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Case Report

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# Neonatal Type-2 Unilateral Herpes Simplex Blepharokeratoconjunctivitis after Cesarean Delivery

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## Abstract

**Introduction and Objectives:** To describe the presentation and management of an isolated type-2 Herpes Simplex Virus (HSV) ocular unilateral infection in a neonate born by cesarean delivery in the absence of clinical maternal genital disease.

**Case Report:** A 18 days newborn with a history of mucopurulent discharge in the Left Eye (LE) presented via teleconsulting due to a Coronavirus pandemic in her General Practice Doctor. Despite the treatment with gentamicin, the clinical condition worsened and three days after she presented to Ophthalmology Emergency Department with significant blepharoconjunctivitis with cornea opacification and total epithelial defect. She was medicated with azithromycin plus gel drops. Five days after, the blepharitis and the epithelial defect resolved, but the cornea opacification became worse, with perilimbal neovascularization appearance. The newborn was admitted to Pediatric Department to initiate empirical antiviral treatment with acyclovir plus topic dexamethasone. Polymerase chain reaction were positive for type-2 HSV and maternal serologies confirmed the diagnostic.

**Results:** With the treatment, there was a complete regression of neovascularization, but the central corneal scar persisted. The patient developed LE esotropia. She was discharged with a treatment regimen of oral acyclovir, topic cyclopentolate plus preservative-free hydrocortisone tapering in the LE, and occlusion therapy in the Right Eye. At age of 11 months, she remains without recurrences, but maintains LE esotropia, despite the improvement in the LE fixation and corneal scar.

**Conclusion:** A high level of suspicion is necessary to recognition of HSV in a neonate, mainly if after cesarean delivery in the absence of clinical maternal history. An appropriate and prompt treatment is mandatory to prevent corneal scarring which can lead to deprivation and amblyopia.

**Keywords:** Herpes Simplex Virus; Herpetic Stromal Keratitis; Neonatal Infection; Acyclovir; Strabismus

## Introduction

Herpes simplex virus (HSV) belongs to the family of Herpesviridae, which are an important cause of severe congenital infections. Neonatal herpes simplex virus infection is a rare but life-threatening condition in newborns, mainly due to an immature immune system [1]. The majority of infections are acquired intrapartum (85%), resulting from vertical transmission from mother to fetus during delivery, following direct fetal contact with herpetic lesions [1]. Rarely, infection occurs in the uterus (5%) or in the postpartum period (10%) [2]. The clinical presentation of these infections has been divided into three groups, each of which is associated with different clinical manifestations and outcomes: (1) skin, eye, and mouth (SEM), when infections are confined to the skin, eyes, and mucosa (2) central nervous system (CNS), associated with lethargy, poor feeding, and seizures, in the absence or not of cutaneous lesions and (3) disseminated disease, involving multiple organs and

clinically indistinguishable from bacterial sepsis. The SEM disease has a lower level of morbidity and mortality [1]. In the acute stage of the neonatal herpes infection, conjunctivitis is the most frequent ocular symptom, often coexisting with keratitis. After the acute phase, the disease can subsequently disseminate systemically and serious complications have been reported [1,2]. Because of this risk of dissemination, prompt therapy and careful investigation is mandatory. We report a case of an isolated type-2 HSV ocular unilateral infection presented with blepharokeratoconjunctivitis in a neonate born by an uncomplicated cesarean delivery with an intact chorioamniotic membrane in the absence of clinical maternal genital symptoms or lesions.

## Case Report

A 40-week, 3280g Caucasian girl was born to a healthy 34-year-old primigravida mother by an elective delivery due to arrested labor, with an intact chorioamniotic membrane. The maternal history and laboratory studies were unremarkable. All prenatal ultrasounds before delivery were normal. The gestation was normal, and the patient's mother denied any history of known sexually transmitted diseases, any known contact with an infected partner. She also denied genital symptoms and signs, such as pain, vulvar erythema or pruritus, vaginal discharge, or any lesions suggestive of either orolabial or urogenital herpes simplex infection before or throughout the pregnancy. Apgar scores were 8, 10, 10 at 1, 5 and 10 minutes, respectively. After birth, physical examination revealed a slight plethoric aspect, with good general condition and nutritional status, being the newborn normal active and reactive. Eye examination revealed bilateral eye red reflex, normal ocular motility, and absence of lesions and discharge. No oral, skin, or mucous membrane lesions were identified in her body. Fifteen days after delivery, her mother noted mucopurulent discharge in the LE, associated with tearing and hyperemia. Due to coronavirus pandemic, she avoided presenting to the Ophthalmologic Emergency Department and make a medical teleconsultation with her General Practice Doctor. Because of the clinical history and characteristics of the findings, the case was misinterpreted of a possible conjunctivitis in the context of canal duct obstruction. The baby was medicated with gentamicin 3 times daily during a week, plus massage, with no resolution of the symptoms and signs. Three days after, the mother noticed that the mucopurulent discharge got worse, with the appearance of a "white lesion" and progressive eyelid edema and present to the Ophthalmologic Emergency Department. On examination, there was significant eyelid edema, and the red reflex was absent in the LE. No dendrites, vesicles, or other lesions were present, but the cornea showed opacification with slight diffuse stromal edema and total epithelial defect, trough cobalt blue filter examination. There was a moderate conjunctival injection and mucopurulent LE discharge. She was medicated with azithromycin 2 times daily for three days, plus gel drops lubrification 5 times daily. Five days after, the blepharitis, eyelid edema and the epithelial defect resolved, but the cornea opacification became worse, with perilimbal neovascularization appearance (Figure 1). At this time, the baby presented with excessive crying and irritability. The newborn was admitted to Pediatric Department to for a complete workup, including blood count, liver function tests, lumbar puncture, urinalysis with culture, and blood culture and initiate empirical antiviral treatment with acyclovir 60 mg/kg/day divided into 3 doses parenterally administered plus topic dexamethasone 4 times daily. The analytic study was unremarkable. Bacterial and fungal cultures, and polymerase chain reaction (PCR) for virus from LE were obtained and were positive for type-2 HSV. HSV PCR for types 1 and 2 performed on cerebrospinal fluid was negative, just like the blood and urine cultures. During follow-up, there was a complete regression of neovascularization. However, despite the treatment, the central corneal scar persisted. Maternal antibody titer detected type 2 HSV-IgM antibody with HSV-IgG antibody seroconversion after 15 days. During this period, the newborn always remained afebrile. The patient completed a 14-day course of intravenous acyclovir and was discharged on orally administered acyclovir 300 mg/m$^2$/dose day, divided into 3 doses, to prevent recurrent herpetic keratoconjunctivitis, with topical LE dexamethasone two times daily plus eye drops. Due to the risk of neutropenia and nephrotoxicity, she was alerted to perform an analytical study once a month. One week after the discharge, she returned to evaluation in the Ophthalmology Department, and LE esotropia with nystagmus was noted. The leukoma remained similar, with no improvement (Figure 2). The weaning schedule of dexamethasone was established. The patient initiated in the Right Eye (RE) cyclopentolate 0.5% once daily, and occlusion therapy one hour each day. Currently, at age of 11 months, she remains without recurrences, but maintains LE esotropia, despite the improvement in the LE fixation and corneal scar.

**Figure 1:** Ciliary injection with perilimbal neovascularization appearance and leukoma developmental, five days after the initial presentation in the Ophthalmology Department.

**Figure 2:** At the end of treatment, the leukoma remained similar with no improvement (A and B).

## Discussion

Neonatal herpes simplex virus infection could cause an extensive spectrum of diseases, varying from minor skin infections to severe encephalitis or extensive life-threatening infections. Most of the neonates acquire the infection following direct fetal contact with herpetic lesions from the maternal genital tract during delivery, although the majority of the mothers present no signs or symptoms of genital herpes and have no medical history of contact with a partner with genital HSV, during childbirth or pregnancy [3,4]. In our case report, the first clinical presentation, (with the absence of skin vesicles, unilateral blepharokeratoconjunctivitis, mucopurulent discharge, and geographic corneal ulcer), could be compatible with other bacterial keratoconjunctivitis. Thus, we decided to start empiric treatment with topical antibiotics with no resolution, which delayed the correct diagnoses. The visceral dissemination was ruled out clinically, imagological and analytically, and we classified the herpetic infection as a SEM disease. Although SEM disease has a lower level of morbidity and mortality, because of the excessive crying and irritable status of the baby, and the high risk of dissemination due to the delayed diagnose, we opted for systemic acyclovir therapy 60 mg/kg/day divided in 3 doses for 14 days, with progressive improvement. In a recent review, the authors determined that this was the best treatment method in the pediatric population, including for neonatal herpes, being safe and well tolerated [5,6]. This regimen it was preferable to toxic and complicated eye-drop regimens, because of the crying during topical drop administration, which dilutes drops and reduces efficacy [7]. Given the high rate of recurrence of herpetic keratitis in children, long-term oral prophylactic acyclovir doses should be applied, especially in stromal disease. In line with the literature, we opted to implement the current recommendation for antiviral-suppressive therapy, with oral acyclovir at 300 mg/m$^2$/dose, three times a day for a minimum period of 6 months. This regimen could be extended for at least 1 year after the last episode of recurrence and must have be monitored by absolute neutrophil count and periodic kidney and liver function while on therapy [4,5]. Besides, in our case, we also implement a weaning schedule of dexamethasone to reduce corneal leukoma and prevent severe visual impairment of LE. However, despite the treatment, the corneal leukoma remained dense and we opted for RE penalization and patch occlusion therapy hourly a day, trying to minimize the impact of a corneal scar in the development of visual acuity and amblyopia.

HSV infections following a cesarean delivery are possible but quite rare. Although two hypothesis for contamination were admitted in our case, because the baby could have acquired the infection during delivery or in the immediate postpartum period, by accidentally transmission by contaminated mother hands carrying virus, these complications has rarely been described and the management of ocular lesions and squeals are also less often reported. There has been only one article describing type-2 HSV keratoconjunctivitis in a newborn after cesarean delivery with intact amniotic membranes in an asymptomatic mother with no history of maternal genital HSV [8] and another similar report of two cases of unilateral type-2 HSV keratitis, after cesarean delivery, in neonates whose twin and had died, because of disseminated infection [9].

Although HSV keratoconjunctivitis in this setting has been reported, this is the first case report presented with isolated blepharokeratoconjunctivitis. In our case, besides the presentation, the unique factor was the delayed diagnosis, at first, because of a delayed observation by an ophthalmologist due to Coronavirus pandemic and because of the initial misdiagnose of other etiological agents for the blepharokeratoconjunctivitis.

Because of the rarity of congenital Type-2 HSV keratitis after cesarean delivery, this case highlights the importance to include HSV in the differential diagnosis of any neonatal blepharokeratoconjunctivitis, mainly in the first 30 days of life, when nonspecific discharge is observed, especially in those who presented with an epithelial defect and with no improvement after initial treatment. HSV neonatal infections are often delayed because of nonspecific symptoms but given the high morbidity and mortality of untreated neonatal HSV, an immediate and accurate diagnosis is desirable. Thus, a high level of suspicion is necessary to prompt recognition and appropriate treatment to prevent corneal scarring as in our patient, which can lead to deprivation and refractive amblyopia.

## Conclusion

A high level of suspicion is necessary to recognition of HSV in a neonate, mainly if after cesarean delivery in the absence of clinical maternal history. An appropriate and prompt treatment is mandatory to prevent corneal scarring which can lead to deprivation and amblyopia.

## Declarations of Interest

The authors report no conflicts of interest.

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