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Prevalence of SARS–CoV–2 among central retinal artery occlusion patients: A case series–HORA study report No. 3

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ABSTRACT

Introduction: COVID-19 patients are susceptible to hypercoagulability, thromboembolic, and vasculitis state; central retinal artery occlusion (CRAO) could be caused by hyperviscosity syndrome, thromboembolic accidents, and vasculitis. Evolving case reports are correlating CRAO with COVID-19 patients. Our case series aims to reveal the prevalence of SARS-CoV-2 among CRAO patients under the COVID-19 pandemic.

Methods: Medical records of all CRAO patients who attended our tertiary referral hospital, during COVID-19 local outbreak (March to November 2020), were reviewed. Respiratory tract samples were tested for SARS-CoV-2 by the validated Xpert Xpress SARS-CoV-2 assay. If patients were able to cooperate, oropharyngeal saliva samples were obtained. Otherwise, nasopharyngeal and deep throat swabs were taken by registered nurses.

Results: A total of 15 CRAO patients (7 males, 8 females) were identified during the 9-month study period. The mean age was 72.1-years (range 45-88 year). None of the patients were infected by SARS-CoV-2 before their CRAO disease episodes. Three patients had a history of CRAO over the contralateral eye. No patient was diagnosed with COVID-19 up to their last follow-up (mean 255.4 days, range 152-341 days). Without any COVID-19 positive case, correlation statistical tests on SARS-CoV-2 infection and CRAO were not established.

Conclusions: Some of the presumed COVID-19 related CRAO cases may be just coincident with at-risk patients, as COVID-19 is prevalent across the world. More in-depth research, with adjustment to known confounding risk factors, is needed to establish a genuine correlation.

KEYWORDS: COVID-19; Coronavirus; SARS-CoV-2; Retinal artery occlusion; Central retinal artery occlusion; Hyperbaric oxygen therapy

1. Introduction

SARS-CoV-2 virus infection causes coronavirus disease 2019 (COVID-19), in which multi-organ involvements were observed. COVID-19 patients are susceptible to hypercoagulability state, thromboembolic event, and vasculitis, therefore COVID-19 related cerebral stroke was widely reported[1]. There were evolving case reports published on central retinal artery occlusion (CRAO), aka ocular stroke, in COVID-19 patients[2-4]. There seems to be a correlation between COVID-19 and CRAO. CRAO is a rare disease entity with an incidence of 0.85/100000/year[5]. Our tertiary hospital is equipped with a hyperbaric oxygen therapy chamber, thus receives all locate acute CRAO referrals, serving >7 million population. Hyperbaric oxygen for central retinal artery occlusion study, in short, HORA study[6,7], aims at evaluating the efficacy of hyperbaric oxygen therapy (HBOT) for treating CRAO in Hong Kong, China[8]. To study the correlation between COVID-19 and CRAO, our retrospective study aims to reveal the prevalence of SARS-CoV-2 among acute CRAO patients in the COVID-19 era.

Significance

Association of COVID-19 and central retinal artery occlusion is evolving with more and more published case reports. Central retinal artery occlusion is a rare disease in the normal population. This case series reported the prevalence of SARS-CoV-2 among central retinal artery occlusion patients. Correlation of COVID-19 and central retinal artery occlusion is not established.

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2. Patients and methods

2.1. Patients

Medical records of all CRAO patients referred to us during the local COVID-19 outbreak period (from March 1st, 2020 to November 30th, 2020) were reviewed retrospectively. Patients with a history of contralateral eye CRAO were also included in this case series. However, ophthalmic artery occlusion or internal carotid artery occlusion patients who presented with similar retinal ischemic findings were excluded. Patients were monthly followed up after completion of the first 5-day course of HBOT.

2.2. SARS-CoV-2 screening

Since the local COVID-19 outbreak, SARS-CoV-2 was screened for all CRAO patients receiving HBOT. This practice aimed to avoid SARS-CoV-2's human-to-human transmission from asymptomatic viral carriers to others entering the same HBOT multi-place chamber simultaneously[9]. Patients could either provide oropharyngeal saliva samples if they were capable of performing the rinsing maneuver[10-12], or nasopharyngeal and deep throat swabs could be taken by our registered nurses[13-15]. Respiratory tract samples were tested for SARS-CoV-2 by the validated Xpert Xpress SARS-CoV-2 assay[16-19].

2.3. Ethical consideration

This study was approved by the Hospital Authority Hong Kong East Cluster Research Ethics Committee with the reference number HKECREC-2020-116.

2.4. Statistical analysis

Statistical analyses were calculated with SPSS version 25 (IBM SPSS Statistics for Windows, IBM Corporation, Armonk, NY), normal distributions of data were tested before choosing the appropriate parametric or non-parametric statistical tests. Correlation analysis was done on SARS-CoV-2 positivity and CRAO, gender, age, and across the 2 groups of respiratory tract samples.

3. Results

A total of 15 CRAO patients (7 males, 8 females) were identified from the retrospective review with a mean age of 72.1-year-old (range 45-88 years). No patient got a COVID-19 infection before the onset of CRAO. Among the 15 patients, oropharyngeal saliva samples were tested from 10 patients, whereas 5 patients were tested by nasopharyngeal and deep throat swabs. No patients got SARS-CoV-2 RNA detected by a reverse-transcription polymerase chain reaction. There was no loss to follow-up. The follow-up was

the mean of 255.4 d (range 152-341 d), and none got COVID-19 infection. Furthermore, 3 patients had a history of CRAO over the contralateral eye before the index eye's acute CRAO episode. However, none of the remaining 12 patients got subsequent contralateral eye CRAO upon their follow-up.

Among all CRAO cases, 9 (60.0%) got hypertension, 8 (53.3%) got hyperlipidaemia, whereas 4 (26.7%) of them got both hypertension and hyperlipidaemia. Without any COVID-19 positive case present in our CRAO case series, correlation by either parametric or non-parametric statistical tests on COVID-19 and CRAO or different types of respiratory tract samples were not established.

4. Discussion

We searched *via* PubMed, Medline, EMBASE, Scopus, Cochrane Library, and Google Scholar with the search terms ["Retinal Artery Occlusion" OR "CRAO"] AND ["coronavirus" OR "COVID"] but only found few case reports[2-4]. Our study is a CRAO case series reporting on its prevalence of SARS-CoV-2.

Following our HORA study group's first and second report[7,8], this retrospective review of data serves as the HORA study report No. 3. Despite a negative result, HORA 3 is important to address the rising concern of CRAO in COVID-19 patients. Hypertension, hyperlipidaemia, coronary artery diseases, smoking, *etc.* are all well known metabolic risk factors for CRAO[5]. By reviewing other cases concerning COVID-19 and CRAO, it was not difficult to discover these middle-aged patients all had the risk factor of hypertension[2-4]. It could just be a coincidence that some studies reported CRAO patients with COVID-19 infection, and COVID-19-related thromboembolic tendency is not real etiology.

Given the weak correlation between COVID-19 and CRAO, practitioners could look to find more literature with concerns about COVID-19-related ocular findings by an ophthalmologist. There were few cases of CRAO as the ocular manifestations of COVID-19[20-23]. The evidence on the correlation of CRAO and COVID-19 is rather weak, despite 9 months of COVID-19 pandemic with a billion infected cases. Our HORA study report No. 3 would add some values to future determinants on the correlation of CRAO with COVID-19.

5. Study strengths and limitations

HORA study was primarily designed to assess the effectiveness of HBOT for acute CRAO in the urban city of Hong Kong, China[7,8]. It receives territory-wide acute CRAO referrals from both the public and private healthcare systems round the clock, even under the local COVID-19 outbreak, serving the local population of >7 million. All patients continued their follow-ups within our study period. With the evolving issue on CRAO and COVID-19, we reviewed our pool of acute CRAO patients. Despite the efforts on

this issue, the incidence of COVID-19 was 0 among our cases, thus further analysis on different correlations with statistical tests was not feasible. Being an important negative result study, HORA 3 supplemented the evidence gap currently available in the literature.

6. Conclusions

In short, we believe some of the presumed COVID-19 related CRAO cases were just coincident with those at risk hypertensive patients amid COVID-19 pandemic. Further investigations are needed, especially over those COVID-19 patients without any metabolic diseases risk factor, to concrete the evidence on the correlation of CRAO with COVID-19.

Conflict of interest statement

The authors report no conflict of interest.

Authors' contributions

S.C.L.A.: Concept and design of study, acquisition of data, drafting the article; C.K.L.K.: Acquisition of data, revising the article for major intelligence.

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