Corneal transplantation and concomitant SARS-CoV-2 infection: a case report

Transplante de córnea e infecção concomitante por SARS-CoV-2: relato de caso

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ABSTRACT

This report was aimed at presenting a case of neurotrophic keratitis and concomitant SARS-CoV-2 infection in a patient who has recently undergone a corneal DALK transplant. One month after corneal transplantation with adequate corneal epithelialization, the patient presented neurotrophic keratitis with a torpid course of the corneal transplant coinciding with a SARS-CoV-2 infection, with an excessive host immune response. In addition, the patient presented a re-positivization of nasopharyngeal polymerase chain reaction of SARS-CoV-2 with past disease after starting treatment with autologous serum eye drops. The implications at the ophthalmological level of SARS-CoV-2 infection may be clarified as the time the illness progresses and we learn more about how it acts. In this case, the disparity of signs and symptoms, the antecedent of corneal surgery, and the possibility of a herpetic infection as a cause of the primary leukoma suggested neurotrophic keratitis. Nonetheless, the involvement of systemic SARS-CoV-2 infection in the process, triggering an excessive host immune response at the corneal level with an increase in inflammatory cytokines must be taken into account. No relationship was found between treatment with autologous serum and re-positivization of nasopharyngeal polymerase chain reaction, presenting the patient a favorable response to treatment.

RESUMO

O objetivo deste relato foi apresentar um caso de ceratite neurotrófica e infecção concomitante por SARS-CoV-2 em paciente submetido recentemente a transplante de córnea DALK. Um mês após o transplante de córnea com adequada epitelização da córnea, o paciente apresentou ceratite neurotrófica com curso tórpido do transplante de córnea, coincidindo com infecção por SARS-CoV-2, com resposta imune excessiva do hospedeiro. Além disso, o paciente apresentou repositivização da reação em cadeia da polimerase nasofaríngeo de SARS-CoV-2, com doença pregressa após iniciar tratamento com colírio de soro autólogo. As implicações a nível oftalmológico da infecção por SARS-CoV-2 podem ser esclarecidas à medida que a doença progride e aprendemos mais sobre sua forma de atuação. Neste caso, a disparidade de sinais e sintomas, o antecedente de cirurgia de córnea e a possibilidade de infecção herpética como causa do leucoma primário sugeriram ceratite neurotrófica. No entanto, deve-se levar em consideração o envolvimento da infecção sistêmica por SARS-CoV-2 no processo, desencadeando uma resposta imune excessiva do hospedeiro no nível da córnea, com aumento de citocinas inflamatórias. Não foi encontrada relação entre o tratamento com soro autólogo e a repositivização da reação em cadeia da polimerase nasofaríngea, apresentando ao paciente uma resposta favorável ao tratamento.

INTRODUCTION

Coronaviruses can cause eye infection in different animals, with a wide spectrum of ophthalmological manifestations, from pathologies of the anterior segment such as conjunctivitis and anterior uveitis to retinitis and optic neuritis.[1] In addition, the possibility that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has ocular implications cannot be ignored. Especially, cases of conjunctivitis have already been reported and also some cases of retinal of microhemorrhages and cotton wool spots, suggesting potential neurological manifestations.[2,3]

CASE REPORT

A 77-year-old pseudophakic patient who underwent a deep anterior lamellar keratoplasty (DALK) of the right eye for central corneal leukoma secondary to keratitis more than 20 years ago. The intervention was carried out without incident, with prophylactic coverage of valaciclovir (500mg/24hours). In the early postoperative period, a complete pseudochamber was observed (Figure 1), which was resolved by injecting intracameral 20% sulfur hexafluoride (Figure 2). One month after surgery, the patient complained about vision loss starting 4 days before. Biomicroscopy revealed a de-epithelialization of the inferior hemicornea with loosening of the tension of the inferior suture, corneal melting and hypotonia without evidence of Seidel. Corneal cultures were negative. Due to the SARS-CoV-2 pandemic, all patients underwent a nasopharyngeal polymerase chain reaction (PCR) test by protocol prior to surgery. Despite the fact that the patient was asymptomatic, the result was positive and a pulmonary involvement suggestive of SARS-CoV-2 with bilateral interstitial infiltrates was observed on the X-ray chest plate, with an analytical increase of C-reactive protein (1.12mg/dL). Treatment for SARS-CoV-2 was established with cefixime, azithromycin, and hydroxychloroquine and a resuture surgery was performed with intravenous bolus of 500mg of methylprednisolone administration. The patient presented a complete pseudochamber again and seidel in one of the corneal transplant points 24 hours after the surgery. A new resuturing and a gas tamponade attained full attachment of the graft.

In subsequent reviews, a minor inferior crescent-shaped corneal epithelium defect remained. Contact lens bandage, preservative free topical treatment (ciprofloxacin 3mg/mL and dexamethasone phosphate 1mg/mL one drop three times a day) and oral treatment with: doxycycline (100mg/24hours), vitamin C (500mg/24hours),

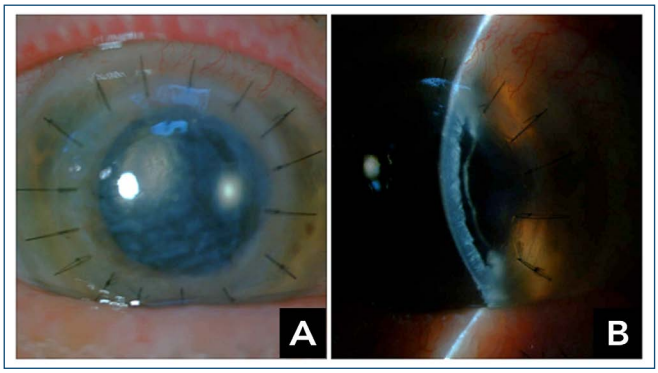

Figure 1. Slit lamp images. (A) Corneal edema the first day after Dalk. (B) Complete pseudochamber.

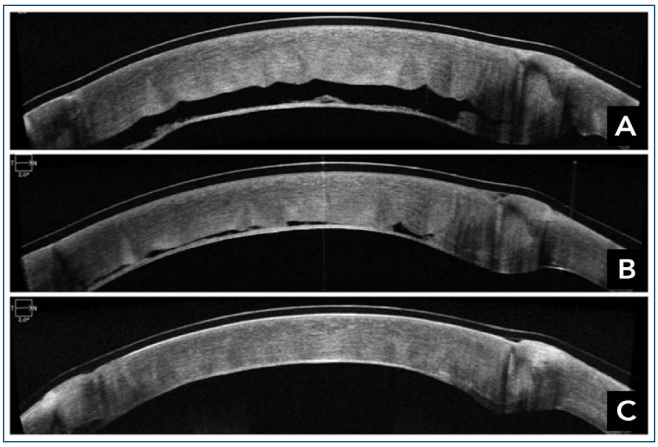

Figure 2. Anterior segment optical coherence tomography (Cirrus HD-OCT 5000®) images. (A) Complete pseudochamber with graft detachment. (B) Complete attachment of the graft minutes after injecting intracameral 20% sulfur hexafluoride. (C) One week after sulfur hexafluoride injection, complete attachment of the graft with normalization of the corneal profile.

nicergoline (10mg/12hours), and valaciclovir treatment (500mg/8hours) was prescribed. Three weeks later, a new epithelial defect of the whole inferior hemicornea with melting and loosening sutures appeared (Figure 3A).

A multilayer amniotic membrane transplantation was performed (Figure 3B) and intravenous bolus of 500mg of methylprednisolone was administered. A corneal sample was taken for SARS-CoV-2 and herpes PCR, which turned out to be negative. The patient presented good evolution with the improvement of melting and corneal thinning.

After reabsorption of the membranes, an inferior paracentral corneal neurotrophic ulcer persisted with decreased corneal sensitivity (Figure 3C). After two negative nasopharyngeal PCRs, positive immunoglobulin (Ig) G, and Ig M negative for SARS-CoV-2, it was decided to perform autologous serum eye drops with a good response. A new amniotic membrane transplant was proposed, but

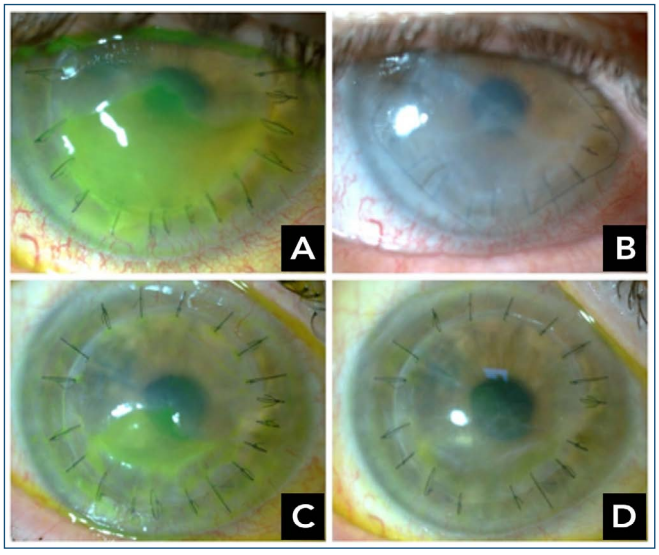

Figure 3. Slit lamp images. (A) Inferior hemicornea ulcer with melting and loosening of the tension of the inferior suture. (B) Image four days after multilayer amniotic membrane transplantation showing the reabsorption of the membranes. (C) Persistence of inferior paracentral corneal ulcer after reabsorption of the membranes. (D) Residual corneal leukoma after closure of the ulcer.

by repeating the nasopharyngeal PCR prior to surgery, it turned out to be positive again, ruling out contamination of the sample. Surgery was postponed, autologous serum eye drops were analyzed by means of PCR and a new nasopharyngeal PCR was performed. All samples were negative for SARS-CoV-2. Autologous serum treatment was continued due to the good corneal response, achieving complete closure of the ulcer with the consequent residual corneal leukoma (Figure 3D).

DISCUSSION

SARS-CoV-2 can bind to the angiotensin-converting enzyme 2 (ACE2) cellular receptor and interact with transmembrane protease, serine 2 (TMPRSS2) of the host cell, which are known to be expressed in the human cornea, retina, and conjunctival epithelium.[4] It has also been shown that an inflammatory response occurs with a significant increase in 14 different cytokines.[5]

In this case, the disparity of signs and symptoms, the antecedent of corneal surgery and the possibility of a herpetic infection as a cause of the primary leukoma suggested a neurotrophic keratitis. Nonetheless, the involvement of systemic SARS-CoV-2 infection in the process, triggering an excessive host immune response with an increase in inflammatory cytokines, similar to those seen to occur in other parts of the body (pneumonitis, encephalitis),[5,6] must be taken into account. Coinciding the appearance of the inflammatory response with the primary SARS-CoV-2 infection, one month after corneal transplantation with an adequate corneal epithelialization at first after surgery.

We were unable to demonstrate the presence of local virus involvement in the corneal scraping performed, which was rather superficial, and have seen in other reports that the sensitivity of detection of SARS-CoV-2 in the conjunctiva of patients is around 2 to 7%. These results have been attributed to the relatively low and unstable viral load in the conjunctival sac, as well as to the different detection techniques and to the sampling time.[2]

Different cases of SARS-CoV-2 reactivation and reinfection have been reported.[7] Our patient returned to positivity for nasopharyngeal PCR after verifying that the disease had resolved both by PCR (two negative PCRs) and by serology (positive IgG and negative IgM), a condition for which we decided to begin autologous serum treatment. After SARS-CoV-2 reactivation, it was decided to continue with the treatment because of the negative analysis of viral load in the autologous serum, the new negative of the nasopharyngeal PCR, the absence of symptoms and the good response to treatment.

The inoculation of SARS-CoV-2 into the respiratory tract through the anatomical link provided by the nasolacrimal system has been demonstrated.[2] This route of contagion is the one that could be involved in the case in which the presence of the virus in blood derivatives is demonstrated. In our case, no relationship was found between treatment with autologous serum and re-positivization of nasopharyngeal PCR, with the patient presenting a favorable response to treatment. However, we believe that the treatment with blood derivatives should be monitored in patients with recent history of SARS-CoV-2 infection until more information about it is available.

SARS-CoV-2 is a newly emerging virus that has generated a global pandemic. The implications at the ophthalmological level may be clarified as the illness progresses, and we learn more about how it acts. In our case, we emphasize the inflammatory response at the corneal level and the re-positivization of nasopharyngeal PCR with past disease.

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