



Branch Retinal Vein Occlusions as a Serious Complication of Covid 19 Infection

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Abstract

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BACKGROUND: Branch retinal vein occlusion (BRVO) has an incidence of 0.5–1.2%. COVID-19 is associated with both venous and arterial thromboembolisms due to excessive inflammation, hypoxia, immobilization, and diffuse intravascular coagulation.

AIM: The present study aims to describe our experience with BRVO in Egyptian COVID-19 patients.

PATIENTS AND METHODS: The present retrospective study included 17 polymerase chain reaction (PCR)-proven COVID-19 patients with BRVO. Data obtained from the studied patients included detailed history taking. In addition, patients were diagnosed with BRVO based on a comprehensive ophthalmic evaluation, including logMAR Best-corrected visual acuity assessment, slit-lamp bio-microscopy, funduscopy, fundus fluorescein angiography, and optical coherence tomography macular assessment.

RESULTS: The present study included 17 PCR-proven COVID-19 patients with BRVO. They comprised 9 males (52.9%) and 8 females (47.1%) with an age of 52.8 ± 13.3 years. Fundus examination revealed BRVO as superior temporal in 9 patients (52.9%), inferior temporal in 5 patients (29.4%), superior nasal in 2 patients (11.8%), and inferior nasal in 1 patient (5.9%). The reported retinal thickness was 355.7 ± 41.7 μ m. In addition, fundus fluorescein angiography identified ischemic changes in 2 patients (11.8%).

CONCLUSION: BRVO is a rare severe complication of COVID-19 infection. In patients with proven or suspected infection with a diminution of vision, there should be high suspicion of BRVO and prompt full-scale ophthalmological examination to exclude the condition.

Introduction

Retinal vein occlusion (RVO) is the second most common retinal vascular disorder after diabetic retinopathy. Branch RVO (BRVO) has an incidence of 0.5–1.2% [1]. BRVOs have two major forms, non-ischemic and ischemic, which are detected in one-third and two-thirds of cases, respectively [2]. Typically, patients present with sudden painless vision loss or visual field defect [3]. Funduscopy examination may reveal flame hemorrhages, dot and blot hemorrhages, cotton wool spots, hard exudates, retinal edema, and dilated tortuous veins [4]. Characteristic findings of BRVO on optical coherence tomography (OCT) include cystoid macular edema, intraretinal hyper-reflectivity from hemorrhages, shadowing from edema and hemorrhages, and occasionally subretinal fluid [5], [6].

The pathogenesis of BRVO is multifactorial, including a combination of mechanical compression, degenerative changes in vessel walls, and/or hypercoagulable factors [7]. Macular edema is the

main cause of vision loss in BRVO. The pathogenesis of macular edema is believed to be a result of multiple inflammatory cascades. Analysis of vitreous samples from patients with BRVO has established an association with increased levels of VEGF, IL-6, IL-8, and monocyte chemoattractant protein-1 compared to controls [8], [9].

COVID-19 is associated with both venous and arterial thromboembolisms due to excessive inflammation, hypoxia, immobilization, and diffuse intravascular coagulation [10], [11]. The prevalence of venous thromboembolic events has been found to be as high as 27% [12], [13]. In addition, microangiopathic retinal changes have been observed in COVID-19 patients [14]. However, it's not clear whether these changes are due to prolonged hypoxemia or direct viral etiology [15], [16].

In fact, the SARS-CoV-2 virus had been detected in many diverse ocular specimens, including in the tears and conjunctival secretions of patients with coronavirus conjunctivitis [17], [18]. Furthermore, SARS-CoV-2 has been identified in retina samples of deceased patients with confirmed COVID-19 disease [19]. Interestingly,

angiotensin-converting enzyme 2 receptors known to be used by COVID-19 to gain entry into human cells are expressed in the retina [20], [21].

The present study describes our experience with BRVO in Egyptian COVID-19 patients.

Patients and Methods

The present retrospective study was conducted at Al-Azhar University Hospitals, Cairo, Egypt. Approval from the Ethics Committee was obtained. Written informed consent was taken from all patients for participation in the study after explaining the purpose of the study based on the Helsinki Declaration of clinical studies, including human subjects.

The study included 17 polymerase chain reaction (PCR)-proven COVID-19 patients with BRVO. Data obtained from the studied patients included detailed history taking. For laboratory assessment, two blood samples were obtained from all patients, including 2 ml of blood on an EDTA tube for assessment of CBC and 5 ml of blood in a serum tube for serum assessment of C-reactive protein, ferritin, lactic dehydrogenase (LDH), and D-dimer and performing anti-COVID IgM/IgG Antibody Test (Artron Laboratories, Canada).

Based on the comprehensive ophthalmic evaluation, patients were diagnosed with BRVO, including logMAR best-corrected visual acuity (BCVA) assessment, slit-lamp bio-microscopy, funduscopy, fundus fluorescein angiography, and OCT macular assessment.

Patients with macular edema were treated using monthly intravitreal injections of ranibizumab (0.5 mg/0.05 ml) for 3 months. Patients were subjected to a full ophthalmic examination 1 week after every injection. In addition, OCT was done 1 month after the last injection, together with an assessment of logMAR BCVA. Data obtained from the present study were presented as number and percent or mean and standard deviation.

Results

The present study included 17 PCR-proven COVID-19 patients with BRVO. They comprised 9 males (52.9%) and 8 females (47.1%) with an age of 52.8 ± 13.3 years. Clinical and laboratory findings in the studied patients are shown in Table 1. Fundus examination revealed BRVO as superior temporal in 9 patients (52.9%), inferior temporal in 5 patients (29.4%), superior nasal in 2 patients (11.8%), and

Table 1: Clinical and laboratory findings in the studied patients (n=17)

Parameters	Value
Age (years)	52.8 ± 13.3
Male/female, n	9/7
Diabetes mellitus, n (%)	7 (41.2)
Hypertension, n (%)	5 (29.4)
Anti-coagulants, n (%)	4 (23.5)
CRP (mg/L)	5.2 ± 0.4
LDH (IU/L)	262.3 ± 42.1
D-Dimer (µ/mL)	0.58 ± 0.12
TLC (×10 ³ /ml)	7.2 ± 2.6
Lymphocytes (%)	32.2 ± 11.3
Neutrophils (%)	65.7 ± 12.2

CRP: C-reactive protein, LDH: Lactate dehydrogenase, TLC: Total leucocytic count.

inferior nasal in 1 patient (5.9%). The reported retinal thickness was 355.7 ± 41.7 µm. Fundus fluorescein angiography identified ischemic changes in 2 patients (11.8%) (Table 2). The OCT retinal thickness had a clear, strong positive correlation that was highly significant with site BRAVO, FFA, Intraocular pressure, BCVA, lymphocytes, Hb, D-dimer, and total leucocytic count (TLC). Furthermore, the OCT retinal thickness significantly negatively correlated with the cataract, neutrophils, PLT, and LDH (Figure 1).

Table 2: Ophthalmic findings in the studied patients (n=17)

Parameters	Value
BCVA, mean ± SD	0.36 ± 0.14
IOP (mmHg), mean ± SD	15.94 ± 3.05
Cataract, n (%)	2 (11.8)
Site of BRVO, n (%)	
Superior temporal	9 (52.9)
Inferior temporal	5 (29.4)
Superior nasal	2 (11.8)
Inferior nasal	1 (5.9)
Retinal thickness (µm), mean ± SD	355.7 ± 41.7
Fundus fluorescein angiography, n (%)	
Ischemic	2 (11.8)
Nonischemic	15 (88.2)

BCVA: Best-corrected visual acuity, IOP: Intraocular pressure, SD: Standard deviation.

Discussion

Hypercoagulability and hyperinflammatory response are major contributors to morbidity and mortality in patients with COVID-19 [22], [23]. The reported clinical spectrum included deep venous thromboses, pulmonary emboli, and ischemic strokes resulting from COVID-19 [24]. Many ocular manifestations have been reported in association with COVID-19, the most common being conjunctivitis seen in 0.8% of patients [25].

In this retrospective study, we documented the largest series of BRVO related to COVID-19 infection to the best of our knowledge. Unfortunately, most published data on this issue involve single-patient case reports. In addition, our study included only BRVO patients with PCR-proven COVID-19 infection.

Sheth *et al.* [26] reported a case of vasculitic RVO secondary to COVID-19 in a 52-year-old patient who presented with a diminution of vision in the left eye 10 days after he tested positive for SARS-CoV-2. Furthermore, Venkatesh [15] reported a case of a

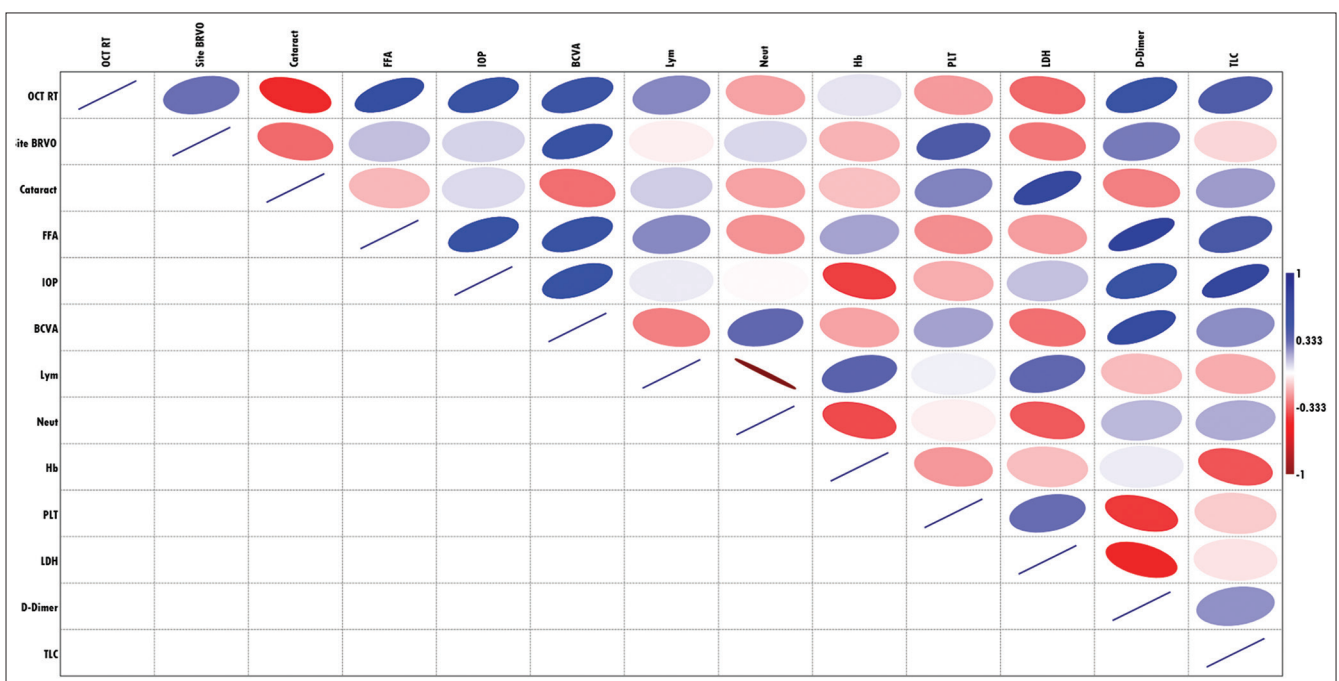


Figure 1: Heat map Pearson correlation shows the relationship between parameters. OCT retinal thickness with site BRAVO, FFA, IOP, BCVA, lymphocytes, Hb, D-dimer, TLC, cataract, neutrophils, PLT, and LDH

56-year-old female with CRVO. She tested positive for SARS-CoV-2 IgG and negative for IgM, denoting old COVID-19 infection. In another work, Walinjar [27] reported a case of a 66-year-old male with combined CRAO and CRVO with proven COVID-19 infection, diagnosed after the presentation. Moreover, Duff *et al.* [28] reported a 74-year-old female patient who initially presented with blurry vision in her left eye in the setting of symptomatic COVID-19 infection. She was diagnosed with a BRVO.

The current investigation was subject to a number of limitations. First, the small number of patients who were investigated was one limitation. Future research should include larger sample size, be broken up into more specific phases, and be categorized by severity. Nevertheless, since there were only 17 eyes included in the research, we could not incorporate a variety of BRVO eyes. Second, every test strategy should examine several retinal regions. Therefore, our deficient data analyses should be explained by conducting more extensive, prospective research.

Conclusion

BRVO is a rare serious complication of COVID-19 infection. The exact pathogenic factors involved remain to be elucidated. In patients with proven or suspected infection with a diminution of vision, there should be high suspicion of BRVO and prompt full-scale ophthalmological examination to exclude the condition.

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Declarations

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Ethics approval

The study followed the instructions of Al Azhar Medical research Ethical, Cairo, Egypt, with reference No. 0000053. All authors have read and agreed to the published version of the manuscript.

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