embolism caused by the vascular alterations which were described in the severe forms of COVID-19 infection.

To the best of our knowledge, this is the first time that retinal vascular abnormalities have been described in patients with COVID-19 ARDS intubated in an ICU.

References

Feroze KB & Azevedo AM. (2020). 'Retinopathy Hemoglobinopathies'. in, StatPearls (Treasure Island (FL)).

Marinho PM, Marcos AAA, Romano AC, Nascimento H & Belfort R Jr (2020): Retinal findings in patients with COVID-19. Lancet **395**: 1610.

Mathur G, Ratra D, Bhuibhar SS & Roy R (2015): Clinical outcomes of retinal detachment surgery following cytomegalovirus retinitis in patients on highly active antiretroviral therapy for acquired immune deficiency syndrome. Ocul Immunol Inflamm **23**: 400–404.

Wu P, Duan F, Luo C, Liu Q, Qu X, Liang L & Wu K (2020): Characteristics of ocular findings of patients with Coronavirus disease 2019 (COVID-19) in Hubei Province, China. JAMA Ophthalmol **138**: 575–578.

Received on July 27th, 2020.
Accepted on November 29th, 2020.

Correspondence:
Tomaso Caporossi, MD
Department of NEUROFARBA,
Ophthalmology
University of Florence
Careggi
Via Largo Brambilla 3
50139, Florence
Italy
Fax/Landline: 0039 055 7948595;
00393924469477

Detection of severe acute respiratory syndrome coronavirus 2 in corneas from asymptomatic donors

Stefano Ferrari,[1] Claudia Del Vecchio,[2] Andrea Leonardi,[3] Giuseppe Feltrin,[4] Angeli Christy Yu,[5,6,7] Massimo Busin,[5,6,7] Andrea Crisanti[2] and Diego Ponzin[1]

[1]Fondazione Banca degli Occhi del Veneto, Zelarino-Venice, Italy; [2]Department of Molecular Medicine, University of Padua, Padua, Italy; [3]Department of Neuroscience, Ophthalmology Unit, University of Padua, Padova, Italy; [4]Regional Centre for Transplant Coordination, Padua, Italy; [5]Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, Italy; [6]Department of Ophthalmology, Ospedali Privati Forlì "Villa Igea", Forlì, Italy; [7]Istituto Internazionale per la Ricerca e Formazione in Oftalmologia, Forlì, Italy

doi: 10.1111/aos.14692

Editor,

In response to the coronavirus disease 2019 (COVID-19) pandemic, public health authorities worldwide have released enhanced guidelines for corneal donor screening aimed at reducing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission through corneal transplantation (Busin et al. 2020). These include immediate exclusion of donors with signs and symptoms of COVID-19 and/or suspected close contact with confirmed cases. Prior to the release of any donated tissue for transplantation, the Centro Nazionale Trapianti (Rome, Italy) has required a single negative post-mortem nasopharyngeal SARS-CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) test from all potential donors within 24 hr of death.

Considerable attention to the possible role of corneal transplantation in viral transmission has been drawn from recent evidence including the recovery of SARS-CoV-2 in tears and conjunctiva (Xia et al. 2020), as well as the interaction between SARS-CoV-2 and ACE2 receptor, which in turn is expressed to a limited extent in the cornea and conjunctiva (Hoffmann et al. 2020).

From 20 February to 31 May 2020, the Veneto Eye Bank Foundation has collected 1161 corneas from 588 donors who had neither medical (clinical,

Table 1. Donor characteristics.

Donor* (Age/ Sex)	Cause of death	Post-mortem time	SARS-CoV-2 RT-PCR testing			
			Nasopharyngeal specimen	Laterality	Cornea	Corneal storage medium
1 (52/F)	Lung cancer‡	4 hr 25 min	Positive	Right	Not detected	Not assessed
				Left	Positive	Not assessed
2 (59/M)	Prostate cancer‡	15 hr 55 min	Positive	Right	Not detected	Not assessed
				Left	Not detected	Not assessed
3 (74/F)	Glioblastoma‡	8 hr 40 min	Positive	Right	Not detected	Not detected
				Left	Positive	Positive
4† (41/M)	Lung cancer‡	3 hr 30 min	Negative	Right	Not detected	Not assessed
				Left	Not detected	Not assessed
5 (72/F)	Breast cancer‡	20 hr 20 min	Negative	Right	Not detected	Not detected
				Left	Not detected	Not detected
6 (76/F)	Breast cancer‡	16 hr 10 min	Negative	Right	Not detected	Not detected
				Left	Not detected	Not detected

COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; RT-PCR = reverse-transcriptase polymerase chain reaction.
* All cases had no medical (clinical, laboratory or radiological) evidence of COVID-19 prior to death.
† Donor had a history of close contact with a confirmed COVID-19 case prior to death.
‡ End-stage disease.

laboratory, radiological) evidence nor epidemiological links to COVID-19 cases. Nasopharyngeal samples were collected using liquid-based transport systems (FLOQSwabs, COPAN SpA, Brescia, Italy). Real-time RT-PCR on swabs and corneal specimens was carried out using One Step Real-Time kits (Thermo Fisher Scientific, Waltham, MA, USA), according to the manufacturer's instructions, while viral isolation was performed using VeroE6 cells (https://www.lgcstandards-atcc.org/; ATCC#CRL-1586).

All testing was compliant with the 2013 tenets of the Declaration of Helsinki, and the tissues were used in accordance with the laws of the Centro Nazionale Trapianti. Informed consent for research was obtained from the donors' next-of-kin.

Only three of 588 nasopharyngeal RT-PCR samples (0.5%) tested positive; and from these, corneal specimens of two cases (0.3%) also yielded SARS-CoV-2 RNA. Furthermore, SARS-CoV-2 RNA was also found in the corneal tissue storage medium of a corneal sample that had tested positive, most likely from sloughing of infected cells. Viral-induced cytopathic effects and plaque formation were not documented in cell cultures of any corneal tissue or storage medium specimens that tested positive for SARS-CoV-2 RNA.

During the same period, three donors with negative nasopharyngeal RT-PCR were also tested as controls. From two randomly selected donors, corneal tissues and preservation media were RT-PCR negative for SARS-CoV-2. Additionally, the cornea of one donor with history of close contact with a COVID-19 case tested negative (Table 1).

With several studies demonstrating asymptomatic carriage in a significant percentage of COVID-19 cases (Sutton et al. 2020), the detection of SARS-CoV-2 among asymptomatic donors, who had already fulfilled the enhanced eligibility criteria for tissue donation, supports the use of complete personal protective equipment and scrupulous disinfection protocols during recovery of potentially infective ocular tissues. In areas with a high prevalence of COVID-19, these measures remain essential for protecting the staff and preventing further spread of infection.

As we were unable to isolate viable virus from cell cultures of SARS-CoV-2-positive corneal specimens, the risk of transmission through keratoplasty seems low. In fact, to date, there have been no reported cases of transmission of SARS-CoV-1, Middle East respiratory syndrome coronavirus, or any other coronaviruses through transplantation of ocular tissue. Although the Eye Bank Association of America does not recommend routine SARS-CoV-2 screening, larger-scale studies regarding viral transmissibility are needed to guide decisions on whether SARS-CoV-2-positive corneas could indeed be treated similarly to those obtained from deaths related to influenza virus, which has also been isolated from the cornea and conjunctiva (Creager et al. 2018), but not excluded from tissue donation.

The detection of SARS-CoV-2 RNA in corneas from asymptomatic donors underscores the need for further research to better understand the role that corneal transplantation may play in viral transmission.

REFERENCES

Busin M, Yu AC & Ponzin D (2020): Coping with COVID-19: an Italian perspective on corneal surgery and eye banking in the time of a pandemic and beyond. Ophthalmology **127**: e68–e69.

Creager HM, Kumar A, Zeng H, Maines TR, Tumpey TM & Belser JA (2018): Infection and replication of influenza virus at the ocular surface. J Virol **92**: e02192-17.

Hoffmann M, Kleine-Weber H, Schroeder S et al. (2020): SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell **181**: 271–280.e8.

Sutton D, Fuchs K, D'Alton M & Goffman D (2020): Universal screening for SARS-CoV-2 in women admitted for delivery. N Engl J Med **382**: 2163–2164.

Xia J, Tong J, Liu M, Shen Y & Guo D (2020): Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. J Med Virol **92**: 589–594.

Received on July 27th, 2020.
Accepted on November 4th, 2020.

Correspondence:
Diego Ponzin, MD
Fondazione Banca degli Occhi del Veneto via Paccagnella 11 30174 Zelarino – Venice
Italy
Tel: +39 041 9656400
Fax: +39 041 9656471
Email: diego.ponzin@fbov.it

†These authors contributed equally to this article as first authors.

Bilateral retinal vein occlusion and diabetic retinopathy after COVID-19

Daniela Rego Lorca, Andrea Rouco Fernandez, Maria Jimenez Santos, Federico Saenz-Frances, Barbara Burgos-Blasco and Juan Donate Lopez

Servicio de Oftalmología, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, Spain

doi: 10.1111/aos.14718

Dear Editor,

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, responsible for the coronavirus disease 2019 (COVID-19), has been linked to coagulation abnormalities and a prothrombotic state. Characteristic findings in COVID-19 patients include an increased D-dimer concentration and prolongation of the prothrombin time, which are more common in severe forms of the disease and have been associated with an increased risk of death (Levi et al. 2020).

Diabetes mellitus has also been associated with worse outcomes due to a pre-existing pro-inflammatory state and the downregulation of the angiotensin-converting enzyme 2 (ACE2) (Pal & Bhadada 2020), the SARS-CoV-2 internalization receptor (Liu et al. 2020). Angiotensin-converting enzyme 2 (ACE2) converts angiotensin II to angiotensin 1–7, acting as a vasodilator and a counter regulator of the renin–angiotensin system (Liu et al. 2020). A downregulation of ACE2 during COVID-19 viral infection has been reported, which results in a state of hypertension, inflammation and increased risk of thrombosis, these being more frequent in patients with a previous downregulation of this