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CASE REPORT

INTERMEDIATE UVEITIS SECONDARY TO COVID-19 INFECTION: A CASE REPORT

VINICIUS STIVAL VENEZIANO SOBRINHO[1,2]; AUGUSTO PEREIRA[1,3], FRANCISCO DIAS LUCENA NETO[1]

ABSTRACT

Objective: a case of intermediate uveitis, post-acute period infection, mediated by SARS-CoV-2, documenting the multiform clinical presentation of COVID-19. Materials and method: case report and image exams, with bibliographic review. Results: A 50-year-old man, with a positive Polymerase Chain Reaction (PCR) in a nasal swab for SARS-CoV-2, 10 days after isolation, complained of low visual acuity and bilateral blurring. Vitreitis in both eyes, 2 + / 4 in OR and 1 + / 4 + in OS and vitreous haze were documented in retinography. 15 days after the early diagnosis and the start of treatment, the patient evolved with improved visual acuity. In the reassessment of biomicroscopy and fundscopy, there was an improvement in the vitreitis pattern. Conclusions: the patient denied a medical history of chronic autoimmune and inflammatory diseases, and possible etiologies were excluded. Clinical apresentation, early diagnosis and clinical response, with gradual reduction and satisfactory response, shows an intermediate uveitis. We present this case of ocular involvement, days after a systemic inflammatory condition by COVID - 19, to document the extraordinary and multifaceted capacity for clinical viral manifestation.

KEY-WORDS: INTERMEDIATE UVEITIS; COVID-19; PUBLIC HEALTH

INTRODUÇÃO

A new RNA virus epidemic, with envelopes belonging to the Coronaviridae [1] family, capable of causing a severe acute respiratory syndrome coronavirus - 2 (SARS-CoV-2), at the end of 2019, emerged from China. Literature descriptions conceptualize "COVID-19" as an inflammatory storm, sustained by cytokines, of a multisystemic character [2].

Coronaviridae viruses (CoVs) are also known to manifest in other regions besides the respiratory tract, including the gastrointestinal tract and eye tissues 1. In 2004, near the end of the SARS-CoV crisis, the polymerase chain reaction (PCR) in tears of patients with SARS-CoV infection demonstrated the presence of the virus. The discovery of SARS-CoV in tears was the first of its kind to emphasize the need for adequate precautions to prevent potential transmission through eye tissues and secretions [3].

In cats and murine models, it is known that viruses of the Coronaviridae family are known to cause various ocular disorders, with conjunctivitis, anterior uveitis, retinitis and optic neuritis. In SARS-CoV-2, ocular pathology manifests, as expected, in different ways [3].

Recently, in the study "SERPICO-19", 54 patients among the 133 exposed were foundc to have retinal alterations, where the main alterations were microvascular, especially microhemorrhages and cotton wool exudates4. It is believed that this correlation between retinal manifestations and uveal and COVID-19 is related to the ACE 2 cell receptor, detected in the human retina, retinal pigmented epithelium, choroid, cornea and conjunctival epithelium [1,4].

A recent survey showed that the main eye complaints of patients with SARS-CoV-2 are dry eyes, blurred vision and foreign body sensation. It is believed that they are related much more to the more intense use of electronic devices in quarantine phases than to the infectious manifestation. However, in some patients, keratoconjunctivitis was the first clinical manifestation5. Some studies indicate that the presentation of SARS-CoV-2 and keratoconjunctivitis may be associated with a more severe form of the disease [3,5]. May be present in conjunctival secretions,

1 – Instituto e Hospital Oftalmológico de Anápolis – Ihoa
2 – Universidade Federal de Goiás – Ufg
3 – Hospital Oftalmológico de Anápolis – Hoa

ADDRESS
VINICIUS STIVAL VENEZIANO SOBRINHO
*Instituto e Hospital Oftalmológico de Anapolis
R. Mozart Soares, 45
Cidade Jardim, Anápolis - GO, 75080-690
e-mail: neto640@gmail.com
vstival@me.com

requiring greater attention and caution on the part of the patient and the multidisciplinary team that will manage the patient [3].

In addition, there are, in the literature, varied descriptions of infrequent ocular presentations of COVID-19. Bettach and collaborators, for example, postulated the first case of bilateral anterior uveitis secondary to multisystemic inflammation of SARS-CoV-2 [6]. The word uveitis was created to describe an inflammatory process in the uvea, the region that constitutes the bulbi vasculature (iris, ciliary body and choroid), but the current term is synonymous with intraocular inflammation [7].

There are several etiologies, of autoimmune or infectious origin, that can develop the pathology, the forms of clinical presentation are also varied, depending on the inflammatory anatomical site. However, it is known that all are mediated by the immune system, where the MHC complex genes regulate the production of cytokines and are involved in the susceptibility to the development of uveitis [7].

CASE REPORT

A 50-year-old man sought care at the Ophthalmology Emergency Room with a visual loss complaint after treatment for COVID-19 infection, confirmed in a nasopharyngeal swab chain reaction (PCR). He reports that he was hospitalized for the treatment of dyspnea, fever and cough with analgesics associated with systemic corticosteroids.

He complained of bilateral visual haze after 10 days of hospital discharge, with no previous ocular pathological history, on examination: visual acuity at 20/50 in the right eye and 20/40 in the left eye (Snellen table at 6 meters). The biomicroscopy examination showed an anterior chamber with a mild anterior chamber reaction and fine paracentral precipitates (PKs) in both eyes. The retinal mapping exam showed a clinically preserved retina until the serrata, however vitreitis in both eyes (AO), 2+/4 in the right eye (OD) and 1 + / 4 + in the left eye (OE), documented by simple retinography (figure 1).

It is worth remembering that, for the evaluation of the vitreous haze scale, characteristic of this clinical presentation, it is graded from 0-4, where the main factors evaluated are the presence of blurring of the optic nerve and retinal vessels. For the evaluation of the anterior chamber, the cell count scale dispersed in the light beam in biomicroscopy is used. However, vitreous haze, according to the American Academy of Ophthalmology (AAO), is the best way to indicate intermediate uveitis activity[7].

On angiofluoresceinography (figure 1), no vascular, macular or papillary abnormalities were observed in both eyes and the Optical Coherence Tomography (figure 3) showed a macula with preserved neurosensory architecture and retinal pigment epithelium. A diagnostic hypothesis of subacute, bilateral, asymmetric intermediate uveitis was raised, secondary to COVID-19.

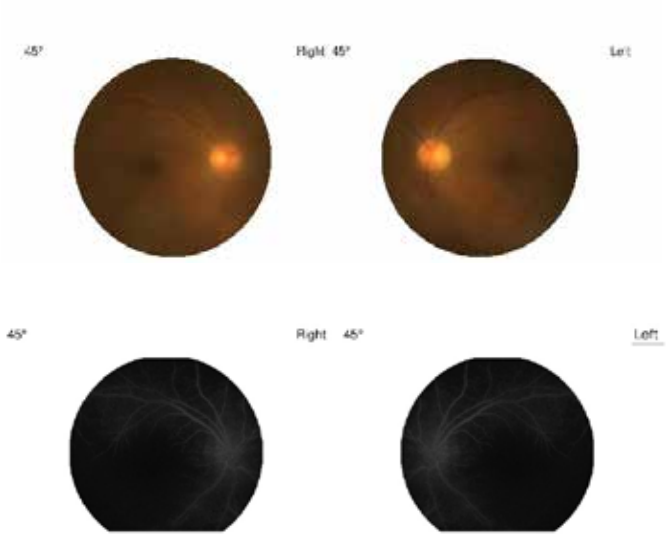

Figure 1. Color Retinography (upper): Vitreous haze 2+/4+ in the right eye and 1+/4+ in the left eye. Angiofluoresceinography (lower): Intermediate phase of the examination without changes in circulation under sodium fluorescein.

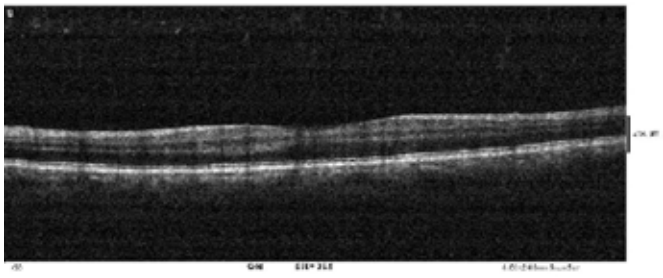

Fig 2. Macular optical coherence tomography right eye (OD): Spot of posterior optical shadow coming from the vitreous cavity.

Topical treatment was started with 1.0% prednisolone acetate eye drops, a 4/4hrs drop in both eyes. The patient evolved with a significant improvement in visual acuity, and on examination after 15 days: in the right eye 20/25 and 20/20 in the left eye. In the reassessment of biomicroscopy and fundscopy, there was an important resolution of the vitreitis pattern and placid anterior chamber without ceramic precipitates (PKs). There was weaning from topical treatment and progressive improvement without reactivation of the condition.

Infectious diseases such as syphilis, herpes, tuberculosis, HTLV, toxocariasis and viral hepatitis were ruled out. Cat scratch disease, sarcoidosis, Lyme disease and multiple sclerosis were also excluded. It is worth mentioning that the patient does not have a medical history of other previous autoimmune, inflammatory and systemic infec-

tious eye or chronic diseases.

DISCUSSION

It is known that SRAS-CoV-19 resembles a hyperferritinemic syndrome, in its main stages, with: lymphopenia, reduction in the number and activity of NK lymphocytes, coagulopathy and hyperferritinemia, which demonstrates the great proinflammatory capacity, which induces the expression of different inflammatory mediators, mainly IL-1β [1].

According to Colanfresco et al., despite the numerous etiologies that can develop hyperferritinemic syndrome, they can converge in at least two mechanisms that cause hyperferritinemia: hyperactivation of T lymphocytes and hyperactivity of IFN-γ [1,2]. However, recent evidence has described the direct role of the ferritin H chain in the activation of macrophages to increase the secretion of inflammatory cytokines, evolving with macrophage activation syndrome (MAS), catastrophic antiphospholipid syndrome (cAPS) and septic shock [1].

This pro-inflammatory condition can be found in several observational studies, where the number of autoimmune conditions, such as Kawasaki syndrome, has increased. In children in cities like Paris[8], in France, and Bergamo, in Italy[9], the SARS-CoV-2 epidemic has been associated with a high incidence of a severe form of Kawasaki disease, such as children's multisystemic inflammatory syndrome (KDSS) and macrophage activation syndrome (MAS) [8,9].

In a peculiar way, the Kawasaki syndrome is an acute vasculitis of medium-caliber vessels, with systemic decompensation, with an immunomediated trigger, which often courses with anterior uveitis[8,9]. The correlation between intraocular inflammations and Kawasaki syndrome is believed to be in the major inflammatory storm present in the pathology, with high levels of IL-6, C-reactive protein and procalcitonin[8,9].

There are reports of bilateral acute anterior uveitis (iridocyclitis), associated with visual haze, associated with a multisystemic inflammatory condition secondary to COVID-19, leading to corneal edema, diffuse descemet folds and keratic precipitates (PKs) in both eyes, with good prognosis after topical and systemic therapeutic follow-up of corticosteroids described in the literature [1,3,5].

Incidentally, intermediate uveitis is a subgroup of uveitis, where the main site of inflammation is the vitreous, peripheral retina and pars plana, epidemiologically it is not usually associated with sex or race and the involvement tends to be bilateral in 70% of cases . The most frequent initial symptom is the perception of floaters and decreased visual acuity [7].

The eye usually has a lower inflammatory pattern when compared to presentations of anterior uveitis, with mild hyperemia and moderate anterior chamber reaction. Also part of the clinical presentation are small, white, fine keratic precipitates, usually in the lower half of the cornea. Vitreitis is the marker of the disease, ranging from mild to severe, becoming more condensed and classically focal, such as snowballs, are observed during progression 7.

Snowballs are peculiar vitreous infiltrations, containing mononuclear leukocytes and cells similar to fibrocytes, Müller cells and fibrous astrocytes. Apparently, the pathophysiology is related to a disease mediated by T cells, which due to immunotaxis initiated by an unknown antigen, leads to a picture of vasculitis and vitreous inflammation [7].

It is possible that the antigen is infectious because intermediate uveitis is seen in infectious diseases like Lyme, syphilis and cat scratch fever. The disease can be autoimmune, as the pathology is also seen in non-infectious diseases, such as multiple sclerosis and sarcoidosis. Collagen type II in the vitreous can be an autoantigen in some patients [7].

HLA associations have been reported in intermediate uveitis, in which HLA-DR is the most significant, occurring in 67-72%. Promising studies correlate Human Leukocyte Antigen (HLA), which are proteins encoded in the main histocompatibility complex, for recognition and immune defenses to COVID-19, which may condition an individual more susceptible or more resistant to the inflammatory storm typical of the acute phase of the disease, such as HLA-B*46: 01 and HLA-B*15: 03 [10].

In general, the picture of intermediate uveitis is usually benign, where its complications are due to chronicity. Glaucoma, cataracts, macular edema and maculopathy, secondary to intraocular inflammation, are possible complications [7]. The diagnosis and early therapeutic intervention can avoid these aggravations, therefore, it is of fundamental importance to discuss the clinical and inflammatory presentations, as well as the therapeutic approach of this multisystemic viral condition, in this ongoing Pandemic, and consequently being an important public health issue.

CONCLUSION

In relation to this COVID – 19 case, it was not possible to perform the PCR of lacrimal swab or the PCR of vitreous humor, so we cannot say that the uveitis presented was caused by the coronavirus. The good response to early clinical treatment speaks for self-limited subacute intermediate uveitis. After excluding other causes and possible etiologies, we considered the presumed diagnosis of intermediate uveitis secondary to coronavirus.

The manifestation of intermediate uveitis, in this case reported, occurred shortly after the treatment of acute systemic disease by COVID-19. One hypothesis raised is the post-infectious immune-mediated presentation. Another hypothesis raised is that uveitis did not manifest early due to the concomitant use of systemic corticosteroids and that after its suspension, intraocular inflammation was installed.

We report this case of ocular involvement, days after the systemic inflammatory condition by SARS-CoV-2, to document the extraordinary and multifaceted capacity for clinical viral manifestation, as a cause of low visual acuity, in an alarming pandemic scenario.

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