presence of posterior synechiae at 2 o'clock and there was no relative afferent pupillary defect. There was granulomatous panuveitis evidenced by mutton-fat keratic precipitates, anterior chamber cells, anterior vitreous cells and dense vitritis. Optic disc was swollen with dilated and tortuous vessels (Figure 2A). Retina appeared ischaemic with

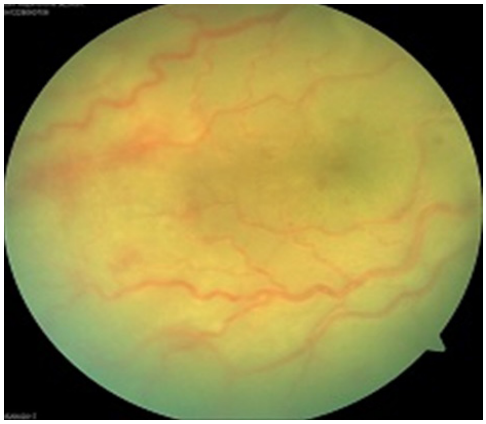

Figure 2C: Fundus photography at presentation showing pale retina with dilated, tortuous vessels and inferior serous retinal detachment.

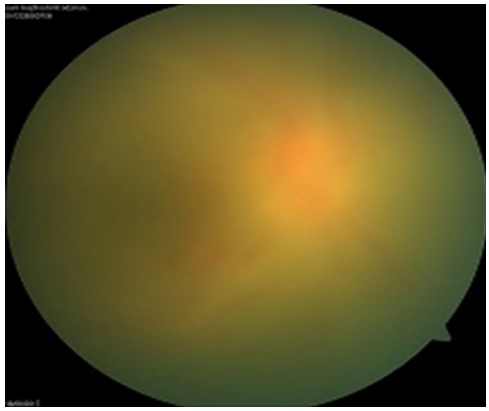

Figure 3: Fundus photography showing rapidly worsening ocular inflammation at day 4 of presentation.

multiple patches of retinitis; largest at the superotemporal quadrant (Figure 2B) and haemorrhages at mid-periphery with inferior serous retinal detachment (Figure 2C). Left eye and systemic examinations were otherwise unremarkable. There were no lesions over the lips, fingers or genitalia.

Inflammation and secondary cataract progressed rapidly in 4 days obscuring the fundus view (Figure 3). After consultation with uveitis specialist, the diagnosis of acute retinal necrosis (ARN) following viral keratitis made. Hence, intravenous acyclovir 300mg, 3 times a day was initiated immediately and completed for 14 days, followed by oral acyclovir 800mg, 5 times a day for a total of 3 months. Oral prednisolone 20mg daily, was introduced a week after the initiation of intravenous acyclovir and tapered slowly over 3 months. Vitreous fluid obtained, was sent for polymerase chain reaction (PCR), which came back positive for Herpes Simplex Virus-1 a week later. All other infective screening, including HSV-1 and HSV-2 serology were negative.

Rapid improvement of inflammation and retinitis were observed (Figure 4) but 3 weeks later, she developed vitreous haemorrhage as well as worsening cataract. Laser panretinal photocoagulation administered 360° peripherally for vitreous haemorrhage secondary to proliferative retinopathy, and laser uptake was satisfactory in spite of media opacity. However, fundus fluorescein angiography (FFA)

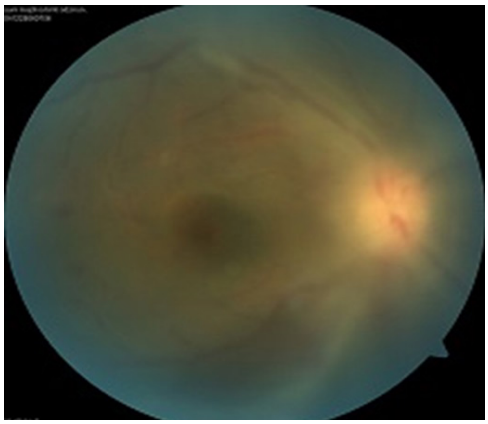

Figure 4A: Fundus photography of the right eye at 1 month, after initiation of antiviral.

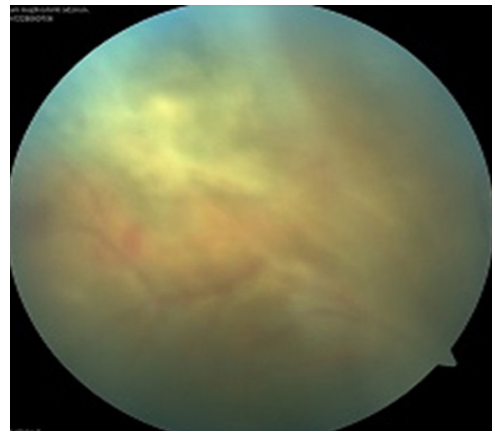

Figure 4B: Fundus photography of the right eye at 1 month after initiation of anti-viral, showing improving vitritis and contracting retinitis at the superotemporal quadrant.

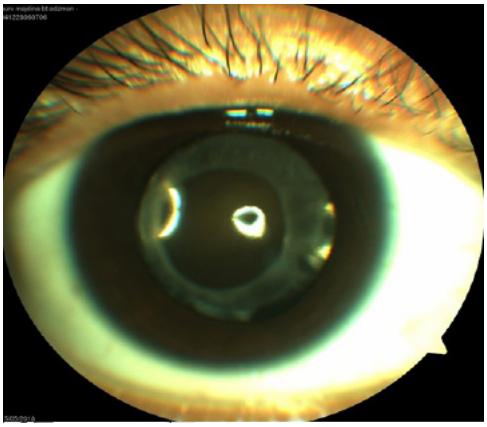

Figure 5A: 3 months post cataract extraction and intraocular lens implantation with clear cornea

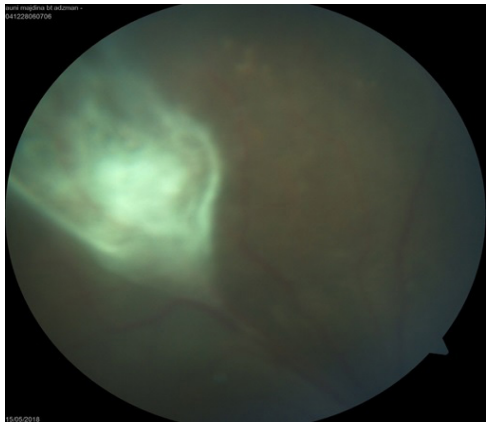

Figure 5B: Scarring of the previous superotemporal retinitis.

was not performed due to the poor fundus view. A month later, she was subjected to lens aspiration and posterior chamber intraocular lens implantation. Vitreous hemorrhage, intraocular inflammation and retinitis gradually resolved (Figure 5A & 5B), and she achieved best corrected visual acuity of 6/12, three months later.

DISCUSSION

HSV gains entry into ocular cells mostly by reactivation of a latent infection either via anterograde transport of HSV from the trigeminal ganglia or from the densely innervated cornea itself (Farooq et al. 2010). However, exogenous exposure and direct invasion of the virus into corneal epithelium is possible too (Farooq et al. 2010; Shah et al. 2010). ARN in this child may possibly be the result of direct HSV invasion following foreign body (sand) entry. The virus can survive on inanimate surfaces between few hours up to 7 days (Kramer et al. 2006). HSV-1 uses a pH-dependent process involving herpes virus entry mediator (HVEM), nectin-1 and paired immunoglobulin-like 2 alpha (PIL-α) receptors to gain entry into human corneal epithelial cells (Shah et al. 2010; Shukla et al. 2009). Thereafter, the virus reaches the retina through neural pathways (Shukla et al. 2009).

ARN is characterized by a triad of panuveitis with occlusive vasculitis and necrotising retinitis Shantha et al. 2015). The American Uveitis Society criteria for the diagnosis of ARN includes: one or more focus of peripheral retinal necrosis, rapid progression and circumferential spread of the disease without antiviral, evidence of occlusive vasculopathy with arteriolar involvement and a prominent inflammatory reaction in the vitreous and anterior chamber (Lauren et al. 2017). Inflammation which progressed rapidly in 4 days, alerted us of the possibility of ARN and antiviral was started even before vitreous sample was taken. Increasing evidence shows that overall immune dysfunction affects the severity of ARN. Herpetic

necrotising retinopathy is a spectrum with two disease entities at either end, namely ARN and progressive outer retinal necrosis (PORN). Those with normal cellular defence have either a milder form of disease or typical ARN with prominent vitritis, while in the immunocompromised, the disease is more severe. However, in the complete absence of cellular immunity, as seen in AIDS, PORN with minimal vitritis develops (Guex-Crosier et al. 1997; Rochat et al. 1996). This suggests that heightened inflammatory responses seen in younger patients may be due to immaturity of the cellular immunity.

Increased vitreous turbidity occurs during the acute phase due to enormous breakdown of the blood-ocular barrier, associated with proliferative and chemotactic effects on retinal pigment epithelium and fibroblasts, where as, in the cicatricial phase, proliferative vitreoretinopathy develops as a result of membrane formation and vitreous contraction (Ahmadieh et al. 2003). In the present case, the acute phase led to the development of proliferative retinopathy with the evidence of vitreous haemorrhage. Occlusive vasculitis and severe inflammation contributes to retinal hypoxia (Shantha et al. 2015) which in turn, stimulates the production of vasoproliferative factors, leading to neovascularisation. Laser panretinal photocoagulation converts the ischaemic retina to an anoxic stage, thereby, removing the stimulus and promotes regression of neovascularisation. FFA to look for areas of non perfusion was not done in view of poor fundus view. Although rhegmatogenous retinal detachment developed in about 50-85% of patients with ARN (Shantha et al. 2015; Ahmadieh et al. 2003), this complication was not seen in our patient. She presented with serous retinal detachment and as stressed in previous reports, exudative retinal detachment in the presence severe posterior segment inflammation, should alert the possibility of an underlying HSV infection (Duker et al. 1990). Another complication seen in this patient was cataract, a common sequelae as a result of uncontrolled, prolonged inflammation. It is the cause of poor vision in up to 40% of those with uveitis (Durrani et al. 2004).

To date, there is no consensus on the optimal treatment of ARN due to inadequate clinical trials as the disease is rare. It is mostly treated using the conventional regime of intravenous acyclovir 10 mg/kg, 3 times daily for 5 to 10 days, followed by oral acyclovir 400-800mg, 5 times daily for at least 6 weeks (Tam et al. 2010). However, treatment solely with oral antiviral is increasingly being employed as supported by the largest consecutive case series (Aizman et al. 2007).

Yoav et al. 2014, in a case report, advocated high dose methylprednisolone pulse therapy in addition to antiviral after achieving excellent outcome in a 4-year-old child with poor prognosis. Corticosteroids in ARN however, is controversial and should be used cautiously as it may potentiate viral replication. Thus, worsening the disease outcome and affecting the healthy eye (Shantha et al. 2015; Yoav et al. 2014). Typically, oral prednisolone (0.5-2.0 mg/kg/day)

is used as adjuvant therapy to combat intense inflammatory response in ARN, 24-48 hours after initiation of antiviral for up to 6-8 weeks.

CONCLUSION

The rarity of the disease makes a definitive approach to its management difficult and since the diagnosis is essentially clinical, close monitoring, early recognition and treatment is important. Although, PCR is helpful in identification of the disease, high index of suspicion is necessary and it should not contribute to the delay in diagnosis. The clinical course of ARN although rare, could be complicated by vitreous hemorrhage as seen in our patient. However, with timely intervention, good visual outcome can be achieved.

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