Dacryolithiasis: A Review

Kapil Mishra, M.D.*, Karen Y. Hu, B.S.*, Saurabh Kamal, M.S.†, Aleza Andron, M.D.‡, Robert C. Della Rocca, M.D., F.A.C.S.*‡§, Mohammad Javed Ali, M.D., F.R.C.S.\(\mi\), and Akshay Gopinathan Nair, D.N.B.‡¶\(\mi\)

*Icahn School of Medicine at Mount Sinai, New York, New York, U.S.A.; †ProAdnexa Oculoplasty Solutions, Faridabad, Haryana, India; ‡Ophthalmic Plastic, Orbital, and Reconstructive Surgery, New York Eye & Ear Infirmary of Mount Sinai, New York, New York, U.S.A.; §Department of Ophthalmology, Mount Sinai West Hospital & Mount Sinai St. Luke's Hospital, New York, New York, U.S.A.; ¶Institute of Dacryology, LV Prasad Eye Institute, Hyderabad, India; ¶Ophthalmic Plastic Surgery & Ocular Oncology Services, Advanced Eye Hospital & Institute, Navi Mumbai, Maharashtra, India; and #Department of Ophthalmology, Lokmanya Tilak Municipal Medical College & General Hospital, Sion, Mumbai, India.

Purpose: To review and summarize the clinical features, presentations, diagnostic modalities and management of dacryolithiasis.

Methods: A comprehensive PubMed search of all English articles on dacryolithiasis was reviewed. Although this review primarily relied on articles written in English, non-English-language articles that had abstracts translated into English were also reviewed. Data reviewed included epidemiology, pathogenesis, appearance and composition, clinical features, presentations, diagnostic modalities, management of dacryolithiasis and the implications of incidental dacryoliths found during lacrimal surgery.

Results: Although an unknown proportion of dacryolithiasis cases may remain asymptomatic; epiphora, acute and/or recurrent dacryocystitis, punctal discharge, and localized swelling are the most common presenting features of dacryolithiasis. It may also present as partial nasolacrimal duct obstruction. Dacryoliths exhibit a variety in external appearances. While some minimally invasive techniques for the removal of dacryoliths have been described, dacryocystorhinostomy with removal of the dacryoliths remain the most effective treatment in cases of symptomatic dacryolithiasis. The expression and production of certain proteins and peptides, namely those of the trifoil factor family play a significant role in the pathogenesis of dacryoliths.

Conclusions: The management of dacryolithiasis is driven by the goal of resolution of secondary obstruction and/or inflammation. Although a large number of dacryoliths are incidentally found during dacryocystorhinostomy, certain clinical features such as unilateral sac distension, particularly those with a palpable firm medial canthal mass, might lead one to have a high index of suspicion. It remains unclear if the incidental finding of a dacryolith during a dacryocystorhinostomy has a favorable prognostic value.

(Ophthal Plast Reconstr Surg 2016;XX:00-00)

Accepted for publication June 24, 2016.

The authors have no financial or conflicts of interest to disclose.

Address correspondence and reprint requests to Akshay Gopinathan Nair, D.N.B., Department of Ophthalmic Plastic Surgery and Ocular Oncology, Advanced Eye Hospital & Institute, 30 The Affaires, Sector 17, Sanpada, Navi Mumbai 400 705, India. E-mail: akshaygn@gmail.com

DOI: 10.1097/IOP.0000000000000769

First described by Cesoin in 1670, dacryoliths are concretions formed in the lacrimal sac and duct. These concretions may be found throughout the lacrimal drainage system and more rarely in the lacrimal gland and associated ductules. Those found in the lacrimal drainage system can be generalized into 2 categories: infectious canalicular stones and noninfectious lacrimal sac/duct stones. Noninfectious stones in the lacrimal drainage system have been called several names, including "dacryoliths," "canaliculith," and "mucoliths." More recently, Perry et al. have proposed renaming noninfectious dacryoliths to "mucopeptide concretions" as more is becoming known about their composition and structure.

Canalicular concretions have historically been investigated more than lacrimal sac concretions due to their association with canaliculitis, most commonly caused by Actinomyces, a Gram-positive rod-shaped organism and also because of the accessibility of the canaliculus to being examined. 11-13 For the sake of brevity, canalicular infections, concretions and canaliculitis will not be included in the discussion in this review article. Symptoms of canaliculitis commonly reported in the literature include epiphora, chronic conjunctivitis, swelling over the medial canthus, a "pouted" or everted punctum, and purulent discharge. 11,14,15 Although concretions in the lacrimal sac and duct can produce similar symptoms, especially when they cause obstruction, many are found incidentally during dacryocystorhinostomy (DCR) and thus have not been as fully explored. Many recent studies have better categorized the composition, theories on pathophysiology, and their relation to DCR and prognostic factors. Therefore, in this communication, the authors present a review of literature on such latest advances.

EPIDEMIOLOGY

Lacrimal obstruction is a common problem, constituting 3% of all ophthalmology clinic visits. ¹⁶ The overall incidence of dacryoliths is difficult to assess as studies thus far have only examined patients with symptoms requiring the need for DCR. ¹⁷ In fact, the presence of a dacryolith cannot be definitively concluded unless a DCR with direct visualization is done. Even certain imaging modalities, such as a dacryocystogram or CT, can only identify a mass but not necessarily characterize it. ¹⁷ There are a few reports when a dacryolith was diagnosed without DCR, however these few instances were discovered after the patient passed an intact stone, sometimes in the shape of the lacrimal duct and sac, although these are quite rare and unlikely to add to incidence

rates. ^{18,19} These confounding factors make it difficult to assess the true incidence of dacryolithiasis in the general population.

The reported incidence of dacryoliths in all DCR procedures ranges from 5.7% to 18%. 59,17,20-24 One study found dacryoliths only in primary acquired nasolacrimal duct obstruction (PANDO), but not in any other indication for DCR. 17 One report found a greater incidence of dacryoliths in patients with prior trauma. 25 Marthin et al. 26 published their findings tabulated from a retrospective review of all pathology reports from 1910 to 1999 that described any lesion of the lacrimal drainage system in the files of the Eye Pathology Institute, University of Copenhagen. From a total of 643 lesions that were collected, dacryocystitis was the most frequent lesion, constituting 508 cases (79%) and the second most common lesion was dacryolithiasis (62 cases; 7.9%). However, this reflects the percentage of dacryolithiasis from only the cases in which a specimen was sent and not all lacrimal surgeries.

A female preponderance for dacryoliths has also been challenged in recent studies. Although most studies reflect that females form a majority among patients undergoing DCR for PANDO, 9,17,21,22,24,27 it is less clear if these studies produce more women than men with dacryoliths due to selection bias. 27 When comparing patients with dacryoliths to those without, researchers found no statistical difference in female incidences. 24,27 Paulsen et al. 28 found a near equal gender distribution (male 11:9), while Yazici et al. 17 found more women overall with PANDO, but only 33% of these women had dacryoliths. Further analysis showed that the male gender was in fact more statistically likely to have dacryoliths (p=0.004). Linberg's 29 response to these results pointed out that conflicting gender ratios for PANDO and dacryoliths might weaken their association.

Lee-Wing and Ashenhurst³⁰ reported that in their clinicopathologic analysis of 202 lacrimal sac biopsies that were obtained during 202 DCR procedures in 166 patients, dacryoliths were found in 8 patients (5%), and the mean age of this group was 52.5 years (range, 22–73 years). In the series by Yazici et al., 17 the average age of patients with dacryoliths at DCR was 59.3 years; among those without calculi, the average age was 64.9 years. Andreou and Rose²⁷ reported that the mean age of patients with dacryolithiasis in their study was comparable with the mean age of patients of nasolacrimal duct obstruction (NLDO) without dacryolithiasis. While currently available literature indicates that the average patient with dacryolithiasis is most commonly in the sixth decade of life, there does not appear to be any statistically significant difference between the average age of patients with and without dacryoliths at lacrimal surgery.9 Therefore, there is not enough evidence to substantiate the previously held belief that dacryoliths tend to occur in younger patients.31

Smoking has long been associated with dacryoliths, first reported by Jones²² in 1965 when he found 70% of patients with dacryoliths to be moderate to heavy smokers. It is unclear if this high association is a reflection of all patients with nasolacrimal obstruction, or more simply a prevalence of smoking in the population. Repp et al. found that in their cohort, 9 of 21 (42.9%) patients with dacryoliths had a history of smoking. It is important to note that the sample size here was very small and the numbers were not compared with a control group undergoing DCR. One study did find a higher prevalence for smoking in a dacryolith group compared with a group without dacryoliths undergoing DCR, although it did not reach significance (25% to 8%; p = 0.09). A possible limitation may be that the duration or amount of smoking was not quantified. While it is difficult to determine the association between smoking and dacryoliths, Repp et al.9 astutely pointed out that tear film composition may be a link between the 2, as lower tear lysozyme level was found in both chronic smokers and in patients with dacryoliths. 32,33

PATHOGENESIS

Although more is becoming known about the composition of dacryoliths, the pathogenesis of its formation is still unclear. In response to Yazici et al.'s¹⁷ findings showing a greater male preponderance in dacryoliths despite a higher female incidence overall in PANDO, Linberg²⁹ called to question any causal relationship between dacryoliths and PANDO. Linberg²⁹ pointed out the greater frequency in association between dacryoliths and partial or incomplete closure of the lacrimal passage compared with complete closure likely discounts debris accumulation with subsequent dacryolith formation as a simple cause-effect mechanism.^{22,28} Indeed, the unlikelihood of complete closure as the main cause of dacryoliths is evidenced by instances of spontaneous stone passage. ^{18,19}

While a relationship between nasolacrimal obstruction and dacryolith pathogenesis cannot be clearly defined, there are many findings that suggest some form of obstruction has a role in formation. Several studies have shown an increased incidence of partial obstruction in patients with dacryoliths compared with those without dacryoliths. ^{17,20,22,28} Yazici et al. ¹⁷ and Paulsen et al. ²⁸ found that dacryoliths were found only in patients with PANDO. Paulsen et al.³⁴ described the pathophysiology of PANDO from findings of several studies,35-37 saying that descending inflammation from the eye or ascending inflammation from the nose leads to fibrous remodeling of the helical arrangement of connective tissue fibers, loss of specialized blood vessels in the subepithelial cavernous body, and epithelial metaplasia of the mucous membrane in a confined area. This leads to a nonfunctioning segment in the lacrimal passage that is clinically seen on irrigating and does not transport tear fluid. The newly formed epithelial metaplasia leads to a slow loss of goblet cells and columnar epithelial cells as well as formation of a noncornifying squamous epithelium, leading to an alteration in mucin and trefoil factor family (TFF) peptide production. Trefoil factor family comprises a group of small peptides which are highly expressed in tissues containing mucus-producing cells and are crucial for epithelial restitution and may work via other pathways than the conventional factors involved in mucosal protection and repair.³⁸

A pertinent outcome of immunohistochemistry studies in dacryolithiasis is the strong staining of TFF peptides implying upregulation of TFF peptides in dacryolithiasis.²⁸ Real-time polymerase chain reaction and immunohistochemistry showed expression and production of all three TFF peptides, whereas in the healthy situation only TFF1 and TFF3 were expressed and produced, indicating that induction of TFF2 occurs in dacryolithiasis. Further analysis by real-time polymerase chain reaction revealed increased expression levels of TFF1 and TFF3.²⁸ Therefore, TFF2 appears to be induced in dacryolithiasis, whereas TFF1 and TFF3 are augmented. Interestingly, in the setting of hepatolithiasis, a similar finding has been noted where all 3 TFF peptide levels were found to be increased in the biliary tract.³⁹

Paulsen et al.²⁸ found 1 dacryolith in their study that did not stain for any of the antibodies or contain any epithelial cell debris but still maintained the same amorphous core as the other samples. The authors on the basis of their study have postulated that dacryolithogenesis may first start with an alteration in tear fluid dynamics, which leads to formation of uncharacterized amorphous material. This material then initiates an epithelial reaction that leads to increased mucins and TFF peptides and immigration of granulocytes and antimicrobial substances. Although speculative, there does appear to be evidence of tear composition playing a role in dacryolith formation. Other factors hypothesized to have a possible role include prior inflammation of the nasolacrimal duct, allergies, fungal colonization, and changes in the hormonal status.

Lew et al.³³ compared the tear constituents of patients with PANDO and dacryoliths to patients with PANDO but without dacryoliths. This prospective study showed that, compared with patients without dacryoliths, patients with dacryoliths had a tear composition with decreased lysozyme levels, decreased K+ concentration, decreased overall protein levels, but no difference in Ca2+ levels. Both groups had a higher tear pH compared with healthy controls.⁴⁰ The authors note that low lysozyme levels may affect proteolysis and create a permissive environment for dacryolith formation due to the aggregation of organic substances, coupled with electrolyte instability and crystal formation in a more alkaline environment.

Many studies have looked to find a link between dacryoliths and infection but there have been mixed outcomes. ^{23,41,42} Two studies found no fungi in their samples, ^{20,22} while others found only isolated fungi in a small percentage of specimens. ^{9,17,28}

There are reports that have shown an eyelash as a possible nidus, 5-7,43 a grass seed,44 long-term mascara use,45 and even from epinephrine metabolites from glaucoma treatment.46,47 Further research is needed to understand what role these foreign materials played in the course of the dacryolith development, however.

Piaton et al.⁴⁸ have hypothesized that anatomical abnormalities of the valve of Hasner could play a role in the development of dacryolithiasis. In their series of 797 surgeries performed for epiphora (including 150 meatotomies at the valve of Hasner), they reported that anatomical abnormalities of the valve of Hasner seen during preoperative endoscopy and mucopurulent discharge at the valve were predictors of the presence of dacryolithiasis.

APPEARANCE AND COMPOSITION

Dacryoliths have been described in the literature with a variety of macroscopic appearances. In color, they range from black in the case of epinephrine dacryoliths, ^{44,47} which classically develop in association with chronic epinephrine application as a historical glaucoma therapy, to yellowish or light brownish in color.⁴⁴ Clinically appreciable dacryoliths are described as ranging in size from 3 mm to a maximum length of 2.9 cm²⁸ and a maximal width of 9 mm⁴⁴ in some case series. They commonly take the shape of the lacrimal sac or the nasolacrimal duct in which they arise, with roughened ridges and notches from the ductal mucosa.^{24,44} One series additionally differentiates between macroscopic appearances of dacryoliths found in the lacrimal sac versus in the canaliculus, the former appearing doughy, pliable, and putty-like and the latter appearing irregular, granular, and friable.¹⁰

The majority of dacryoliths analyzed in the literature have been found to be primarily composed of organic substances. 10 In one case study, analysis demonstrated high proportions of phosphate and urate. 19 The authors of this case speculated that phosphate from an intracellular source and urate from genetic material breakdown might imply a chronic process of cell turnover contributing to growth of the stone. In cases wherein stone development is suspected to be secondary to chronic epinephrine therapy, stones are predictably found to be composed largely of epinephrine. 46,47 However, in the majority of studies, wherein the development of dacryoliths is idiopathic, dacryoliths are commonly described on histopathology as consisting of lobes and lobules built on an amorphous eosinophilic hyaline core material.^{28,46,49} A chemical and mineralogical analysis of 86 dacryoliths by Komínek et al.44 found them to be almost exclusively composed of organic material, including proteins and mucoproteins. In an earlier histopathologic study, Perry et al. 10 evaluated 30 lacrimal drainage system concretions removed from the lacrimal sac and canaliculi and found significant

calcium or stone-like density to be absent from all samples, with negative calcium and iron stains at the surface and in the middle of the concretions.

The authors go on to propose that concretions removed from the lacrimal sac and canaliculi be alternatively referred to as mucopeptide and bacterial concretions, respectively, as terms more accurately describing their histomorphologic, histochemical, and microbiologic characteristics than the traditional terms "dacryolith" and "canaliculith." The composition of the concretions examined were also strongly correlated with location, where mucopeptide concretions largely devoid of cells were found exclusively within the lacrimal sac and more heterogeneous and cellular concretions with internal meshworks of filamentous were found predominantly in the canaliculi. Similar findings have been described in other studies, where fungal hyphae and yeast-like structures are seen in portions of analyzed samples in contrast to those comprised only of amorphous material. 28,48,50 The strong correlation of mucopeptide versus bacterial character with location may imply a difference in mechanisms of formation of concretions found in the lacrimal sac versus the canaliculi. Perry et al. 10 proposed that mucopeptide concretions may be primary precipitants, with only peripheral incidental organisms found on histopathology, whereas bacterial concretions may arise from a process incited by infection. Many studies identify Actinomyces as a common isolate, possibly providing further support for a shared infectious origin of bacterial concretions that is differentiable from the pathogenesis of mucopeptide concretions. 10,11,14,51-53

In contrast to the findings described above, other published cases have described dacryoliths composed largely of inorganic material. In one case report, x-ray fluorescence spectrometry determined the main nature of the analyzed dacryolith to be inorganic and composed of calcium, potassium, iron, titanium, and magnesium with their oxidized forms. The authors have hypothesized that a rural environment and chronic soil exposure may have contributed to the formation and particular composition of the analyzed dacryolith. In addition, a case report of a patient diagnosed with dacryolithiasis by CT scan described the lacrimal sac mass as having a "rice kernel" appearance, with a peripheral rim of calcification, suggesting deposition of higher molecular weight inorganic material. It is possible then that some dacryoliths undergo a secondary calcification process. A

The variable macroscopic and histological appearance of dacryoliths points to the heterogeneity of their origin and composition. However, they share clinical significance as potential causes or exacerbating factors of NLDO and inflammation of nasolacrimal structures.

CLINICAL PRESENTATION

Classically, dacryoliths become symptomatic when they obstruct the nasolacrimal duct system. This can produce a variety of symptoms including, most commonly epiphora, 9.27,30,44,52,55 acute, 27 and in some cases recurrent 19,28 episodes of dacryocystitis with mucoid punctal discharge, medial canthal swelling, and sometimes a palpable firm mass. 46 Uncommonly, dacryoliths have also been associated with recurrent conjunctivitis 9 and maxillary sinusitis. 28

Of the clinical characteristics associated with NLDO, certain presentations have been suggested to appear more commonly in cases of underlying dacryoliths. In a study comparing 12 patients found to have dacryoliths at DCR with 103 patients without dacryoliths at DCR, Yazici et al. ¹⁷ found a significantly higher incidence of sac distension, otherwise known as acute dacryocystic retention syndrome, in patients with dacryolithiasis (p = 0.001). The study defined sac distension as swelling

of the medial canthal region without excessive tenderness, with purulent discharge and localized erythema.

In the same study, the authors suggested that dacryoliths may be more strongly associated with partial obstruction, with epiphora despite patent lacrimal passages on syringing by the evaluating ophthalmologist, recapitulating an association described in a much earlier study. However, this finding only approached significance, with 6 of 12 of the dacryolith group versus 24 of 103 of the nondacryolith group presenting clinically with partial obstruction (p = 0.08). On the other hand, Piaton et al. found that a history of acute noninfectious dacryocystic retention and the presence of partial obstruction of the lacrimal pathway were clinical signs seen significantly more in patients with dacryolithiasis.

Of note, in one series of 76 cases, all patients with dacryoliths who received dacryocystography (DCG) were found to have large lacrimal sacs.²⁴ However, the authors only performed dacryocystography rarely in unclear or complicated cases and do not provide the quantity of that group of patients. If this finding is generalizable, then it may have implications as a prognostic factor predicting success of DCR in treating obstructive and inflammatory symptoms (see "Implications of Incidental Dacryolith Found During DCR" for further discussion).

In their study comparing 4 groups with and without dacryocystitis and with and without dacryolithiasis, Andreou and Rose²⁷ found that patients with dacryoliths and dacryocystitis episodes typically had a shorter duration of symptoms in comparison to those with dacryocystitis but without stones at DCR, and typically sought treatment after one episode of dacryocystitis versus multiple episodes in the group without stones. This finding was recapitulated in a study by Komínek et al.,24 where patients found to have dacryoliths at DCR had sought care after a significantly shorter period of time (p = 0.014). In addition, the presence of dacryoliths at DCR was associated with a higher clinical incidence of acute dacryocystitis (p < 0.001). It is arguable that dacryolithiasis, when presenting with dacryocystitis, may produce a more severe infection. Andreou and Rose²⁷ also argue that patients with dacryoliths are likely to develop dacryocystitis if left untreated as a direct result of obstruction by dacryoliths. This is echoed in a case report by Dhillon et al., wherein a patient with epiphora and chronic dacryocystitis had complete resolution of symptoms following incision and drainage without DCR, implying that dacryoliths were central to the pathogenesis of the patient's dacryocystitis.54

In summary, symptomatic dacryoliths commonly produce epiphora, acute and/or recurrent dacryocystitis, punctal discharge, and localized swelling. Unilateral sac distension, particularly with a palpable firm medial canthal mass, might lead one to have increased suspicion for the presence of a dacryolith. In addition, one may have increased suspicion in settings of partial obstruction of the nasolacrimal ductal system. However, further investigation is necessary to rigorously demarcate symptoms implying the presence of a dacryolith.

DIAGNOSIS

Examination of the outer structures and blind probing with irrigation are integral for the initial evaluation of epiphora with suspected NLDO and may qualitatively characterize the extent of NLDO as well as reveal findings suspicious for a dacryolith.⁵⁶

A variety of imaging modalities have demonstrated utility in further evaluating disorders of the nasolacrimal duct. Dacryocystography has been the traditional radiological investigation for epiphora,⁵⁷ wherein contrast is injected into the lacrimal ducts and radiographic films visualize drainage into the nasopharynx or failure thereof.⁵⁷ Dacryocystography is

considered to be superior at eliciting anatomical detail. However, it does subject patients to radiation and requires injection, which distort the results of the study and obscure functional drainage characteristics.⁵⁷

Dacryoscintigraphy is an alternative imaging technique wherein radionuclide drops are placed in the inferior fornix of the eye and tracer distribution is visualized by a collimator camera. Wearne et al.⁵⁷ demonstrated that dacryoscintigraphy is a comparably sensitive option to dacryocystography, with the benefit of avoiding the need for injection, and perhaps providing functional information over anatomical detail.

Ultrasound was first used to detect a mass in the nasolacrimal duct system in 1988,46 and advancements in imaging technology have increased the applicability of ultrasound in the evaluation of small anatomical structures. Stupp et al.⁵⁶ showed that ultrasound could be used to identify dacryoliths in 9 of 10 patients ultimately found to have stones at DCR, compared with 2 of 10 identified by dacryocystography, and described the added benefit of ultrasound of being able to characterize additional diagnostic criteria such as compressibility of the lacrimal sac and flow dynamics via Doppler. However, a shortcoming of traditional ultrasound is that, in most cases, it cannot visualize the lacrimal ductal lumen or wall unless there is inflammation. dilation, or intubation that increase the echogenicity of the tissues.⁵⁶ In 2011, Al-Faky et al.⁵⁸ applied traditional ultrasound technology to biomicroscopy by using very high frequencies, achieving resolutions on the order of 20-60 µm. The utility of this technology is limited as increasing resolution decreases penetrance. Al-Faky et al.⁵⁸ addressed this challenge with a technique wherein the area of interest was immersed in fluid. The authors were able to identify inflammatory changes, fistulas, masses, and dacryoliths. In general, ultrasound has the advantage of avoiding radiation exposure to the patient and characterizing the lacrimal drainage system proximal and distal to any point of obstruction. As stated before, however, the utility of ultrasound is limited by penetrance, and ultrasound largely cannot be used to visualize intraosseous structures, including the lower lacrimal sac in most patients.

CT has broad applications in assessing the lacrimal system along with surrounding bony structures, structures within the orbit, the paranasal sinuses, and the nasal cavity,54,59-61 with demonstrated ability to directly visualize dacryoliths in select cases.51 More commonly CT is used to evaluate the lacrimal drainage system in cases of epiphora and suspected NLDO. CT-DCG can be performed where contrast is applied to the lacrimal drainage system, either passively via the inferior fornix or directly via syringing, and drainage subsequently visualized.61-63 A significant disadvantage of using CT imaging is that the radiosensitive structures of the orbit are subjected to high doses of ionizing radiation as compared with other imaging modalities. This disadvantage is somewhat mitigated by applying cone beam CT to dacryocystography, as dose levels for cone-beam CT imaging are significantly lower than those of multislice CT.^{60,63} In a 2014 study, Tschopp et al.⁶³ found that cone beam CT-DCG was able to identify the site of obstruction in all clinically diagnosed obstructions (n = 11) and correctly define all patent lacrimal systems studied (n = 9). The authors cannot expect studies directly comparing results of cone beam CT-DCG and multislice CT-DCG or traditional radiographic DCG due to unnecessary increased radiation exposure to patients, but these results imply the competitive diagnostic ability of cone beam CT-DCG.

Similarly, MRI may be applied to imaging the nasolacrimal drainage system, with the option of instilling contrast agents for DCR.⁶⁴ It has the particular strengths of producing contrast resolution superior to CT and lack of ionizing radiation,⁶⁵ with comparability to identify the presence and level of NLDO when present.⁶⁶ Visualization of a dacryolith in the lacrimal gland by MRI has been documented in the literature;⁶⁷ however, no studies have been conducted comparing the ability of CT or MRI versus traditional DCG to diagnose dacryolithiasis, which would help to argue for or against their diagnostic reliability for this application.

Rogers and DelGaudio⁶⁸ have reported the case of a patient with a diagnosis of NLDO who was found to have a large dacryolith obstructing the nasolacrimal duct orifice on endoscopic examination of the inferior meatus. The dacryolith was easily removed under endoscopic visualization in the office. In the eventuality that such a patient may be taken up for endoscopic DCR, a preoperative endoscopic evaluation would most definitely have yielded the cause for epiphora. However, in scenarios where external DCR is the preferred surgery of choice, as is the case in many developing countries, it is possible that cases such as this may be missed, as routine nasal endoscopy is not necessarily performed preoperatively.⁶⁹

Dacryoendoscopy is a procedure utilizing microendoscopic techniques to visualize the entire lacrimal system from the puncta to the inferior meatus. 70 Küstner et al. 71 in their series have described a patient who presented with tearing and discharge but was found to have a patent NLD on irrigation. The case was subsequently diagnosed as a tear-film disorder. However, dacryoendoscopy showed a dacryolith in the lacrimal sac and was fragmented using a microdrill system and fully removed through the nasolacrimal duct, as well as the lacrimal canaliculus. Such transcanalicular viewing and operating systems have evolved dramatically in the past few years. However, high costs and a paucity of data on long-term results continue to limit the use of transcanalicular surgery.⁷² Furthermore, dacryoendoscopic surgery is an additional skill set that has its own associated learning curve. It appears logical and likely that dacryoendoscopy can be useful to diagnose dacryoliths within the lacrimal sac. However, given the limited data available and the fraction of cases of NLDO that are in fact due to dacryolithiasis, there is not enough evidence to suggest that all cases of epiphora should undergo dacryoendoscopic examination as a part of routine evaluation.

MANAGEMENT

The management of dacryolithiasis is driven by the goal of resolution of secondary obstruction and/or inflammation. The important factor, therefore, that needs to be established before any intervention is confirming the diagnosis of dacryolithiasis. Preoperative diagnosis of dacryoliths can be difficult due to the variability of clinical presentation.⁶⁷ In most cases, dacryoliths are identified incidentally on imaging or by direct visualization during therapeutic interventions undertaken to alleviate epiphora or dacryocystitis. Diagnosing dacryolithiasis requires a high degree of clinical suspicion, following which appropriate investigations may be carried out to confirm the diagnosis.

There are multiple cases in the literature wherein spontaneous passage has been documented with subsequent resolution of symptoms. ^{17,19} When spontaneous passage does not occur and symptoms become bothersome, a variety of therapeutic techniques are available. Local tissue massage, lacrimal irrigation probing, and percutaneous aspiration can be used initially in the clinic to attempt to induce expulsion of dacryoliths. ¹⁷ With failure of less invasive methods, techniques such as dacryoplasty, ⁵⁵ possibly with snaring, laser, or microdrill fragmentation can be undertaken ^{71,73}

Guthoff and Lieb⁷⁴ have reported successful outcomes in 2 cases of dacryolithiasis diagnosed preoperatively with the

help of DCG. In these 2 cases, dacryocystotomy with primary microsurgical lacrimal sac reconstruction combined with silicone intubation was done, suggesting that an osteotomy may not always be required. However, unless the pretest probability of the preoperative investigations to diagnose dacryolithiasis improves significantly, and sufficient long-term outcomes for the above mentioned minimally invasive technique to treat it becomes available, DCR remains the gold standard to treat NLDO due to dacryolithiasis. Debates about optimal DCR approaches and techniques are outside of the scope of this review and will not be discussed in further detail.

IMPLICATIONS OF INCIDENTAL DACRYOLITHS FOUND DURING DCR

There is clearly some merit in evaluating patients for the presence and characteristics of dacryoliths preoperatively, particularly in cases where surgery can be avoided. Dacryoliths are so often diagnosed incidentally during DCR, however, that it is of particular interest whether the presence of an incidental dacryolith is predictive of outcomes in DCR cases.

Some recent studies have suggested an association between success of DCR and the presence of dacryoliths. In a study of 908 DCRs with 76 identified cases of dacryoliths conducted between 1995 and 2011, Komínek et al. found the presence of dacryoliths to be significantly associated with success of DCR and persistent resolution of symptoms, with a 100% (76 of 76) success rate for cases with dacryoliths compared with a 91.1% (633 of 695) success rate overall (p < 0.001).²⁷ These findings were carried forward in a study published in 2014, with an expanded sampling of 967 primary EDCRs conducted between 1994 and 2012, wherein 86 dacryoliths were found and analyzed.44 In this study, too, surgical success defined as complete improvement and resolution of symptoms occurred significantly more frequently in cases where dacryoliths were found. It is possible that patients were shared between the 2 studies, decreasing their generalizability; however, taken together, they nevertheless convincingly argue that for this population of patients, the presence of incidental dacryolith on DCR can be a favorable prognostic finding.

Current evidence suggests that the positive prognostic value of dacryoliths at DCR is that dacryoliths may be a direct cause of epiphora and other symptoms via obstruction of the nasolacrimal ductal system, one that can be addressed in totality by DCR and removal of the stone. In other words, failure of the surgeries can be considered exceptionally rare and the presence of a dacryolith is a good predictive factor for successful DCR. There however are certain gray areas: do cases of partial NLDO have higher chances of harboring dacryoliths as opposed to complete NLDOs? Is advising imaging modalities in all cases of NLDO to rule out dacryolithiasis justifiable? Our understanding of the pathophysiology and formation of dacryoliths, although nascent, is evolving rapidly. There is a need for focused studies that can throw light on the clinical features that can predict the presence of dacryoliths with considerable success, the predictive value of the diagnostic modalities in diagnosing dacryoliths, and consensus guidelines regarding the management of the dacryolithiasis.

REFERENCES

- Duke-Elder S, MacFaul PA. The Ocular Adnexa. London: Henry Kimpton, 1974:768–70.
- Naito H, Oshida K, Kurokawa K, et al. Atypical intermittent exophthalmos due to hyperplasia of lacrimal gland associated with dacryolithiasis. Surg Neurol 1973;1:84–6.
- Duke-Elder SS. Text-book of ophthalmology, volume 5. The Ocular Adnexa. Am J Med Sci 1952;224:711.

- Baker RH, Bartley GB. Lacrimal gland ductule stones. Ophthalmology 1990;97:531–4.
- Baratz KH, Bartley GB, Campbell RJ, et al. An eyelash nidus for dacryoliths of the lacrimal excretory and secretory systems. Am J Ophthalmol 1991;111:624–7.
- Mawn LA, Sanon A, Conlon MR, Nerad JA. Mawn LA, Sanon A, Conlon MR, et al. Pseudomonas dacryoadenitis secondary to a lacrimal gland ductule stone. *Ophthal Plast Reconstr Surg* 1997;13:135–8.
- Zafar A, Jordan DR, Brownstein S, et al. Asymptomatic lacrimal ductule dacryolithiasis with embedded cilia. Ophthal Plast Reconstr Surg 2004;20:83–5.
- 8. Halborg J, Prause JU, Toft PB, et al. Stones in the lacrimal gland: a rare condition. *Acta Ophthalmol* 2009;87:672–5.
- Repp DJ, Burkat CN, Lucarelli MJ. Lacrimal excretory system concretions: canalicular and lacrimal sac. *Ophthalmology* 2009;116:2230–5.
- Perry LJ, Jakobiec FA, Zakka FR. Bacterial and mucopeptide concretions of the lacrimal drainage system: an analysis of 30 cases. *Ophthal Plast Reconstr Surg* 2012;28:126–33.
- Briscoe D, Edelstein E, Zacharopoulos I, et al. Actinomyces canaliculitis: diagnosis of a masquerading disease. *Graefes Arch Clin Exp Ophthalmol* 2004;242:682–6.
- 12. Varma D, Chang B, Musaad S. A case series on chronic canaliculitis. *Orbit* 2005;24:11–4.
- Seal DV, McGill J, Flanagan D, et al. Lacrimal canaliculitis due to Arachnia (Actinomyces) propionica. Br J Ophthalmol 1981;65:10–3.
- Yuksel D, Hazirolan D, Sungur G, et al. Actinomyces canaliculitis and its surgical treatment. *Int Ophthalmol* 2012;32:183–6.
- McKellar MJ, Aburn NS. Cast-forming actinomyces israelii canaliculitis. Aust N Z J Ophthalmol 1997;25:301–3.
- 16. Traquair HM. Chronic dacryocystitis: its causation and treatment. *Arch Ophthalmol* 1941;26:165–80.
- Yazici B, Hammad AM, Meyer DR. Lacrimal sac dacryoliths: predictive factors and clinical characteristics. *Ophthalmology* 2001;108:1308–12.
- Rosen WJ, Rose GE. Intranasal passage of dacryoliths. Br J Ophthalmol 2000;84:799–800.
- Kaye-Wilson LG. Spontaneous passage of a dacryolith. Br J Ophthalmol 1991;75:564.
- Rb W, Jp P. Diagnosis and incidence of lacrimal calculi. Ophthalmic Surg 1980;11:787–9.
- Hawes MJ. The dacryolithiasis syndrome. Ophthal Plast Reconstr Surg 1988;4:87–90.
- 22. Jones LT. Tear-sac foreign bodies. Am J Ophthalmol 1965;60:111–3.
- Berlin AJ, Rath R, Rich L. Lacrimal system dacryoliths. *Ophthalmic Surg* 1980;11:435–6.
- Komínek P, Červenka S, Zeleník K, et al. Lacrimal sac dacryolith (76 cases): a predictive factor for successful endonasal dacryocystorhinostomy? Eur Arch Otorhinolaryngol 2014;271:1595–9.
- Herzig S, Hurwitz JJ. Lacrimal sac calculi. Can J Ophthalmol 1979;14:17–20.
- Marthin JK, Lindegaard J, Prause JU, et al. Lesions of the lacrimal drainage system: a clinicopathological study of 643 biopsy specimens of the lacrimal drainage system in Denmark 1910-1999. *Acta Ophthalmol Scand* 2005;83:94–9.
- Andreou P, Rose GE. Clinical presentation of patients with dacryolithiasis. *Ophthalmology* 2002;109:1573–4.
- Paulsen FP, Schaudig U, Fabian A, et al. TFF peptides and mucins are major components of dacryoliths. *Graefes Arch Clin Exp Ophthalmol* 2006;244:1160–70.
- Linberg JV. Discussion by John V. Linberg, MD. Ophthalmology 2001;108:1312.
- Lee-Wing MW, Ashenhurst ME. Clinicopathologic analysis of 166 patients with primary acquired nasolacrimal duct obstruction. Ophthalmology 2001;108:2038–40.
- 31. Smith B, Tenzel RR, Buffam FV, et al. Acute dacryocystic retention. *Arch Ophthalmol* 1976;94:1903–4.
- Satici A, Bitiren M, Ozardali I, et al. The effects of chronic smoking on the ocular surface and tear characteristics: a clinical, histological and biochemical study. *Acta Ophthalmol Scand* 2003;81:583–7.

- Lew H, Lee SY, Yun YS. Measurement of pH, electrolytes and electrophoretic studies of tear proteins in tears of patients with dacryoliths: a novel concept for dacryoliths. *Ophthalmologica* 2004;218:130–5.
- Paulsen FP, Thale AB, Maune S, et al. New insights into the pathophysiology of primary acquired dacryostenosis. *Ophthalmology* 2001;108:2329–36.
- Ayub M, Thale AB, Hedderich J, et al. The cavernous body of the human efferent tear ducts contributes to regulation of tear outflow. *Invest Ophthalmol Vis Sci* 2003;44:4900–7.
- Paulsen F, Hallmann U, Paulsen J, et al. Innervation of the cavernous body of the human efferent tear ducts and function in tear outflow mechanism. *J Anat* 2000;197(pt 2):177–87.
- 37. Thale A, Paulsen F, Rochels R, et al. Functional anatomy of the human efferent tear ducts: a new theory of tear outflow mechanism. *Graefes Arch Clin Exp Ophthalmol* 1998;236:674–8.
- Kjellev S. The trefoil factor family small peptides with multiple functionalities. Cell Mol Life Sci 2009;66:1350–69.
- Sasaki M, Ikeda H, Ohira S, et al. Expression of trefoil factor family 1, 2, and 3 peptide is augmented in hepatolithiasis. *Peptides* 2004;25:763–70.
- 40. Norn MS. Tear fluid pH in normals, contact lens wearers, and pathological cases. *Acta Ophthalmol (Copenh)* 1988;66:485–9.
- Wolter JR, Stratford T, Harrell ER. Cast-like fungus obstruction of the nasolacrimal duct; report of a case. AMA Arch Ophthalmol 1956;55:320–2.
- 42. Song HY, Jin YH, Lee HK, et al. Nonoperative management of dacryolithiasis. *J Vasc Interv Radiol* 1995;6:647–50.
- 43. Jay JL, Lee WR. Dacryolith formation around an eyelash retained in the lacrimal sac. *Br J Ophthalmol* 1976;60:722–5.
- Komínek P, Doškářová S, Svagera Z, et al. Lacrimal sac dacryoliths (86 samples): chemical and mineralogic analyses. *Graefes Arch Clin Exp Ophthalmol* 2014;252:523–9.
- Ciolino JB, Mills DM, Meyer DR. Ocular manifestations of longterm mascara use. Ophthal Plast Reconstr Surg 2009;25:339

 –41.
- Bradbury JA, Rennie IG, Parsons MA. Adrenaline dacryolith: detection by ultrasound examination of the nasolacrimal duct. Br J Ophthalmol 1988;72:935–7.
- Spaeth GL. Nasolacrimal duct obstruction caused by topical epinephrine. Arch Ophthalmol 1967;77:355–7.
- Piaton JM, Keller P, Sahel JA, et al. Dacryolithiasis: diagnosis using nasal endoscopy. J Fr Ophtalmol 2003;26:685–98.
- Orhan M, Onerci M, Dayanir V, et al. Lacrimal sac dacryolith: a study wit atomic absorption spectrophotometry and scanning electron microscopy. Eur J Ophthalmol 1996;6:478–80.
- 50. Ozer S, Ozer PA, Ortarik Z, et al. Analysis of inorganic elements in a dacryolith using polarised X-ray fluorescence spectrometry: a case report. *Eye (Lond)* 2012;26:887.
- Asheim J, Spickler E. CT demonstration of dacryolithiasis complicated by dacryocystitis. AJNR Am J Neuroradiol 2005;26:2640–1.
- Kubo M, Sakuraba T, Wada R, Kubo M, Sakuraba T, Wada R. Clinicopathological features of dacryolithiasis in Japanese patients: frequent association with infection in aged patients. ISRN Ophthalmol 2013;2013:406153.
- 53. Park A, Morgenstern KE, Kahwash SB, et al. Pediatric canaliculitis and stone formation. *Ophthal Plast Reconstr Surg* 2004;20:243–6.
- Dhillon N, Kreis AJ, Madge SN. Dacryolith-induced acute dacryocystitis: a reversible cause of nasolacrimal duct obstruction. *Orbit* 2014;33:199–201.
- Wilhelm KE, Hofer U, Textor HJ, et al. Dacryoliths: nonsurgical fluoroscopically guided treatment during dacryocystoplasty. *Radiology* 1999;212:365–70.
- Stupp T, Pavlidis M, Busse H, et al. Presurgical and postsurgical ultrasound assessment of lacrimal drainage dysfunction. Am J Ophthalmol 2004;138:764–71.
- Wearne MJ, Pitts J, Frank J, et al. Comparison of dacryocystography and lacrimal scintigraphy in the diagnosis of functional nasolacrimal duct obstruction. *Br J Ophthalmol* 1999;83:1032–5.
- Al-Faky YH. Anatomical utility of ultrasound biomicroscopy in the lacrimal drainage system. Br J Ophthalmol 2011;95:1446–50.
- McCormick A, Sloan B. The diameter of the nasolacrimal canal measured by computed tomography: gender and racial differences. *Clin Experiment Ophthalmol* 2009;37:357–61.

- Wilhelm KE, Rudorf H, Greschus S, et al. Cone-beam computed tomography (CBCT) dacryocystography for imaging of the nasolacrimal duct system. Klin Neuroradiol 2009;19:283–91.
- 61. Gandhi RA, Nair AG. Role of imaging in the management of neuroophthalmic disorders. *Indian J Ophthalmol* 2011;59:111–6.
- Udhay P, Noronha OV, Mohan RE. Helical computed tomographic dacryocystography and its role in the diagnosis and management of lacrimal drainage system blocks and medial canthal masses. *Indian* J Ophthalmol 2008;56:31–7.
- Tschopp M, Bornstein MM, Sendi P, et al. Dacryocystography using cone beam CT in patients with lacrimal drainage system obstruction. *Ophthal Plast Reconstr Surg* 2014;30:486–91.
- Rubin PA, Bilyk JR, Shore JW, et al. Magnetic resonance imaging of the lacrimal drainage system. *Ophthalmology* 1994;101: 235–43.
- Conneely MF, Hacein-Bey L, Jay WM. Magnetic resonance imaging of the orbit. Semin Ophthalmol 2008;23:179

 –89.
- Cubuk R, Tasali N, Aydin S, et al. Dynamic MR dacryocystography in patients with epiphora. Eur J Radiol 2010;73:230–3.
- 67. Alten F, Domeier E, Holz FG, et al. Dacryoliths in the lacrimal gland ductule. *Acta Ophthalmol* 2012;90:e155–156.

- Rogers GA, DelGaudio JM. Inferior meatus dacryolith: an easily managed cause of epiphora. Arch Otolaryngol Head Neck Surg 2008;134:1110–1.
- Nair AG, Kamal S. Indian survey on practice patterns of lacrimal and eyelid disorders (iSUPPLE) report 1: congenital nasolacrimal duct obstruction. *Int J Ped Otorhinolaryngol*. 2016. doi:10.1016/j. ijporl.2016.06.009.
- Ali MJ. Dacryoendoscopic examination of the lacrimal system In: Ali MJ, ed. *Principles and Practice of Lacrimal Surgery*. New Delhi: Springer, 2015: 87–92.
- Küstner M, Clemens S, Tost F. [Minimally invasive endoscopic surgery of the lacrimal drainage system—two case reports]. Klin Monbl Augenheilkd 2005;222:928–32.
- Athanasiov PA, Prabhakaran VC, Mannor G, et al. Transcanalicular approach to adult lacrimal duct obstruction: a review of instruments and methods. *Ophthalmic Surg Lasers Imaging* 2009;40:149–59.
- Meyer-Rüsenberg HW, Emmerich KH. Modern lacrimal duct surgery from the ophthalmological perspective. *Dtsch Arztebl Int* 2010;107:254–8.
- Guthoff R, Lieb WE. [Dacryocystostomy and microsurgical lacrimal sac reconstruction in dacryolithiasis]. Ophthalmologe 2002;99:113–5.