DOI - 10.37951/CEREM.2022.V2I6.13-16

CASE REPORT

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

VINICIUS STIVAL VENEZIANO SOBRINHO[1,2], AUGUSTO PEREIRA[1], 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 fundoscopy, there was an improvement in the vitritis pattern. Conclusions: the patient denied a medical history of chronic autoimmune and inflammatory diseases, and possible etiologies were excluded. Clinical presentation, 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.

KEYWORDS: INTERMEDIATE UVEITIS; COVID-19; PUBLIC HEALTH

INTRODUCTION

A new epidemic of the RNA virus, with envelopes belonging to the family Coronaviridae [1], capable of causing a severe acute respiratory syndrome coronavirus - 2 (SARS-CoV-2), emerged from China in late 2019. Literature descriptions conceptualize "COVID-19" as an inflammatory storm, supported by cytokines, of a multisystem nature[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 from patients with SARS-CoV infection demonstrated the presence of the virus. The discovery of SARS-CoV in tears was the first of its kind in emphasizing the need for adequate precautions to prevent potential transmission through ocular tissues and secretions [3].

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

Recently, in the "SERPICO-19" study, 54 patients, among the 133 exposed, were identified with retinal changes, where the main changes were microvascular, especially microhemorrhages and cotton-wool exudates [4]. 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 pigment 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 manifestation 3,5. 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, varied descriptions of infrequent ocular presentations of COVID-19. Bettach et al., as an 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 of the ulvea,

1 – INSTITUTO E HOSPITAL OFTALMOLÓGICO DE ANÁPOLIS – IHOA/GO
2 – UFG/GO

ADDRESS
FRANCISCO DIAS LUCENA NETO
Rua 3, Quadra 5 - Residencial Cidade Jardim - bloco 1, apartamento 502, Anápolis - IHOA/GO - CEP: 75080-710
E-mail: fneto640@gmail.com

the region that constitutes the bulbi vasculosa (iris, body ciliary 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, 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 genes of the MHC complex 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 Ophthalmological Emergency Room with a complaint of low vision after treatment for a COVID-19 infection, confirmed in a nasopharyngeal swab Polymerase Chain Reaction (PCR). He reports that he was hospitalized for treatment of dyspnea, fever and cough with analgesics associated with systemic corticosteroids.
He complained of bilateral blurring of vision 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 chart at 6 meters). Biomicroscopy 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 the 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 evaluation of the anterior chamber, the scale for counting cells scattered 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 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 intermediate uveitis secondary to COVID-19 was raised.

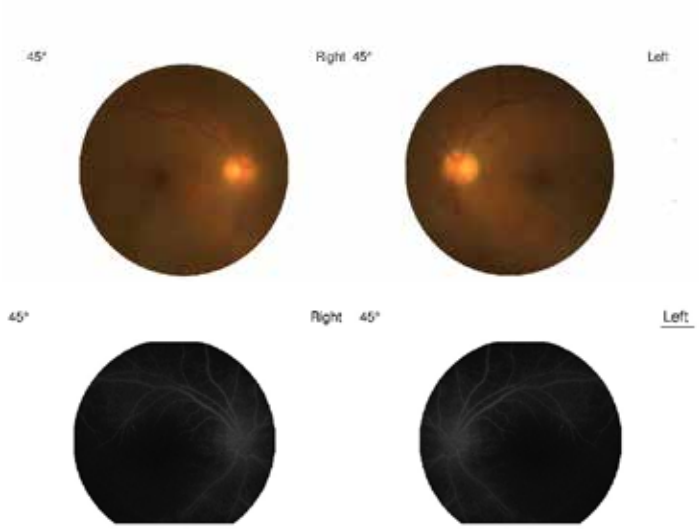

Figure 1. Color Retinography (upper): Vitreous haze 2+/4+ in the right eye and 1+/4+ in the left eye. Fluorescein angiography (lower): Intermediate phase of the exam without changes in circulation under sodium fluorescein.

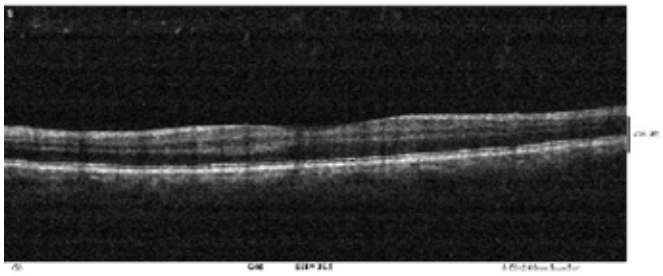

Fig 2. RE macular optical coherence tomography: Posterior optical shadow foci from the vitreous cavity.

Topical treatment was started with 1.0% prednisolone acetate eye drops, one drop, in both eyes, every 4 hours. The patient evolved with significant improvement in visual acuity, and on examination after 15 days: 20/25 in the right eye and 20/20 in the left eye. In the reassessment of biomicroscopy and funduscopy, there was 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 mentioning that the patient has no medical history of other previous eye diseases or chronic systemic autoimmune, inflammatory and infectious diseases.

DISCUSSION

It is known that SARS-CoV-19 resembles a hyperferritinemic syndrome, in its main stages, coursing with:

lymphopenia, reduction in the number and activity of NK lymphocytes, 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 [1,2] hyperactivity. However, recent evidence has described the direct role of ferritin H chain in macrophage activation to increase the secretion of inflammatory cytokines, 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 Paris8, 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 children's multisystem inflammatory syndrome (KDSS) and macrophage activation syndrome (MAS) [8,9].

In a peculiar way, kawasaki syndrome is an acute vasculitis of medium-sized vessels, with systemic decompensation, with an immune-mediated trigger, which often leads to anterior uveitis [8,9]. It is believed that the correlation between intraocular inflammation and Kawasaki syndrome lies in the large 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 blurred vision, 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 therapy with 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 not usually 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 lower inflammatory pattern compared to presentations of anterior uveitis, with mild hyperemia and moderate anterior chamber reaction. The clinical presentation also includes small, white, thin keratic precipitates, usually in the lower half of the cornea. Vitreitis is the hallmark 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 fibrocyte-like cells, muller cells, and fibrous astrocytes. Apparently, 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 may be autoimmune as the pathology is also seen 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 of 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 condition 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]. Early diagnosis and therapeutic intervention can avoid these conditions, 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 a self-limited subacute intermediate uveitis. After excluding other causes and possible etiologies, we considered a presumptive diagnosis of intermediate uveitis secondary to coronavirus.

The manifestation of intermediate uveitis, in this case reported, occurred shortly after treatment of acute systemic illness 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 discontinuation of the same, intraocular inflammation set in.

We report this case of ocular involvement, days after the systemic inflammatory condition 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.

REFERENCES

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395 (10223):497–506.doi:10.1016/S0140-6736(20)30183-5.
2. Colafrancesco S, Alessandri C, Conti F, Priori R. COVID-19 gone bad:a new character in the spectrum of the hyperferritinemic syndrome?. Autoimmun Rev. 2020;19:102573.
3. Dawn Ho, Rebecca Low, Louis Tong, Vishali Gupta, Aravamudan Veeraraghavan & Rupesh Agrawal (2020) COVID-19 and the Ocular Surface: A Review of Transmission and Manifestations, Ocular Immunology and Inflammation, 28:5, 726-734.
4. Invernizzi A, Torre A, Parrulli S, Zicarelli F, Schiuma M, Colombo V, Giacomelli A, Cigada M, Milazzo L, Ridolfo A, Faggion I, Cordier L, Oldani M, Marini S, Villa P, Rizzardini G, Galli M, Antinori S, Staurenghi G, Meroni L. Retinal findings in patients with COVID-19: Results from the SERPICO-19 study. EClinicalMedicine. 2020 Oct;27:100550.
5. Nuzzi R, Carucci LL, Tripoli F. COVID-19 and ocular implications: an update. J Ophthalmic Inflamm Infect. 2020 Sep 4;10(1):20.
6. Bettach, E., Zadok, D., Weill, Y., Brosh, K. and Hanhart, J. (2021), Bilateral anterior uveitis as a part of a multisystem inflammatory syndrome secondary to COVID-19 infection. J Med Virol, 93: 139-140.
7. Nida Sen H, Albini TA, Burkholder BM, Dahr SS, Dodds EM, Leveque TK, Smith WM, Vasconcelos-Santos AV. Uveitis and ocular inflammation – American Academy of ophthalmology. Basic and Clinical Science Course 2019-2020.
8. Toubiana J, Poirault C, Corsia A, Bajolle F, Fourgeaud J, Angoulvant F, Debray A, Basmaci R, Salvador E, Biscardi S, Frange P, Chalumeau M, Casanova JL, Cohen JF, Allali S. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. BMJ. 2020 Jun 3;369:m2094. doi: 10.1136/bmj.m2094.
9. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, Bonanomi E, D'Antiga L. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet. 2020 Jun 6;395(10239):1771-1778.
10. Iturrieta-Zuazo I, Rita CG, García-Soidán A, et al. Possible role of HLA class-I genotype in SARS-CoV-2 infection and progression: A pilot study in a cohort of Covid-19 Spanish patients. Clin Immunol. 2020;219:108572. doi:10.1016/j.clim.2020.108572.