

Superior ophthalmic vein and cavernous sinus thrombosis associated with COVID-19: a case report

Trombose de veia oftálmica superior e seio cavernoso associada à COVID-19: relato de caso

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ABSTRACT

Cavernous sinus and superior ophthalmic vein thrombosis is a rare clinical condition, and little described in the literature. The clinical presentation is nonspecific and highly variable, and symptoms may include red eye, ophthalmoplegia, coma, and death. The main etiology results from infection of the paranasal sinuses. The final diagnosis must be made through imaging tests such as magnetic resonance imaging. We describe a case of cavernous sinus and superior ophthalmic vein thrombosis after COVID-19 infection in a 64-year-old patient with persistent ocular hyperemia and pain on eye movement. Ophthalmological examination showed preserved visual acuity, conjunctival hyperemia, dilation of episcleral vessels and retinal vascular tortuosity in the right eye. Magnetic resonance imaging confirmed the diagnosis. The association with the COVID-19 was raised, excluding other infectious causes. Enoxaparin and Warfarin were started with significant improvement in the ocular clinical presentation and maintenance of initial visual acuity after 12 months of follow-up.

RESUMO

A trombose de seio cavernoso e veia oftálmica superior é uma condição clínica rara e pouco descrita na literatura. A apresentação clínica é inespecífica e altamente variável. Os sintomas podem incluir olho vermelho, oftalmoplegia, coma e morte. A etiologia principal resulta da infecção dos seios paranasais. O diagnóstico final deve ser efetuado por meio de exames de imagem, como ressonância magnética. Descrevemos um caso de trombose de seio cavernoso e veia oftálmica superior após COVID-19 em paciente de 64 anos e com quadro de hiperemia ocular persistente e dor à movimentação ocular. Ao exame oftalmológico, observou-se acuidade visual preservada, hiperemia conjuntival, dilatação de vasos episclerais e tortuosidade vascular retiniana em olho direito. A ressonância confirmou o diagnóstico. A associação com a COVID-19 foi levantada, excluindo-se demais causas infecciosas. Prescrevemos enoxaparina e varfarina, com melhora do quadro clínico ocular e manutenção da acuidade visual inicial após 12 meses de acompanhamento.

INTRODUCTION

Superior ophthalmic vein thrombosis (SOVT) is a rare eye condition, with high mortality rate and high risk of complications if not diagnosed and treated in time.^(1,2) Clinical signs are due to venous congestion and include painful proptosis, ptosis, eyelid swelling, chemosis, ocular motility restriction, and vision loss. Thrombosis is caused by altered venous blood flow and can be divided into septic and aseptic causes. The aseptic etiologies include orbital arteriovenous malformations (dural arteriovenous fistula, carotid-cavernous fistula), autoimmune, and systemic diseases (systemic lupus erythematosus, thyroid eye disease, ulcerative colitis), facial trauma, hematological diseases, orbital neoplasms and use of hormonal medications (tamoxifen, oral contraceptives).⁽¹⁻⁴⁾ Within the septic causes, infections of the paranasal sinuses, orbit, face, and teeth are included, with infections by *Staphylococcus aureus* and streptococci being reported as the most common causes.^(3,4) The diagnosis is made through the clinical presentation and the use of imaging tests such as contrast-enhanced computed tomography or angiographic magnetic resonance. Cavernous sinus thrombosis (CST) may be present simultaneously with the condition.⁽⁵⁾ The treatment is not well established in literature due to the rarity of the pathology, and the intervention should be focused on the etiological cause when it is found. Possible treatments include antibiotics, anticoagulants, corticosteroids and/or surgery.⁽¹⁻⁴⁾

The acute respiratory infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is potentially severe, highly transmissible and affects the entire planet. Although most people with the coronavirus disease 2019 (COVID-19) develop mild (40%) or moderate (40%) symptoms, approximately 15% may develop severe symptoms that require oxygen support and about 5% may have the critical form of the disease with complications such as respiratory failure, sepsis and septic shock, thromboembolism and/or multiple organ failure.^(6,7)

Objective

To describe a case of cavernous sinus and superior ophthalmic vein thrombosis after COVID-19 infection.

CASE REPORT

A 64-year-old female, from Uberaba (MG), Brazil, sought emergency care with conjunctival hyperemia and retro-orbital pain in the right eye that lasted a month. Ophthalmological examination showed best-corrected

visual acuity of 20/20 in both eyes, with slit-lamp biomicroscopy of the anterior segment showing moderate conjunctival hyperemia, chemosis and substantial tortuosity of conjunctival and episcleral vessels in the right eye (Figures 1 and 2), in addition to restriction of extrinsic ocular movement, mainly during elevation and abduction, with no other changes to the exam. Tonometry was 15mmHg in the right eye and 13mmHg in the left eye. Fundoscopy showed vascular tortuosity in retinal vessels in the right eye, without changes in the left eye. During consultation, the patient reported a history of flu-like symptoms starting one month before eye symptoms and diagnosis of COVID-19 infection with positive polymerase chain reaction (PCR) test, requiring hospitalization for respiratory supplementation. The patient's medical history included anxiety disorder, using sertraline 50mg daily and zolpidem 10mg at night. She denied other comorbidities, the use of other medications and prior vaccination for the SARS-CoV-2. After a diagnostic hypothesis of CST, magnetic resonance imaging (MRI) of the orbits and brain was requested, with an imaging finding compatible with partial thrombosis of the superior ophthalmic vein and the right cavernous sinus (Figure 3). The Neurology Department was called and performed a neurological physical examination that did not show other changes. After carrying out additional tests (Table 1) and discussing the case with the Neurology and Hematology Departments, the other hypotheses were excluded and the hypothesis of a thromboembolic event was considered as a complication of the SARS-CoV-2 infection. Anticoagulation with warfarin 5mg associated with enoxaparin 60mg every 12 hours was performed, maintained until International Normalized Ratio (INR) control between 2 and 3, with subsequent suspension of enoxaparin and maintenance only of warfarin. The patient remained hospitalized for 11 days under the care of the Ophthalmology and Neurology departments. She is followed up at the Ophthalmology outpatient clinic with a significant improvement in her clinical condition and significant regression of chemosis, conjunctival hyperemia and retinal vascular tortuosity after 12 months of treatment (Figure 2). Visual acuity was preserved throughout the ophthalmologic follow-up.

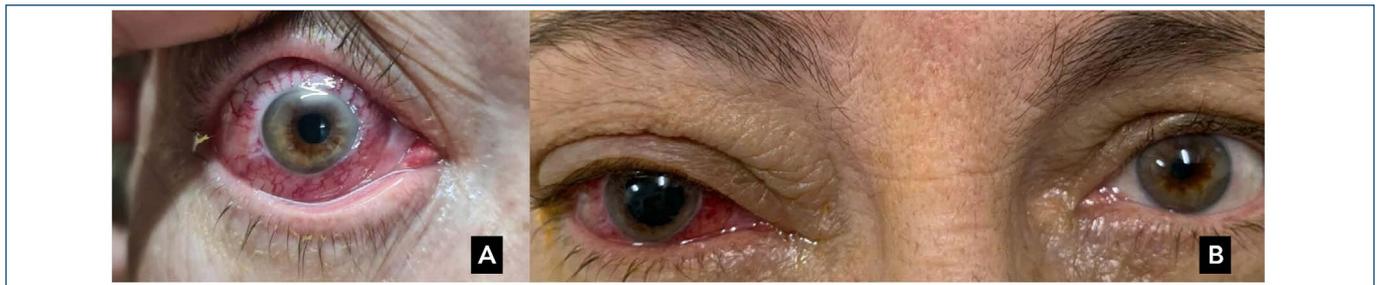
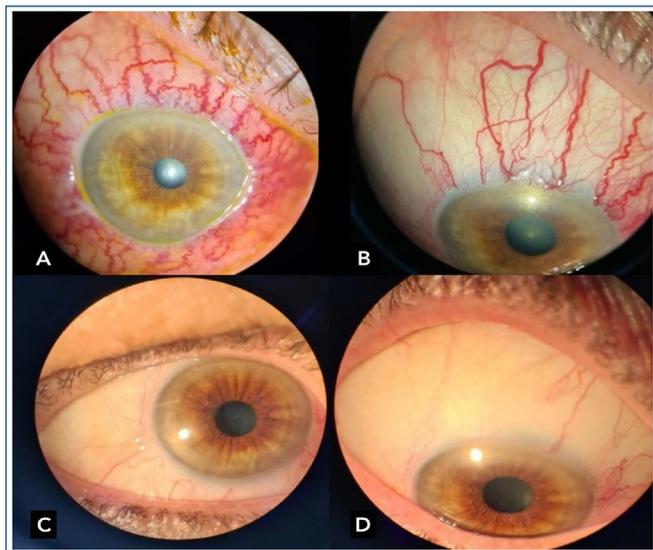
DISCUSSION

Cavernous sinus thrombosis refers to clotting within the cavernous sinus. Features are rapid in onset and may include severe headache, nausea and vomiting, proptosis, chemosis, conjunctival and retinal vein congestion, reduced vision, and limitation of extrinsic ocular muscle

Table 1. Additional tests

Complementary exams	Results	Reference values
Creatinine	1.0mg/dL	0.70-1.20mg/dL
Urea	31.0mg/dL	Less than 50mg/dL
Platelets	275.000/mm ³	150.000-400.000/mm ³
International Normalized Ratio	1.00	1.0-1.4
Activated partial thromboplastin time	28.1 seconds	25-34 seconds
Thyroid stimulating hormone	2.058mLU/mL	0.35-4.94mLU/mL
Free T4	0.980ng/dL	0.70-1.48ng/dL
Antinuclear antibodies	Non-reactive	Non-reactive
Rheumatoid factor	7.20IU/mL	Less than 14.0IU/mL
C-reactive protein	0.7mg/dL	Less than 0.5mg/dL
Blood culture	No bacterial growth	No bacterial growth
Cardiolipin antibodies IgG	9.40LPG	Less than 15.0GPL
Cardiolipin antibodies IgM	9.40MPL	Less than 12.5MPL
Homocysteine	14.58 micromol/L	5.75-18.89 micromol/L
Factor V Leiden	Negative	Negative
D-dimer	1131 ng/mL FEU	Less than 600 ng/mL FEU
Anti-SSA/RO antibodies and Anti-SSB/LA antibodies	Less than 7.0U/mL	Less than 7.0 U/mL
ANCA	p-ANCA non-reactive, c-ANCA non-reactive	Non-reactive
Albumin	4.46g/dL	3.50-4.85g/dL
Folic acid	8.50ng/mL	4.6-18.7ng/mL
Total protein	7.00g/dL	6.50- 8.20g/dL
Protein electrophoresis	Without changes	Without changes
Erythrocyte sedimentation rate	17mm	0-20mm
Fibrinogen	428.0mg/dL	150.0- 450.0mg/dL
HBsAg, Anti-HCV, HTLV 1 and 2, VDRL, Anti-HIV 1 and 2	non-reactive	Non-reactive
Anti-HBS	Less than 2.00IU/L	Less than 10IU/L
Lupus anticoagulant	Not detected	Not detected
Echocardiogram and electrocardiogram	Without changes	
Complete blood count	Without changes	

IgG: immunoglobulin G; IgM: immunoglobulin M; ANCA: antineutrophil cytoplasmic antibodies; HTLV: human T-lymphotropic virus type 1; VDRL: venereal disease research laboratory test

**Figure 1.** Thrombosis of the superior ophthalmic vein and cavernous sinus on the right.**Figure 2.** Clinical evolution.

movement. It has a high mortality rate: 20% if treated, and up to 100% if untreated.⁽⁶⁾

The diagnosis of CST and SOVT is challenging, as the signs and symptoms are extremely varied and nonspecific. Cavernous sinus thrombosis can be classified etiologically as septic or aseptic. The septic form is considered the most frequent and is usually associated with an infectious process of the paranasal sinuses, face, and ears. The aseptic form is due to trauma, sickle cell anemia, and thromboembolic phenomena. The differential diagnosis must be made with orbital cellulitis, orbital apex syndrome, and carotid-cavernous fistula.

In the present case, after the diagnostic confirmation of CST and SOVT through MRI, infectious and thromboembolic causes were investigated. According to the results of the auxiliary tests and due to previous infection by the

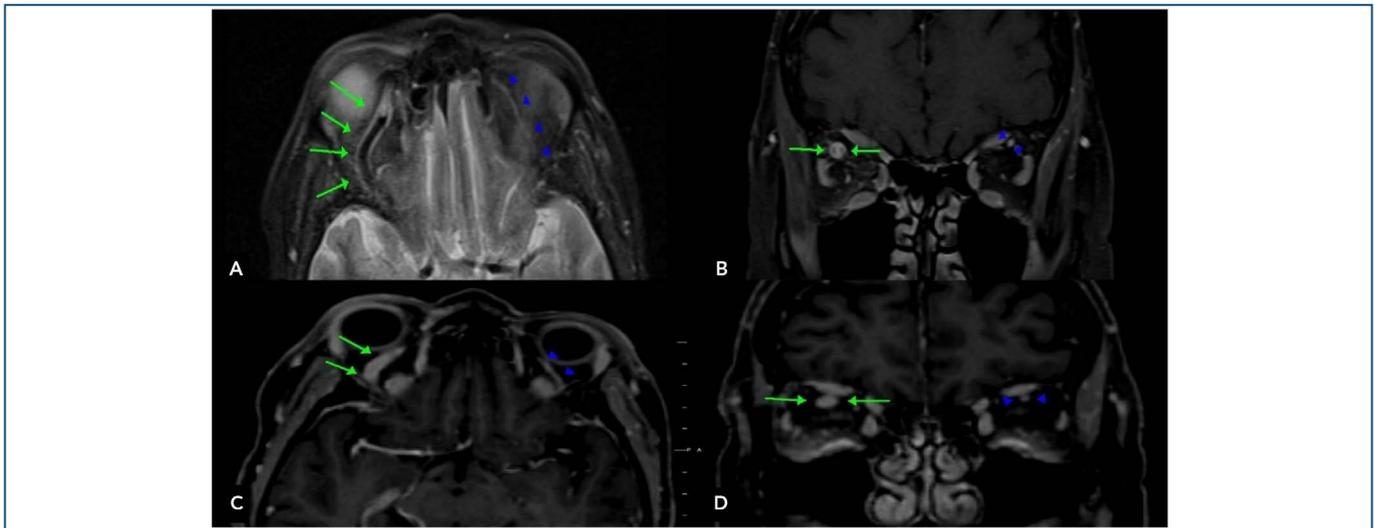


Figure 3. Magnetic resonance imaging (MRI).

SARS-CoV-2, the diagnostic hypothesis of thromboembolic complication resulting from COVID-19 infection was raised and other causes were excluded. It is known that complications related to arterial and venous thrombosis are highlighted due to thromboembolic events caused by SARS-CoV-2. The thrombotic complications arising from the severe inflammatory state, secondary to the virus, describe a state of hemostasis disturbance, associated with hypercoagulability, creating a favorable diagnostic hypothesis for etiological suspicion. Due to the rarity of the clinical picture and lack of scientific evidence demonstrating the best approach in cases of CST and SOVT with COVID 19 infection, treatment with Enoxaparin and Warfarin was recommended since the literature has shown a decrease in the mortality rate and an increase in the recovery rate with anticoagulant treatment in other thromboembolic causes.^(9,10)

Therefore, it is important to have a complete ophthalmologic exam and to request complementary laboratory and imaging exams in order to make the correct diagnosis for a quick start of the appropriate treatment. It is a rare condition, but with a dramatic clinical course and high mortality rates, prompt identification and treatment are mandatory. Furthermore, the case described confirms a new etiology as a cause of CST and SOVT.

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