Keratitis during post COVID convalescence

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Introduction

- Novel coronavirus disease (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)
- Global pandemic
- First case report of ocular transmission- China
- Limited evidence

Introduction

Ocular manifestations and clinical characteristics of 535 cases of COVID-19 in Wuhan, China: a cross-sectional study

Liwen Chen,† Chaohua Deng,† Xuhui Chen,† Xian Zhang, Bo Chen, Huimin Yu, Yuanjun Qin, Ke Xiao, Hong Zhang and Xufang Sun†

Department of Ophthalmology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

<table>
<thead>
<tr>
<th>Chronic eye diseases – no. (%)</th>
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<tbody>
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<td>Conjunctivitis</td>
<td>30 (5.9%)</td>
<td>3 (11.1%)</td>
<td>0.228</td>
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<tr>
<td>Keratitis</td>
<td>13 (2.6%)</td>
<td>1 (3.7%)</td>
<td>0.520</td>
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<tr>
<td>Xerophthalmia</td>
<td>22 (4.3%)</td>
<td>2 (7.4%)</td>
<td>0.345</td>
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<tr>
<td>Cataract</td>
<td>9 (1.8%)</td>
<td>0</td>
<td>1.000</td>
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<tr>
<td>Glaucoma</td>
<td>4 (0.8%)</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>Macular disease</td>
<td>1 (0.2%)</td>
<td>0</td>
<td>1.000</td>
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<tr>
<td>Diabetic retinopathy</td>
<td>5 (1.0%)</td>
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<tr>
<td>Other retinal disease</td>
<td>3 (0.6%)</td>
<td>0</td>
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<tr>
<td>Optic nerve diseases</td>
<td>1 (0.2%)</td>
<td>0</td>
<td>1.000</td>
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</tbody>
</table>

Data are presented as median (IQR) or as frequencies (n, %). Results are supplemented. In some cases, the data were missing for some patients.
Conjunctivitis

Strategies to limit spread

PPE guidelines

Transplantation

Recovery of donor corneas
• Detected in tears and conjunctival secretions of COVID-19 patients with active conjunctivitis
• Little evidence supporting presence of virus in COVID-19 patients without ocular symptoms
• Human influenza virus and animal coronavirus- capable of transmission through ocular surface
• Further studies to prove the hypothesis
Angiotensin-converting enzyme-2 (ACE2) receptor

Transmembrane protease and serine 2 (TMPRSS2) protease

Dendritic cell-specific intercellular adhesion molecule 3-grabbing nonintegrin (DC-SIGN) and DC-SIGN related proteins (DC-SIGNR or L-SIGN)
Long term sequelae of COVID is not well characterized. Usually multiorgan dysfunction is reported.
Keratitis in post COVID convalescence

Study the clinical and demographic profile of keratitis in patients who presented within 3 months of acute COVID-19 infection.
Spectrum of microbial keratitis post COVID convalescence

- 18 eyes of 16 patients with MK during post COVID convalescence between Sep 2020-Sep 2021
- 14 patients—Unilateral.
- Presentation was 1-93 days post COVID.
Risk Factors for post COVID keratitis

- Diabetes: 4
- Hypertension: 5
- Hospitalized: 9
- Oxygen adm.: 5
- Sys.Steroids: 3

* More than one risk factor in each patient
Microbes identified (n=16)

- Fungus, 7
- Microsporidia, 7
- Herpes zoster, 1
- Pythium, 1
Management (n=16)

- Medical management, 9
- Therapeutic keratoplasty, 5
- TA+BCL, 2

All eyes resolved between 1-6 weeks of follow up.
Case Scenario - Microsporidia keratitis

- 14 year old female
- C/o redness and blurred vision in BE x 1 week
- Not tested for COVID

Mother & sister: COVID +ve one month back

Quarantined together at home
1st visit (09/6/21)

RE 20/20p

LE 20/20p

Microbiology:
RE Corneal Scraping ➔
PCR for Adenovirus and Microsporidia
Diagnosis: RE microsporidial keratoconjunctivitis + anterior uveitis

Plan: Topical Medications

E/D CHLORAMPHENICOL 0.5% QID
E/D CMC 0.5% 2 hourly
E/D FLUROMETHOLONE 0.5% four times

Review: 2 week
<table>
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<th>Number</th>
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<tr>
<td>CD /mm²</td>
<td>1378</td>
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<tr>
<td>AVG um²</td>
<td>726</td>
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<tr>
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<tr>
<td>CV %</td>
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<tr>
<td>Max um²</td>
<td>3101</td>
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<tr>
<td>Min um²</td>
<td>237</td>
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2 weeks (30/6/21)

Visual acuity: BE– 20/20
Case Scenario - Microsporidial Stromal keratitis

- 69y male
- Nashik, Maharashtra
- C/o decreased vision RE x 9 months, LE x 3 months
- Multiple consultations
- Multiple medications – topical/oral antivirals, antibiotics, antifungals, steroids
- Current - RE Chloramphenicol 6td, LE Betaxolol BID
- LE cataract Sx Nov 2020
- HTN x 20 y; DM x 10 y; s/p angioplasty
1st visit – 11/05/21

RE HM +

Large central epithelial defect
whitish anterior stromal infiltrate
fuzzy borders
anterior chamber reaction
1\textsuperscript{st} visit – 11/05/21

Central stromal whitish infiltrates
minimal cellularity and stromal edema
anterior chamber activity
keratic precipitates

Imp: BE Stromal Keratitis + uveitis

Plan: RE Corneal Scraping + Corneal Biopsy + Diagnostic AC tap- negative
Small linearly arranged hyper reflective dots along the keratocytes - stromal microsporidial keratitis
RE Corneal biopsy

- Widened interlamellar spaces
- Interlamellar debris & granularity
RE Corneal biopsy

1% acid fast short, stout organisms

1%AF

100x
History re-visited

- H/o herbal eye drop usage
- H/o dip in river water
- H/o COVID-like illness 2-4 weeks prior to ocular symptoms
S/P 3 weeks TPK RE followed by LE

RE
20/400

LE
20/125
RE Full Corneal Button

- Absent epithelium

LE Full Corneal Button

- Interlamellar cleft and debris - up to mid-stroma

- Interlamellar clefts
- Acid fast rod-like short, stout organisms
Post op 2 months OD

- Epithelial recurrence of microsporidiosis
- Fumagilin topical and systemic preparations ordered
Case Scenario HZO

- 71 years/Male, Karnataka, India
- Redness, swelling, watering and discharge in the left eye for the past 6 days
- No prior Diabetes Mellitus and Hypertension

Treated for COVID 19:
- RT PCR positive for COVID-19 -3 weeks ago
- Had moderate disease
- IV Dexamethasone 8mg thrice a day for 5 days and Remdesivir when he was hospitalized for the same
Clinical Picture unavailable at this visit

• Vision- 20/100
• Lower lid- Severe excoriation
• Conjunctival congestion
• Anterior Segment was quiet
• Referred from Oculoplasty Clinic for possible Conjunctival Swabs- deferred as conjunctivitis was suspected to be secondary to lid margin lesion
First Visit

- **Differential diagnosis**: Herpes Zoster
- **Treatment**:
  - E/D MOXIFLOXACIN 0.5% two hourly
  - E/O CHLORAMPHENICOL 1% BD
  - Cap AMOXICYLLIN+ CLAVULINIC ACID TID
- **Review**: 3 days
1 week

LE: 20/400

Pseudo dendrite lesion on cornea

Left Eye Ophthalmic Zoster Sine Herpes
Treatment modified

Treated in lines of HZO

- Tab ACYCLOVIR 800 mg 5 times a day
- Antibiotic ointment on lid application
- Neuroleptic medications for pain relief
Lid lesion resolved
medial ectropion and punctal scarring

Corneal lesion resolved
faint scarring
Case Scenario Fungal Keratitis
Case 1

29/05/21
24yr male
Student
C/o RE redness, watering, pricking sensation and mild pain from 10 days

COVID positive- 13/05/21
COVID negative- 27/05/21– Discontinued medication from 2days

No systemic illness

Was initially treated as RE conjunctivitis—
E/D MOXIFLOXACIN 6t/day
RE: 20/40; N18

29/05/21
29/05/21
RE: 20/40; N18

Infiltrate with feathery borders
DM folds
Scraping- plenty fungal filaments

E/D NATAMET 5% hourly
E/D ATROPINE 1% TID

Review 1 week
E/D NATAMET 5% 8times/day X3weeks
E/D CMC 0.5% 6times/day
Review 1month
Case Scenario Fungal keratitis

Case 2

19/05/21
56yr male works in private sector
BE redness, pain with headache from 10 days

COVID positive 15 April 2021
Hospitalized for 5 days
COVID negative 5 May 2021

Consulted elsewhere 10 May 2021
Diagnosed BE herpes viral keratitis with secondary bacterial infection
LE TA BCL applied
Tab ACYCLOVIR 400mg 5 times/day
E/D GATIFLOXACIN 0.5% Hourly
E/D HOMATROPINE 2% TID
RE 20/500; <6/60
Stromal infiltrate
Epithelial defect 2.5X4mm
Superficial vascularisation

19/05/21
LE CF CF
Stromal infiltrate
TA+BCL
Superficial vascularisation

Hypopyon
Microbiology

21/05/21 – RE corneal scraping —> Negative

22/05/21 – Significant growth in culture —> Aspergillus niger
Resolving corneal infiltrates
Advice: continue same treatment
Lubricants added
Scarring and vascularisation
Central area of thinning 3X2mm- 40-50%
Poor ocular surface
Hypopyon resolved

TA+BCL insitu
AC shallow
Digitally soft globe
Hypopyon resolved

Plan:
BE tarsorrhaphy+ BE punctal cautery+ LE TA+BCL
Last Follow up: 01/09/21 # 4months

S/P Tarsorrhaphy and Amniotic membrane transplantation
Case scenario - Fungal keratitis

Case 3

- 44 year old gentleman, welder by occupation

- Telangana

- LVPEI- 10/6/2021

- C/o - Painful decrease in vision, redness and watering in the LE since 15 days

  - H/o fall of some foreign material into the eye while at work about 15-20 days back
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<td>NA (Still on treatment at home)</td>
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<td>Hospital admission</td>
<td>Yes, 5 days</td>
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<tr>
<td>Oxygen therapy</td>
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<tr>
<td>Steroid treatment</td>
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<tr>
<td>Any other systemic illness</td>
<td>Pneumonitis, HTN (2 years, on treatment)</td>
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</table>
• VA- CFCF
• Ring shaped white infiltrate of about 7*7 mm
• Corneal scrapings performed—TA applied
• Micro-septate hyaline fungal filaments

• Oral ketoconazole 200mg Tab BD, eyedrop natamycin 5% hourly, E/d Atropine TID

100X, oil
Gram stain

LV Prasad Eye Institute
• 2 weeks

• Central corneal perforation with iris plugging

• Planned for Therapeutic Penetrating keratoplasty

• Tenon’s patch graft performed with central tarsorrphy, eye left to heal by adherent leucoma formation
• Globe tectonically stable
• No evidence of infection
• B scan normal
• Planned for PKP+ Cataract surgery
Case scenario 4

- 48 year old gentleman, farmer by occupation
- Nashik, Maharashtra, India
- LVPEI- 17/6/2021
- C/o - Painful decrease in vision, redness and watering in the LE since 10 days
  - H/o injury to the left eye 10 days back
  - On treatment with eyedrop natamycin 5%, voriconazole 1% hourly, moxifloxacin 0.5% 4times, oral ketoconazole 200mg Tab 2 times/day
# Covid related history

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<tr>
<td>Any other systemic illness</td>
<td>NA</td>
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</table>
- One eyed
- VA- HM
- Large >8mm central corneal infiltrate with endoexudates and thinning in the periphery
- Corneal scrapings performed—GPC, GNB
- Fortified vancomycin 5%, ciprofloxacin 0.3% eyedrops hourly
Worsening on treatment
• Culture grew GPC (Staphylococcus Hominis and Fusarium Solani)

• Hence also started on topical natamycin 5%

• In view of large size, worsening again after 2 days, planned for ThPK
• After 15 days, topical steroids were added under antibiotic and antifungal cover

• Graft failing

• Hence planned for a PKP
- POP 1 week
- VA 20/400
- Clear graft, GHJ well apposed
Case scenario 5

- 39 year old gentleman
- Madhya Pradesh, India
- LVPEI- 22/6/2021
- C/o - Sudden loss of vision, watering and redness in right eye since 1.5 months
  - History of fall of some dust particle in the right eye 1.5 months ago
  - Currently using natamycin 5% eyedrops hourly, ofloxacin eyedrops 2 hourly, atropine eye drops TID, and timolol maleate BD
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<tr>
<td>Any other systemic illness</td>
<td>Type 2 DM</td>
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</table>
• VA RE- HM+

• RE – Central large 8*8 corneal infiltrate with corneal melt and perforation, flat AC, B scan shows choroidals

• Planned for ThPk, back button scraping - Septate hyaline filament, Aspergilus flavus grown

22.6.2021
## Summary of severe fungal keratitis

<table>
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<tr>
<th>Case</th>
<th>Date</th>
<th>History</th>
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<tr>
<td>2-10.6.2021</td>
<td>25.5.2021</td>
<td>Covid positive</td>
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<td></td>
<td>Steroid treatment: Record not available</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any other systemic illness: Pneumonitis, HTN (2 years, on treatment)</td>
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</table>

### Case 2 - 10.6.2021
- 44yr, fall of FB in LE since 15 days
- Fungus on smear, tenon patch graft

### Case 3 - 17.6.2021
- 48yr, Injury to LE since 10 days
- Mixed infection, ThPk f/b PKP done

### Case 4 - 22.6.2021
- 39yr, fall of FB in RE since 1.5 months
- Fungus grown, ThPK done

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<tr>
<td>Any other systemic illness</td>
<td>Type 2 DM</td>
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</table>
Case Scenario Pythium

16/6/21
43yr male
Agricultural worker
C/o LE redness, watering, pain from 1 week

COVID positive- 06/05/21
COVID negative- 24/05/21– Home quarantine

No systemic illness

Was initially treated with:
E/D MOXIFLOXACIN BD
E/D TOBRAMYCIN BD
E/D HOMATROPINE TID
E/D NATAMYCIN TID
First visit- 16/6/21

LE- 20/60p; N12p
RE WNL
20/2; N6

LE scraping- Negative

E/D VANCOMYCIN 5%- two hourly
E/D CIPROFLOXACIN 0.3%- Two hourly
E/D ATROPINE 1%- TID
E/D LINEZOLID 0.2%- Hourly
E/O AZITHROMYCIN 1%-%- TID
E/D ATROPINE 1%- TID
Tab AZITHROMYCIN 500mg- OD

VA- 20/60p; N12p

Review 1 week

1 week- 23/6/21
10% KOH CFW 40X
E/D LINEZOLID 0.2%- Hourly
E/O AZITHROMYCIN 1%- TID
E/D ATROPINE 1%- TID
Tab AZITHROMYCIN 500mg- OD

Review 1week

VA- 20/60→
20/30 with pin hole

2 weeks- 30/6/21
Case Scenario Mucor keratitis

73,M
Chatrapati Shivaji Nagar, Maharashtra India

LE 2 weeks H/O of redness and pain

COVID positive in April 2021
Admitted for 8 days
Oxygen –Yes
Steroids- Yes

Undergone cataract surgery on 20 June 2021 in LE
RE lost no details available

Imp: Side port infection with endophthalmitis after cataract surgery
Case Scenario: Mucor keratitis
Mucor *spp.* from corneal scraping
Case scenario Neurotrophic keratitis

52 yr
Male
Farmer
Latur, Maharashtra

C/O LE decreased vision, unable to move eye to left side from 3months
Treated for Mucormycosis elsewhere
Referred to the institute for LE non healing ulcer

H/O pneumonia 3months back; steroids and oxygen supplementation
Denies COVID positive history
H/O uncontrolled sugars then — continuing OHA at present

Bilateral partial maxillectomy
Nasal debridement 3times- negative reports
<table>
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<th>Date/Details</th>
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<td>Pneumonia</td>
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<td>Hospitalization</td>
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<td>Presented to hospital</td>
<td>20/08/21</td>
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<td>Uncontrolled blood sugars</td>
<td>On treatment- Oral Hypoglycemics</td>
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<td>H/o Steroids and oxygen administration</td>
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<td>After 15 days of admission</td>
<td>C/O BE decreased vision and inability to move left eye outwards</td>
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<tr>
<td>Sinus debridement</td>
<td>18/05/21 and 28/05/21</td>
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<tr>
<td>Bilateral partial maxillectomy</td>
<td>05/06/21</td>
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<tr>
<td>LE TRAMB</td>
<td>7 doses- 12/06/21 to 18/06/21</td>
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<tr>
<td>Tab Posaconazole</td>
<td>08/07/21 till date</td>
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VA- 20/600
Abduction limitation

LE neurotrophic keratitis
With sixth nerve palsy

Left eye-
E/D Chloramphenicol 0.5% 6times/day
Lubricants
Could there be a neurotrophic association?

Corneal confocal microscopy identifies corneal nerve fibre loss and increased dendritic cells in patients with long COVID


8 out of 18 eyes had decreased corneal sensations in our series
Conclusions

1. Long COVID may significantly affect activities of daily living

2. Causal association of keratitis with COVID-19 infection cannot be proven, only temporal association is noteworthy.

3. Decreased corneal sensations and neurologic alterations may affect presentation and clinical course of keratitis.

4. Altered host immune responses could be implicated in the pathogenesis of the keratitis.
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Dr Raksheeth Nathan
Dr Vishy Shrivastava
Dr Uma Thigale
Dr Mugundhan
Dr Mariya Doctor