patient underwent uneventful cataract surgery, with anticipated dense deprivational amblyopia, but was lost to follow-up.

Discussion

Orbitopalpebral cysts have been classically described in association with microphthalmos or anophthalmos.[1] They are rare and account for 2% of orbital cystic lesions and <1% of orbital biopsies.[2] These cysts are more commonly unilateral than bilateral.[3] They may occur in isolation or in association with other developmental ocular or systemic anomalies.[3,4] Histopathologically they lack a lining epithelium and must be differentiated from other cystic lesions of the orbit without an epithelial lining, such as a cystic eye, microphthalmia with cystic teratoma, meningoencephaloceles, and ectopic brain tissue.[5] Of these, a cystic eye is likely to be a close masquerader.

Development of a cystic eye is believed to stem from the failure of invagination of the primary optic vesicle at the 2–7 mm stage of the embryo leading to a fluid-filled cavity lined by primitive neuroglial tissue and the absence of all other ocular structures that develop from the surface ectoderm.[5,6] Development of the cyst associated with microphthalmos arises from the failure of the fetal fissure to close at the 7–14 mm embryotic stage. In this case, evidence of development of ocular structures is usually present albeit with smaller dimensions, resulting in a microphthalmic globe.[5,6]

The cyst in the present case resembled neither of these entities histopathologically; rather, it mimicked a typical cyst with microphthalmos clinically and radiologically, although it apparently arose from conjunctival tissue. The presence of a thick fibrous cyst wall and evidence of chronic inflammation may suggest unidentified remote birth trauma or chronic infection or inflammation of undetermined cause, but the pathogenesis of the lesion remains unknown. Table 1 compares the findings in this case with typical features of congenital cystic eye and the cyst with microphthalmos reported in the literature.[5-8]

References

1. McLean CJ, Ragge NK, Jones RB, Collin JRO. The management of orbital cysts associated with congenital microphthalmos and anophthalmos. Br J Ophthalmol 2003;87:860-63.
2. Shields JA, Bakewell B, Augsburger JJ, Flanagan JC. Classification and incidence of space-occupying lesions of the orbit: a survey of 645 biopsies. Arch Ophthalmol 1984;102:1606-11.
3. Demirci H, Peksayar G, Demirci YFK, Buyukbabani N, Demiryont M. Bilateral microphthalmos with colobomatous orbital cyst. J Pediatr Ophthalmol Strabismus 2002;39:110-13.
4. Foxman S, Cameron JD. The clinical implications of bilateral microphthalmos with cyst. Am J Ophthalmol 1984;97:632-8.
5. Guthoff R, Klein R, Lieb WE. Congenital cystic eye. Graefe's Arch Clin Exp Ophthalmol 2004;242:268-71.
6. Hayashi N, Repka MX, Ueno H, Iliff NT, Green RW. Congenital cystic eye: report of two cases and review of the literature. Surv Ophthalmol 1999;44:173-9.
7. Lieb W, Rochels R, Gronemeyer U. Microphthalmos with colobomatous orbital cyst: clinical, histological, immunohistological, and electron microscopic findings. Br J Ophthalmol 1990;74:59-62.
8. Al-Khamiss A, Ayoubi A, Manzoor M, Al-Dandan S. Colobomatous cyst: histopathological characterization. J Case Rep Images Pathol 2015;1:12-16.

Neonatal bilateral acute retinal necrosis in a neonate with a history of severe intrauterine growth restriction

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We present the case of a baby girl born at term with severe intrauterine growth restriction (IUGR) to a gravida 1 mother who was previously healthy and HIV negative. The newborn was evaluated by an ophthalmologist because of her history of IUGR and was diagnosed with intraretinal hemorrhages associated with areas of peripheral retinal necrosis at the posterior pole of both eyes. A diagnosis of acute retinal necrosis of presumed viral origin due to cytomegalovirus virus was considered, and the infant was started on and responded well to valganciclovir.

Acute retinal necrosis (ARN) is a retinopathy of viral etiology that is characterized by 360° of peripheral retinal necrosis, occlusive vasculitis, and vitritis.[1] It can compromise both retinal arteries and veins and cause optic neuropathy and retinal detachment. The annual incidence is estimated at 1 case per 2 million individuals,[2,3] occurring more frequently in adults than children; neonatal cases are exceptional.[4] It affects both sexes and any ethnicity or age group; it occurs in both immunocompetent and immunosuppressed patients.[2] Its etiology is mainly viral and can involve the Herpesviridae family, such as herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2) varicella zoster virus (VZV), cytomegalovirus (CMV) or Epstein–Barr virus.[5]

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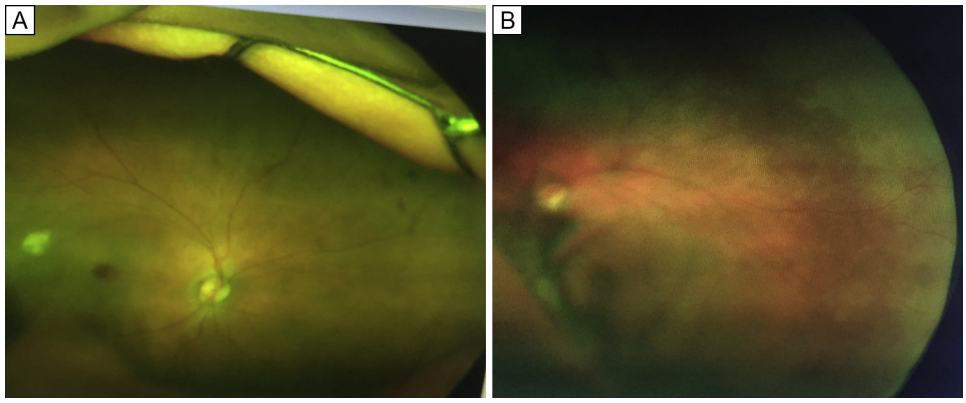

FIG 1. Right eye (A) and left eye (B) before treatment. At the level of the posterior pole, multiple intraretinal hemorrhages are observed, including the macula of both eyes, and toward the periphery, there are pale, peripheral areas of confluent retinal whitening in both retinas, with vasculitis in acute retinal necrosis. Vascular sheathing toward the periphery of the retina is also present.

Table 1. Main assessments performed on mother at week 28 of gestation

Test	Result
Rubella IgM	0.29 negative
Rubella IgG	57.5 positive
CMV IgM	1.6 negative
CMV IgG	44 positive
Toxoplasmosis IgM	0.096 negative
Toxoplasmosis IgG	95.8 positive
HSV 1 IgM	0.3 negative
HSV 1 IgG	18 positive
HSV 2 IgM	0.6 Negative
HSV 2 IgG	10.6 borderline
VDRL	Not reactive
Anti-HBs	Negative
HIV	Negative

Table 2. Main assessments performed on newborn at 2 weeks after birth

Test	Result
Blood PCB	0.02
Urine CMV PCR	Negative[a]
CMV IgM	0.40 not reactive
CMV IgG	>250.0 reactive
Toxoplasmosis IgM	0.19 not reactive
Toxoplasmosis IgG	12.70 reactive
HSV 1 IgM	0.10 not reactive
HSV 1 IgG	1.50 reactive
HSV 2 IgM	0.20 not reactive
HSV 2 IgG	0.50 not reactive
Rubeola IgM	0.29 negative
Rubeola IgG	57.5 positive
HIV	Negative
Cranial CT scan	Normal
Brain US	Normal
CSF	Normal

[a]Carried out after starting treatment with valganciclovir.

VZV is the most prevalent (50%-80% of cases),[2,3] followed by VHS-1, HSV-2, CMV and Epstein-Barr virus.[3] The diagnosis is established clinically and is based on retinal findings and the rapid progression of necrosis in the absence of therapy, regardless of the causative agent and the immune status of the affected host.[6] We reported an unusual case in a newborn with bilateral acute retinal necrosis associated with a history of severe intrauterine growth restriction (IUGR) who was successfully treated with valganciclovir.

Case Report

An infant girl, born to a healthy mother by vaginal delivery at 37 weeks' gestation and weighing 1900 g, was examined by a retinal specialist (LMZ) at Clínica Universitaria Bolivariana in the second week of life because of a history of severe IUGR. On examination, a macular hemorrhage was found in the right eye associated with multiple dot-and-blot and flame-shaped intraretinal hemorrhages in the posterior pole, with peripheral retinal white-color areas indicating necrotizing retina (Figure 1A). The macula of the left eye had hemorrhages toward the periphery with similar characteristics to those found in the right eye but with much more marked peripheral necrosis (Figure 1B).

Maternal history was positive only for smoking in the first trimester of pregnancy. The mother did not report acute infections or nonspecific flulike symptoms during her pregnancy and denied herpetic infection. The mother's was evaluated at 28 weeks to look for causes of IUGR (Table 1).

Because clinical findings were compatible with an ARN of presumed viral cause, the baby was hospitalized. Laboratory tests were performed: serologic testing (IgM) for rubella, toxoplasma, herpes simplex type 1 and 2, and human immunodeficiency virus (anti-HIV), cytomegalovirus were negative; only IgG CMV was reactive with high titre and IgG HSV-1 with low titre (Table 2). Empirical treatment with valganciclovir was initiated. After 4 days of treatment, the infant's eyes showed a very good clinical response, with marked improvement of intraretinal hemorrhaging in both eyes and a slight improvement in the necrosis areas (Figure 2A and 2B). Because clinical signs

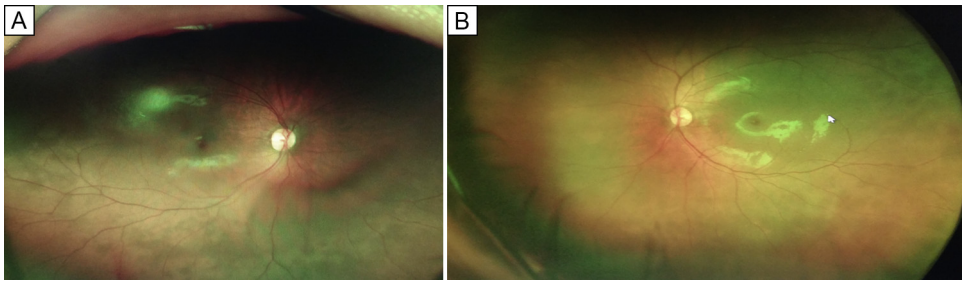

FIG 2. Right eye (A) and left eye (B) 10 days after treatment. Both eyes have attached retinas, healthy nerves, macula with good shine, and retinas without intraretinal hemorrhages; the whitening areas have disappeared. Irregular hyperpigmented areas are observed throughout the retina of the right eye (A).

improved, vitreous samples were suspended. Antiviral treatment with oral valganciclovir was continued for 6 months, with monthly pediatric infectious disease and retinal specialties follow-up. Response to treatment was excellent: all retinal necrosis resolved by 3 months' follow-up, with both retinas attached.

Discussion

The etiology of ARN is mainly viral, with HSV-2 being the most frequent cause in the pediatric and neonatal population; in adults, VZV and HSV-1 are more common.[1] Cases of ARN caused by HSV-1 have also been described in the pediatric population,[7] as have, atypically, cases caused by CMV.[5]

In 1994 the American Society of Uveitis described the clinical criteria that define the diagnosis of ARN syndrome[6]: (1) more than one focal point of retinal necrosis, with defined borders located in the peripheral retina; (2) rapid circumferential progression in the absence of therapy; (3) evidence of occlusive vasculitis with arteriolar involvement; (4) inflammation at the level of the vitreous or anterior chamber; and (5) rapid disease progression without treatment.

In the present case, the degree of necrosis of the peripheral retina, with vasculitis and macular and perivascular hemorrhages was considerable. Because IUGR and ARN were both likely caused by CMV and there was a favorable clinical response to valganciclovir, CMV infection was suspected. The absence of mucocutaneous lesions and significant systemic viral morbidity with normal cerebrospinal fluid made HSV-1 and HSV-2 infection less likely. Furthermore, improvement of the retinal lesions made molecular testing unnecessary, and taking intraocular samples for polymerase chain reaction in this case carried a high morbidity and risk of complications. The clinical characteristics and the positive response at day 4 of valganciclovir treatment allowed continuation of empirical medical management. The literature on ARN indicates that these tests should not be performed at the beginning of the diagnosis and only under special circumstances, such as when there is an inadequate response to the first-line antiviral drug.[8]

Patients with ARN usually have competent immunological status. Cases of infants with ARN born prematurely, or IUGR infants have been reported, however, and in such cases a subclinical dysfunctional and immature immunological state may be contributory. Our patient, with a history of UIGR, may have been at greater risk for congenital ocular infection.[5,9]

ARN in the neonatal population is rare. Although it was not possible to establish the causative agent in our case, a diagnosis of ARN is sufficient to initiate antiviral treatment. The favorable and progressive clinical response after starting valganciclovir was considered a confirmatory positive therapeutic test for ARN secondary to CMV infection. Starting antiviral therapy in a timely fashion is crucial to preventing consequences that can lead to retinal detachment and blindness.

References

1. Ganatra JB, Chandler D, Santos C, Kuppermann B, Margolis TP. Viral causes of the acute retinal necrosis syndrome. Am J Ophthalmol 2000; 129:166-72.
2. Muthiah MN, Michaelides M, Child CS, Mitchell SM. Acute retinal necrosis: a national population-based study to assess the incidence, methods of diagnosis, treatment strategies and outcomes in the UK. Br J Ophthalmol 2007;91:1452-5.
3. Cochrane TF, Silvestri G, McDowell C, Foot B, McAvoy CE. Acute retinal necrosis in the United Kingdom: results of a prospective surveillance study. Eye Lond Engl 2012;26:370-77, quiz 378.
4. LaMattina KC, Wirostko WJ, Costakos DM. Bilateral acute retinal necrosis with concurrent retinopathy of prematurity in two neonates. Ocul Immunol Inflamm 2016;24:115-17.
5. Vemulakonda GA, Pepose JS, Van Gelder RN. Acute retinal necrosis syndrome. In: Cleveland, OH: Elsevier Inc. 2018:1709-18.
6. Holland GN. Standard diagnostic criteria for the acute retinal necrosis syndrome. Executive Committee of the American Uveitis Society. Am J Ophthalmol 1994;117:663-7.
7. Fong CY, Aye AMM, Peyman M, et al. Neonatal herpes simplex virus type-1 central nervous system disease with acute retinal necrosis. Pediatr Infect Dis J 2014;33:424-6.
8. Brydak-Godowska J, Borkowski P, Szczepanik S, Moneta-Wielgoś J, Kęcik D. Clinical manifestation of self-limiting acute retinal necrosis. Med Sci Monit Int Med J Exp Clin Res 2014;20:2088-96.
9. Sharma D, Shastri S, Sharma P. Intrauterine Growth restriction: antenatal and postnatal aspects. Clin Med Insights Pediatr 2016;10: 67-83.