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CASE REPORT

INTERMEDIATE UVEITIS AFTER COVID-19 INFECTION: A CASE REPORT

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ABSTRACT

Introduction: In the medical literature, multiple descriptions of ophthalmological manifestations have been attributed, directly or indirectly, to COVID-19. The increase in ocular surface symptoms, such as dry eye, were correlated by increasing exposure to digital life during the isolation period in pandemia. The signs of vascular involvement are well documented, such as retinal hemorrhages and also of intraocular inflammation, called uveitis. We describe a case of intermediate uveitis after COVID-19 infection. Case report: A 50-year-old man with positive Polymerase Chain Reaction (PCR) in a nasal swab for SARS-VOC-2, ten days after isolation, complained of low visual acuity and bilateral visual blurring. Vitreitis in both eyes, 2 + / 4 OD and 1 + / 4 + OE and vitreous haze were documented in simple retinography. Fifteen days after the early diagnosis and the start of treatment, the patient evolved with improved visual acuity. In the reassessment of biomicroscopy and fundoscopy, there was an improvement in the vitritis pattern. Discussion: The patient denied a medical history of chronic autoimmune and inflammatory diseases, and other etiologies were excluded. The clinical presentation, early diagnosis and satisfactory response suggest a subacute intermediate uveitis. Conclusion: 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 manifestation of this virus.

KEYWORDS: UVEITIS, COVID-19, INFLAMMATION

INTRODUCTION

A new epidemic of RNA virus, with envelopes belonging to the Coronaviridae family[1], 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, supported by cytokines, of a multisystemic character [2].

Viruses of the Coronaviridae family (CoVs) are also known to manifest in regions other than the respiratory tract, including the gastrointestinal tract and ocular 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 ocular tissues and secretions[3].

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

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

A recent survey showed that the main ocular complaints of patients with SARS-CoV-2 are dry eyes, blurred vision and foreign body sensation. It is believed that they are much more related 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 manifestation[5]. 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]. It may be present in conjunctival secretions, requiring greater attention and caution on the part of the patient and the multidisciplinary team that will manage the patient [3].

Furthermore, there are, in the literature, various descriptions of infrequent ocular presentations of COVID-19. Bettach et al., for example, postulated the first case of bi-

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lateral anterior uveitis secondary to multisystemic inflammation of SARS-CoV-2 [6]. The word uveitis was created to describe an inflammatory process in the ulvea, a region that constitutes the tunica vasculosa bulbi (iris, ciliary body and choroid), but the current term is synonymous with intraocular inflammation [7].

There are several ethologies, of autoimmune or infectious origin, that can develop the pathology, and 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 Ophthalmologic Emergency Room complaining of low vision after being treated for COVID-19 infection, confirmed in a nasopharyngeal swab Polymerase 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 blurring after 10 days of hospital discharge, with no previous ocular pathological history, on examination: distance visual acuity of 20/50 in the right eye and 20/40 in the left eye (Snellen's table at [6] meters). Biomicroscopy examination showed an anterior chamber with mild anterior chamber reaction and fine paracentral keratic precipitates (PKS) in both eyes. The retinal mapping exam showed a clinically preserved retina up to the ora serrata, however vitritis in both eyes (BE), 2+/4 in the Right Eye (RE) and 1+/4+ in the Left Eye (LE), documented by simple fundus (figure 1).

It is worth remembering that, for the assessment 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. To assess the anterior chamber, the scale for counting cells scattered in the light beam is used in biomicroscopy. However, vitreous haze, according to the American Academy of Ophthalmology (AAO), is the best way to indicate intermediate uveitis activity[7].

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

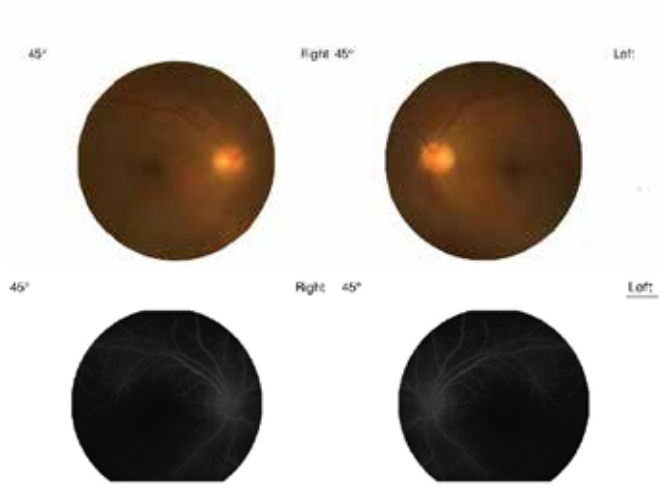

Figure 1. Color Retinography (top): Vitreous Haze 2+/4+ RE and 1+/4+ LE. Fluorescein angiography (bottom) : Intermediate phase of the examination without changes in the circulation under sodium fluorescein.

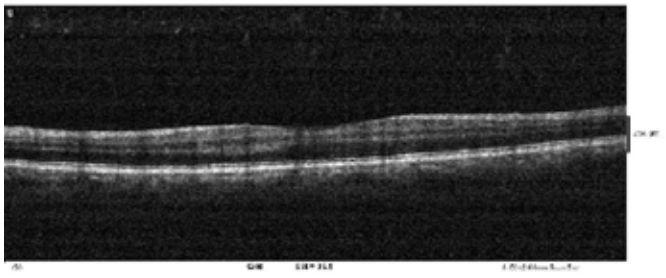

Fig 2. RE macular optical coherence tomography: Posterior optical shadow foci from the vitreous cavity.

Topical treatment was started with 1.0% prednisolone acetate eye drops, one drop, in both eyes, for 4/4hrs. The patient evolved with expressive improvement in visual acuity, and after 15 days on examination: in the right eye 20/25 and 20/20 in the left eye. In the reassessment of biomicroscopy and funduscopy, there was an important resolution of the vitritis pattern and placid anterior chamber without keratic precipitates (PKS). There was weaning from the 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 noting that the patient does not have a medical history of other ocular or chronic autoimmune, inflammatory and systemic infectious diseases.

DISCUSSION

It is known that SARS-CoV-19 is similar to a hyperferritinemic syndrome, in its main stages, with: lymphopenia, reduction in the number and activity of NK lym-

phocytes, coagulopathy and hyperferritinemia, which demonstrates the great pro-inflammatory 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 the hyperferritinemic syndrome, they can converge in at least two mechanisms that cause hyperferritinemia: T lymphocyte hyperactivation and IFN-γ hyperactivity [1,2]. However, recent evidence has described the direct role of ferritin H chain in macrophage activation to increase inflammatory cytokine secretion, evolving with macrophage activation syndrome (MAS), antiphospholipid syndrome (cAPS) and septic shock [1].

This pro-inflammatory condition can be observed in several observational studies, where an increase in the number of autoimmune conditions, such as Kawasaki syndrome, was found. In children, in cities such as Paris[8], France, and Bergamo, Italy9, the SARS-CoV-2 epidemic has been associated with a high incidence of a severe form of Kawasaki disease, such as multisystem inflammatory syndrome in children (KDSS) and macrophage activation syndrome (MAS) [8,9].

In a peculiar way, the kawasaki syndrome is an acute vasculitis of medium-sized vessels, with systemic decompensation, with an immune-mediated trigger, which frequently courses with anterior uveitis [8,9]. It is believed that the correlation between intraocular inflammation and Kawasaki syndrome lies in the great 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 blurring, associated with a multisystem inflammatory condition secondary to COVID-19, coursing with 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].

In time, intermediate uveitis is a subgroup of uveitis, where the main site of inflammation is the vitreous, peripheral retina and pars plana, epidemiologically it is usually not associated with gender 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 generally has a lesser inflammatory pattern compared to the 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. Vitritis is the disease marker, ranging from mild to severe, becoming more condensed and classically focal, such as snowballs, during progression [7].

Snowballs are peculiar vitreous infiltrates containing mononuclear leukocytes and fibrocyte-like cells, muller cells, and fibrous astrocytes. As indicated, the pathophysiology is related to a disease mediated by T cells, which, by 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 such as Lyme, syphilis, and cat-scratch fever. The disease can be autoimmune, as the pathology is also observed in non-infectious diseases, such as multiple sclerosis and sarcoidosis. Type II collagen in the vitreous may 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 major histocompatibility complex, for the recognition and immune defenses to COVID-19, which can 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, intermediate uveitis is usually benign, and its complications are due to chronicity. Glaucoma, cataracts, macular edema and maculopathy, secondary to intraocular inflammation, are possible complications [7]. Early diagnosis and therapeutic intervention can prevent these problems, 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 therefore, an important public health issue.

CONCLUSION

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

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

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

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