Bilateral acute retinal necrosis in premature newborn with skin, eye, and mouth infection presenting with vitreous and subretinal hemorrhage

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A premature newborn with systemic sepsis due to *Candida albicans* and *parapsilosis* developed skin, eye, and mouth herpetic infection. Ocular disease presented atypically with vitritis and pre and subretinal hemorrhage due to herpes simplex virus-1 confirmed fulminant bilateral acute retinal necrosis. Pars plana vitrectomy revealed necrotizing retinitis with poor visual prognosis. The baby has survived suffering from multiple morbidities which include post-hemorrhagic hydrocephalus, chronic lung disease, patent ductus arteriosus, and developmental delay.

Key words: Bilateral acute retinal necrosis, herpes simplex virus type 1, subretinal hemorrhage, vitreous hemorrhage

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Bilateral acute retinal necrosis (BARN) is a severe sight-threatening condition with poor prognosis in all age categories. In a recent report, herpes simplex virus (HSV)-1 was the most frequent cause, followed by HSV-2 and varicella-zoster virus.[1] In children and neonates, HSV-2 has been reported as more frequent causative agent.[2,3] Herpes simplex encephalitis has been postulated as a risk factor.[4-6] Neonatal reports of HSV-1 BARN are rare.[7-9] Herein, we present a case of premature neonate with skin, eye, and mouth (SEM) infection and HSV-1 confirmed fulminant BARN presenting with vitritis and pre and subretinal hemorrhage.

Case Report

A 12-day-old baby boy of Indian origin with a history of extreme prematurity (24 weeks, birth weight of 580 g) was admitted

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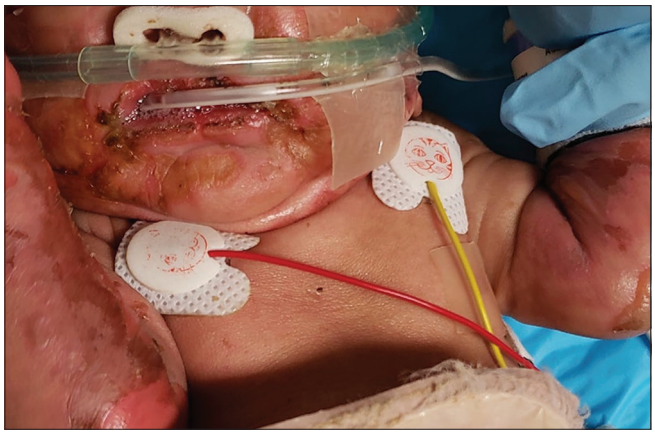

Figure 1: General picture of skin and mouth vesicles and jejunostomy characterizing skin, eye, and mouth (SEM) neonatal herpes simplex virus infection

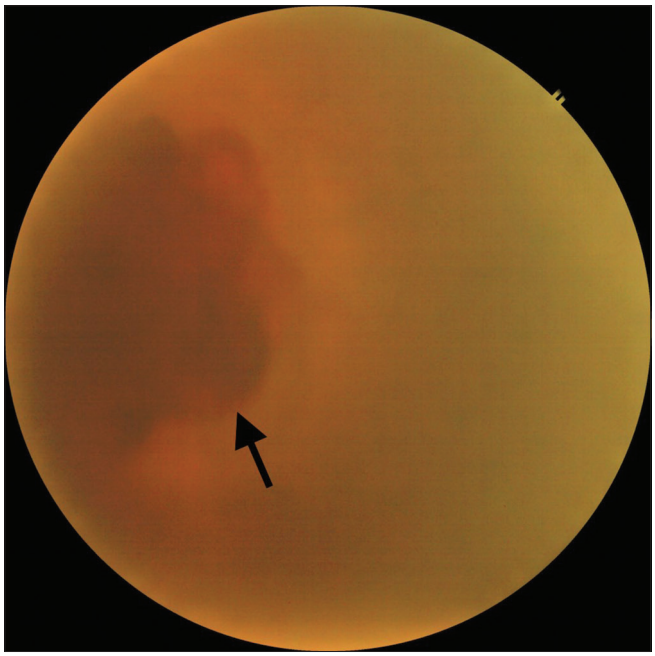

Figure 3: Right eye of the same newborn with culture-positive necrotizing retinitis. Color fundus photography demonstrates vitritis and pre and subretinal hemorrhage (black arrow). The rest of the retina was necrotic with barely visible retinal vessels

in neonatal intensive care unit. Mother was primigravida. Her antenatal blood test for hepatitis B, syphilis, and human immunodeficiency virus was negative. Her vaginal swab was positive for *Candida* growth and she had received treatment for the same. She had gestational diabetes and was treated with metformin and insulin. She did not receive antenatal steroids. Baby was born spontaneously via vaginal delivery. Baby was extremely premature and was intubated electively at birth and received two doses of surfactant. Apgar scores were 4 and 7 at 1 and 5 min, respectively.

Ophthalmology consultation was requested after 1 week to rule out bilateral intraocular inflammation as baby had systemic septic candidiasis with cultured *Candida albicans* and *parapsilosis*

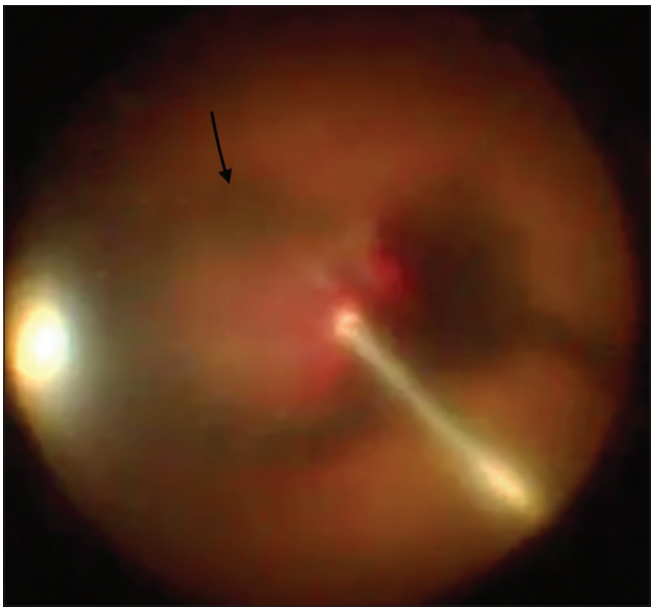

Figure 2: Left eye of premature baby who developed bilateral necrotizing retinitis. Intraoperative image demonstrates vitreous hemorrhage and subretinal hemorrhage (black arrow). The rest of the retina was necrotic with barely visible retinal vessels

from blood culture. Baby had received liposomal amphotericin B, amikacin, metronidazole, and tazocin for fungal sepsis. First ocular examination showed well dilated pupils with mild hazy view secondary to tunica vasculosa lentis in both eyes. No intraocular inflammation was seen. Baby's clinical condition deteriorated after 29 weeks of gestation when he developed right-sided intraventricular hemorrhage grade 4 and also underwent emergency surgery for perforated necrotizing ileitis with Penrose drain. Retinopathy of prematurity (ROP) screening performed at 30 and 32 weeks of gestational age recorded vascularization at zone II with no ROP. Clinically baby developed multiple bowel perforations and again underwent laparotomy and jejunostomy and stoma closure at 33 weeks of gestation.

ROP screening at 34 weeks of gestation showed bilateral rubeosis and fibrinous activity in anterior chamber with mid vitreous hemorrhage. Baby had two attacks of apnea during examination. Due to rubeosis and working diagnosis of aggressive posterior ROP, intravitreal injection of ranibizumab 0.20 mg was given in both eyes and pars plana vitrectomy was scheduled within a week. Baby also developed extensive skin and mouth vesicles at week 35 and polymerase chain reaction (PCR) form scrotal swab was positive for HSV-1 [Fig. 1]. The origin of HSV is unknown. We assume it was a consequence of immunosuppression following fungal candidiasis with sepsis. Systemic antiviral treatment with acyclovir in the dose of 20 mg/kg/dose IV infusion by syringe pump over one hour 3 × day was initiated by neonatologist and infectious disease specialists. The note from neonatology mentioned also disseminated intravascular coagulation and the use of thrombolytic therapy. The baby has survived and is recovering from multiple morbidities which include post-hemorrhagic hydrocephalus, chronic lung disease, patent ductus arteriosus, and developmental delay.

Pars plana vitrectomy performed on left eye showed necrotic peripheral retina with barely visible retinal vessels and vitreous hemorrhage which was surgically cleared. Posterior pole showed retinal necrosis with extensive subretinal hemorrhage and poorly discernable disc or macula [Fig. 2]. Fundus photo of the right eye showed similar picture [Fig. 3]. Anterior chamber fluid and vitreous samples were taken for quantitative PCR analysis from both eyes. This came positive for HSV-1. Baby was diagnosed with BARN with extremely poor visual potential; surgery for the fellow eye after discussion with parents was, therefore, abandoned.

Discussion

We describe a severely immunocompromised premature newborn with systemic *Candida* in association with neonatal HSV infection and bilateral ARN. Neonatal HSV infections are well recognized in literature. The clinical presentation of neonatal HSV (especially type 2) has been classified into three categories: (i) disseminated infection, (ii) encephalitis, and (iii) skin, eye, and mouth (SEM) infection. Disseminated disease usually presents in the second week of life and has the highest mortality. Encephalitis can be a part of disseminated viremia or occur as isolated finding most likely secondary to retrograde axonal transmission of virus into the brain. The third category, called SEM, has the lowest morbidity and mortality.[10] Clinical characteristics of our case fall in the third category. However, neonatal BARN has been reported without external ocular or cutaneous signs.[7]

Throughout the hospitalization the baby was systemically very unstable due to prior multiple bowel perforations, severe coagulopathy, and sepsis. First ocular presentations in this case showed signs of prematurity including the presence of tunica vasculosa lentis—the part of the hyaloid that supplies the developing lens. This was later complicated by severe inflammatory reaction and vitreous hemorrhage. Both precluded the view to retina and, hence, antiangiogenic therapy was used as first step followed by PPV surgery when systemic condition allowed another general anesthesia. The intraoperative clinical picture was typical of necrotizing retinitis which turned out to be culture positive for HSV-1. Preoperative differential diagnosis of vitreous hemorrhage included aggressive ROP given baby's medical history but intraoperative clinical picture revealed necrotizing retinitis. Coexistence of ROP and ARN is extremely rare and only two bilateral cases have been described up to date.[11]

While neonatal ARN can present with vitritis, vitreous opacities, and retinal hemorrhage,[5,12] both vitreous and subretinal hemorrhage are atypical findings. The source of bleeding is thought to be fragile and poorly developed choroidal and retinal vasculature and perhaps impact of some systemic medication administered for multiple medical and post-surgical problems. One of those included intraventricular brain hemorrhage but with no signs of herpetic encephalitis which usually predisposes to ARN.[4-6] Bilaterality of vitreous and subretinal hemorrhages and rapid disease course in this case point to extremely week condition of the newborn. In general, BARN usually occurs sequentially, with the second eye affected weeks to years after the first.[13] Due to severe ocular morbidity, the visual prognosis in this case is dismal.

Conclusion

Physicians should be aware that culture-positive ARN in immunocompromised newborns can present with both pre and subretinal hemorrhage in addition to typical clinical signs of necrotizing retinitis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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