



## Early trends of secondary acquired nasolacrimal duct obstruction in COVID-19 associated sino-orbital mucormycosis: SALDO update study (SUP) – Paper IV

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### ARTICLE INFO

#### Keywords:

Secondary acquired lacrimal duct obstruction  
SALDO  
Rhino-orbital-cerebral mucormycosis  
ROCM  
Lacrimal

### ABSTRACT

**Purpose:** To study the emerging trend of development of secondary acquired nasolacrimal duct obstruction (SALDO) in the cases treated for rhino-orbital-cerebral mucormycosis (ROCM).

**Observations:** Prospective, interventional case series of five patients who developed SALDO post-surgical and medical management of ROCM. The mean age was 45.4 years (range: 40–62 years), all five being males. Right lacrimal drainage pathways was involved slightly more than the left (right:left = 3:2). Epiphora and discharge were the main presenting features. All five patients were treated with extensive debridement of the nose, sinuses, orbit and cerebral involvement as needed followed by medical management for ROCM. CT- Dacryocystography for all 5 patients showed obstruction at the lower end of the nasolacrimal duct. The patients underwent external dacryocystorhinostomy with mitomycin-C with or without intubation with good anatomical and functional outcomes at 6 months follow-up.

**Conclusions and importance:** The present series highlights the possible etiology of development of SALDO in cases treated for ROCM, its management and discusses the role of Computed Tomography Dacryocystography (CT-DCG) in understanding the pathophysiology of the development of SALDO along with delineating the spatial relationship of the lacrimal drainage system with the surrounding structures.

### 1. Introduction

Rhino-orbital-cerebral mucormycosis (ROCM) presented in epidemic proportions during the COVID-19 era. Several factors attributed to this surge include underlying uncontrolled diabetes mellitus, injudicious use of steroids, decreased immune response, diabetic ketoacidosis, hypoxic milieu, and prolonged hospitalization with or without ventilators.<sup>1,2</sup> The ROCM treatment consisted of surgical debulking of all the affected tissues followed by long-term medical management with systemic anti-fungal medications.<sup>3–5</sup> Surgical debulking may involve but is not restricted to the sinuses, maxilla, pterygopalatine fossa, infratemporal fossa, orbit, and other extracranial sites.<sup>3</sup> In most cases, the nasal and sinus debridement was performed using Denker's approach, where the nasolacrimal duct was deliberately cut as a part of the surgery, a possible cause for iatrogenic secondary acquired lacrimal duct obstruction (SALDO).<sup>1</sup> Nevertheless, the extensive involvement of the nose, sinus, and orbit with mucormycosis can initiate inflammation and fibrosis, or

cause a direct invasion of the nasolacrimal ducts or more commonly, can be secondary to the iatrogenic trauma during debridement. The current report presents a series of five cases who, after complete surgical and medical treatment of ROCM, presented with complaints of epiphora. Patient consent and institutional Ethics Committee approval was obtained, and the study adhered to the tenets of the Declaration of Helsinki.

### 2. Case 1

A 62-year-old male presented to the clinic with complaints of epiphora in the right eye of two months duration. Two years ago, there was a history of sino-nasal debridement and partial right-sided maxillectomy for extensive rhino-orbital mucormycosis post-COVID-19 infection (Fig. 1, Panel A & B). The surgical and medical management of mucormycosis was completed, following which the infection resolved. The anterior and posterior segment examinations were within normal

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<https://doi.org/10.1016/j.ajoc.2024.102024>

Received 13 December 2023; Received in revised form 2 February 2024; Accepted 14 February 2024

Available online 22 February 2024

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limits, with the best corrected visual acuity being 20/20, N6 in both eyes. Lacrimal drainage irrigation showed regurgitation of mucoid fluid from the opposite punctum on the right side and was freely patent on the left side. Nasal endoscopy demonstrated expansion of nasal cavity with loss of septum and lacrimal landmarks (Fig. 1, Panel C). Lacrimal probing revealed a hard stop at the distal end of NLD. Computed tomography dacryocystography (CT-DCG) scans were suggestive of disruption at the end of the bony NLD with no gross malposition of the lacrimal sac (Fig. 1, Panel D-F). The patient underwent external dacryocystorhinostomy with mitomycin-C and bicanalicular intubation (Fig. 1, Panel G). A small part of the posterior sac flap was sent for histopathology and microbiology examination and was negative for mucor. The post-operative period was uneventful, and the stent was extubated at one-month post-surgery, and the patient was doing anatomically and functionally well at the six-month follow-up (Fig. 1, Panel H).

### 3. Case 2

A 41-year-old male patient presented with excessive discharge in the right eye of six weeks duration. He had a history of resolved COVID-19 infection complicated with rhino-orbito-cerebral mucormycosis 18 months ago. Extensive orbito-sino-nasal debridement and cerebellar abscess drainage was performed followed by intensive medical therapy for mucormycosis (Fig. 2, Panel A). During infection, he developed right sided fifth and sixth cranial nerve paresis leading to neurotrophic ulcer causing diminished visual acuity. The left eye was unremarkable. The right lacrimal system examination showed regurgitation on pressure over the lacrimal sac (ROPLAS), while the irrigation was freely patent on the left side. Endoscopic examination showed the absence of landmarks on the lateral wall of the nose with absent turbinates and the membranous part of the nasolacrimal duct. The septum was intact (Fig. 2, Panel B). Lacrimal probing showed bony obstruction at the distal end of NLD. CT-DCG scans revealed obstruction at the distal end of the bony NLD (Fig. 2, Panel C,D). External dacryocystorhinostomy with mitomycin -C was performed without intubation due to the presence of an active corneal ulcer. A para-median tarsorrhaphy for corneal protection and to aid in ulcer healing was performed. The sac flap did not show any microbiological growth. Routine post-operative medications were given along with treatment of corneal ulcer. At six months follow-up, the patient was doing well anatomically and functionally, and the corneal ulcer was healing.

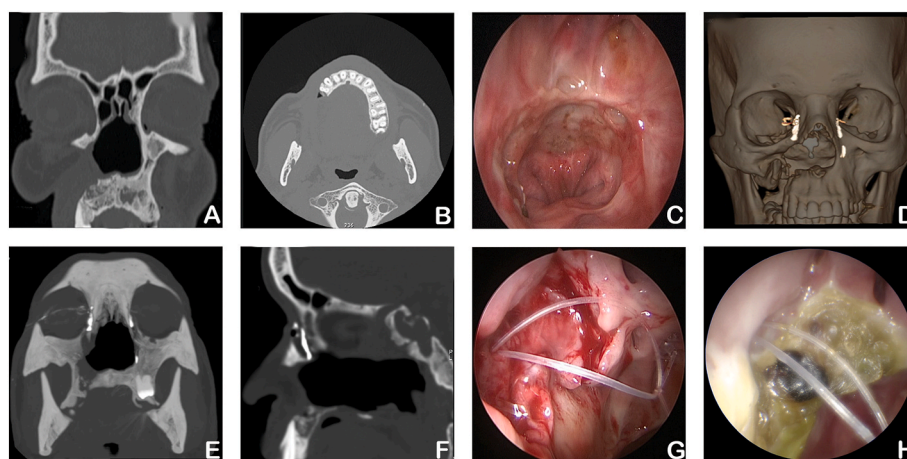
Table 1 lists the details of the five cases.

### 4. Discussion

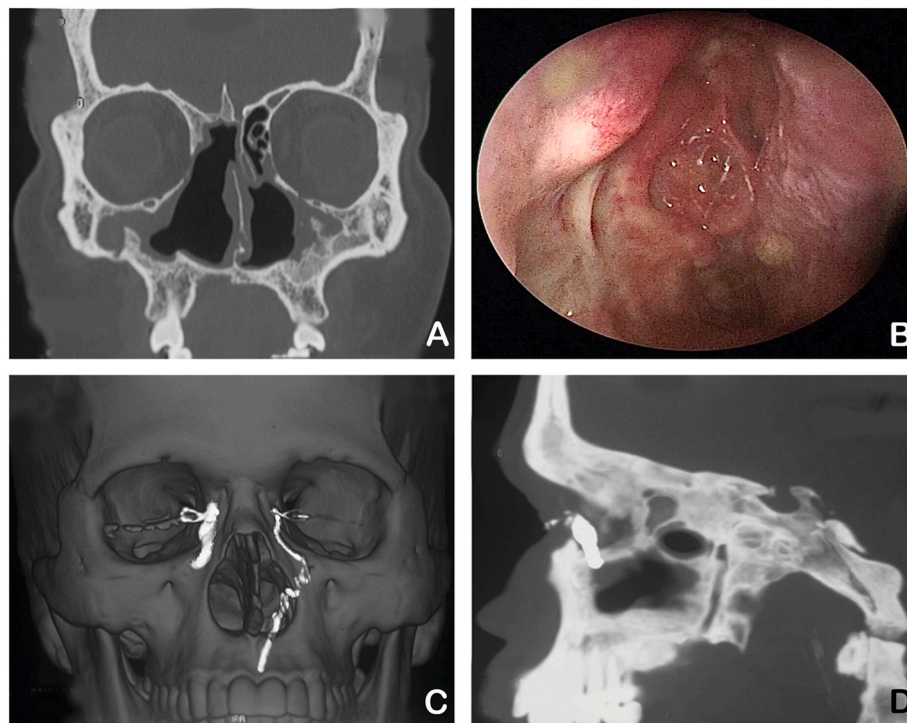
ROCM occurs after the colonization of the nasal and sinus mucosa by the spores, which then subsequently spreads to the adjoining structures, orbit, cavernous sinus, and the brain. Angioinvasion of the fungal hyphae leads to thrombosis and tissue necrosis.<sup>5</sup> Complete debridement of the necrotic tissue is essential to limit the spread of the infection, followed by extensive and long-term medical anti-fungal therapy.

Several surgical procedures are implicated in iatrogenic trauma to the nasolacrimal duct and include uncinectomy, medial maxillectomy, maxillary osteotomy, frontal sinusotomy, rhinoplasty, and inferior turbinatectomy.<sup>6</sup> Most ROCM cases were managed by endoscopic debridement (Denker's approach) of the affected tissue with medical management.<sup>7</sup> Although endoscopic modified medial maxillectomy and the pre-lacrimal approaches help preserve the nasolacrimal duct, the extensive involvement of the sinonasal tissues in ROCM may not favor these procedures.<sup>7,8</sup> The endoscopic Denker's approach involves the removal of the entire medial wall of the maxillary sinus along with the inferior turbinate and transection of the nasolacrimal duct.<sup>7</sup> It allows complete exposure of the anterior, inferior, and lateral recesses of the maxillary sinus. It also facilitates direct and straight entry to the pterygopalatine and infratemporal fossae, helping debulk most necrotic tissue.<sup>9</sup> It is considered a superior alternative approach where access to the pterygopalatine and infratemporal fossae is required. Interestingly, all the cases in the present series had an obstruction at the junction of the bony and membranous part of the NLD, which is where the transection is made. This requires further exploration before we arrive at a conclusion. McCormick et al., in their series of patients undergoing modified endoscopic Denker's approach, reported four cases (6.9%) with post-operative epiphora at an average follow-up of 30 months, requiring additional procedures.<sup>10</sup> Stavrakas et al. used the modified Denker's approach in 22 patients with extensive sino-nasal pathology and reported only transient epiphora post-operatively, which resolved.<sup>9</sup>

Apart from the surgical technique, the direct invasion of the lacrimal drainage pathways with the fungal infection could be a possible reason for the acquired lacrimal duct obstruction. It is postulated that the infection from the nasal cavity spreads via the nasolacrimal duct to directly invade the lacrimal sac and then enter the orbit.<sup>11</sup> There is a single case report of a localized lacrimal sac mucormycosis in an immunocompetent patient treated with surgery followed by medical management using Amphotericin-B. It did not affect any adjacent structure until the last follow-up.<sup>12</sup> A 9-year-old immunocompetent girl developed epiphora, swelling, and discharge, which grew *Saksenaea*



**Fig. 1.** CT scans, bone windows, coronal cuts, demonstrating absence of turbinates and septum in the nasal cavity with clear sinus and well formed orbital bony landmarks and lacrimal sac fossa (Panel A) and partial loss of right-sided maxilla with upper teeth (Panel B). Endoscopic view of nasal cavity pre-operative showing loss of turbinates, septum and membranous NLD (Panel C). CT-DCG scans, 3DR, maximum intensity projection sequence and parasagittal cuts, demonstrating the blockage at the distal end of bony NLD (Panel D-F). Endoscopic view of the post-operative nasal and sac flap anastomosis with the bicanalicular stent in-situ (Panel G) and the post-operative result after 6 weeks showing a well formed ostium with bicanalicular stent in place and minimal crusts (Panel H).



**Fig. 2.** CT scans, orbits, bone windows, coronal cuts, demonstrating the extensive sino-nasal deridement for mucormycosis with absent turbinates (Panel A). Endoscopic view showing absence of the turbinates and membranous NLD on the right side (Panel B). CT DCG, 3DR and para-sagittal cuts reveals obstruction to the flow of dye at the distal end of bony NLD with a dilated lacrimal sac (Panel C&D).

**Table 1**

Details of the five cases presenting with epiphora following treatment for ROCM.

Age	Sex	Eye involved	Duration of Epiphora (months)	Duration since ROCM infection (months)	CT-DCG	Surgery performed	Anatomical and Functional Outcomes	Follow-up duration (months)
62	M	RE	2	24	Obstruction at end of bony NLD with no gross mal-position of the sac	External DCR + MMC + intubation	Irrigation patent, FDDT – no delay	6
41	M	RE	1.5	18	Obstruction at end of bony NLD with mild dilatation of the sac and proximal NLD	External DCR + MMC	Irrigation patent, FDDT – no delay	6
41	M	RE	2	6	Obstruction at the distal half of nasolacrimal duct with lacrimal sac dilatation	External DCR + MMC + intubation	Irrigation patent, FDDT – no delay	6
43	M	LE	2	2	Obstruction at the distal half of NLD without a dilated lacrimal sac	External DCR + MMC + intubation	Irrigation patent, FDDT – no delay	6
40	M	LE	6	8	Obstruction at distal part of nasolacrimal duct with no lacrimal sac dilatation	External DCR + MMC + intubation	Irrigation patent, FDDT – no delay	6

spp. of order Mucorales. The infection rapidly spread to involve the orbit forming an orbital abscess. The infection resolved after prolonged therapy with Posaconazole.<sup>13,14</sup> Concomitant aspergillus and mucormycosis infection causing acute dacryocystitis and spreading to the orbit was reported and needed extensive debridement followed by medical management with liposomal Amphotericin-B and voriconazole.<sup>15</sup>

The SARS-CoV-19 virus has been postulated to pass through between the nasal cavity and ocular surface, transmitting the virus to both anatomical regions and thus, increasing the infectivity.<sup>16,17</sup> Does the nasolacrimal duct become more susceptible to infections due to direct invasion? Does it cause increased inflammation of the nasolacrimal duct epithelium making it more susceptible? These mechanisms are speculative at present and further studies are required to establish the causative mechanisms.

External dacryocystorhinostomy was preferred in these cases as the endoscopic anatomical landmarks were difficult to identify. The surgical procedure for external DCR remained unchanged except minimal

increase in the bone thickness and the understanding of the surrounding identifying anatomical landmarks.

In summary, SALDO is one of the emerging sequelae of post-COVID Rhino-Orbital mucormycosis, which can account for further morbidity in patients who survived. All the patients in the present series were presented with epiphora following extensive endoscopic surgical debridement. CT DCG was a useful tool to identify the exact site of obstruction in these patients and to assess the integrity of surrounding bones for creation of a bony ostium. External dacryocystorhinostomy has excellent outcomes in the clinical scenario of post-mucormycosis SALDO. A prospective study with a larger sample size would help decipher the mechanisms in greater details.

**5. Patient consent**

Consent to publish this case report has been obtained from the patient(s) in writing. This report does not contain any personal identifying

information.

### Funding

Hyderabad Eye Research Foundation.

### Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

### CRedit authorship contribution statement

**Nandini Bothra:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Yamini Priya:** Methodology, Investigation, Conceptualization. **D. Rincy:** Data curation. **Mohammad Javed Ali:** Writing – review & editing, Supervision, Conceptualization.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors have no conflict of interest.

### Acknowledgements

None.

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