



# Lacrimal Sac Dacryoliths-Pathogenesis and Composition

## *Lakrimal Kесе Dakriolitleri-Patogenez ve Bileşim*

Serdar Özer, Pınar Altıaylık Özer

Aksaray State Hospital, Ministry of Health, Aksaray, Turkey

### **Summary**

The Main objective of the present study is to review the literature about the chemical composition and the formation of dacryoliths. Dacryoliths are calculi of the lacrimal system observed incidentally during dacryocystorhinostomy. Theories about the formation of dacryoliths mainly suppose that dacryoliths are simply a secondary phenomenon resulting from a lacrimal pathway obstruction and accumulation of debris. Inflammation caused by fungi, most commonly *Candida albicans*, an eyelash within the sac, or adrenalin use are also considered to be potential causes. It was also reported that the unstable concentrations of electrolytes rather than the supersaturation of some electrolytes are related to the pathogenesis of dacryoliths. Chemical analysis of the dacryoliths in studies had revealed calcium, magnesium, potassium, sulfur, and some phosphorus. Atomic absorption spectrophotometric investigations demonstrated organic proteins and, to a much lesser extent, inorganic material. (*Turk J Ophthalmol* 2013; 43: 186-9)

**Key Words:** Dacriolith, dacryocystorhinostomy, atomic absorption spectrophotometry

### **Özet**

Bu çalışmanın amacı lakrimal kese dakriyolitlerinin kimyasal bileşimi ve oluşumları ile ilgili literatürün taranmasıdır. Dakriyolitler dakriyosistorinostomi sırasında tesadüfen gözlenen lakrimal sistem taşlarıdır. Dakriyolitlerin oluşumu ile ilgili teoriler temel olarak dakriyolitlerin ikincil oluşumlar olduğunu, lakrimal sistem tıkanıklığı ve debris birikimi sonucunda oluştuğunu varsayarlar. Başta *Candida albicans* olmak üzere mantarlara bağlı enflamasyon, kese içindeki bir kirpik ya da adrenalin kullanımı olası nedenler olarak düşünülmektedir. Ayrıca elektrolitlerin doygunluk üzeri konsantrasyonlarından çok dengesiz konsantrasyonlarda bulunmalarının dakriyolitlerin patogenezi ile ilişkili olduğu bildirilmiştir. Dakriyolitlerin kimyasal analizlerinde kalsium, magnezyum, potasyum, sulfur ve fosfor bulunmuştur. Ayrıca Atomik Absorbsiyon Spektrofotometrik çalışmalar dakriyolit yapısında organik proteinler ve çok az oranda inorganik maddeler göstermiştir. (*Turk J Ophthalmol* 2013; 43: 186-9)

**Anahtar Kelimeler:** Dakriolit, dakriyosistorinostomi, atomik absorbsiyon spektrofotometri

### **Introduction**

Dacryoliths were initially described by Cesoni in 1670.<sup>1</sup> They are calculi of the nasolacrimal system which are generally observed incidentally in dacryocystorhinostomy (DCR) operations. Dacryolith formation was reported to occur in between 6 and 18% of patients with nasolacrimal duct obstruction who undergo DCR.<sup>2-7</sup>

A swelling in the medial canthal region, intermittent or constant epiphora, mucoid discharge, acute lacrimal sac

distention, partial obstruction, recurrent acute dacryocystitis can accompany the clinical condition.<sup>3-6,8,9</sup> Interestingly, dacryoliths occur more often in patients with epiphora despite patent lacrimal passages on syringing.<sup>10</sup>

Even though the studies about dacryoliths initiated in very early years, their pathogenesis and composition are still in mystery. Some predisposing factors listed in the literature are female sex, patient age below 50 years, cigarette smoking, facial-sinonasal trauma, and previous attacks of dacryocystitis.<sup>2-5,8,11</sup>

**Address for Correspondence/Yazışma Adresi:** Pınar Altıaylık Özer MD, Aksaray State Hospital, Ministry of Health, Aksaray, Turkey

Gsm: +90 532 501 19 14 E-mail: drpınar@yahoo.com

**Received/Geliş Tarihi:** 18.04.2012 **Accepted/Kabul Tarihi:** 05.09.2012

However, some contradictory studies reported increased frequency in males and patients aged above 50 years.<sup>6-8,11,12</sup> But a recent study showed a male:female ratio of 11:9, suggesting that both sexes are involved in a comparable manner.<sup>13</sup> Some studies supporting the idea of female predominance in dacryolithiasis speculate that the obstruction is caused by gender-specific hormonal or anatomic differences.<sup>14</sup>

#### **Pathogenesis**

No accepted theory exists about the formation of dacryoliths, but some authors suppose dacryoliths are simply a secondary phenomenon, resulting from a lacrimal pathway obstruction and accumulation of debris.<sup>14</sup> Inflammation caused by fungi, most commonly *Candida albicans*, an eyelash within the sac, or adrenalin use are also considered to be potential causes.<sup>2,15,16</sup> In some studies, stones revealed hyphae-like structures although no fungi are recovered by culturing.<sup>17</sup>

Dacryoliths are known to be more common in primary acquired nasolacrimal duct obstruction (PANDO), and PANDO may be related to the early stages of dacryolith formation.<sup>6,14</sup> In PANDO, 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<sup>19,20</sup> and epithelial metaplasia of the mucous membrane in a circumscribed area,<sup>21</sup> which may play a role in dacryolith formation.

A recent study investigated whether there is a relation of dacryolith formation in patients with nasolacrimal duct obstruction with tear constituents and demonstrated a decreased K<sup>+</sup> concentration in tears of PANDO patients with dacryoliths.<sup>14</sup> Since tear K<sup>+</sup> concentration is known to be very important for corneal surface stability particularly light scattering and healthy epithelial cells,<sup>22</sup> general discomfort such as glare and blurring may be explained as the result of PANDO/dacryoliths. Total calcium concentration in tear was found to be in normal limits in PANDO patients with dacryoliths,<sup>14</sup> even the existing histological examination revealed amorphous organic material and limited areas with the characteristics of calcium salt deposition.<sup>23</sup>

Although it is unclear whether this is a cause or a result of the presence of a dacryolith with a nasolacrimal duct obstruction, it is assumed that the unstable concentrations of electrolytes rather than the supersaturation of some electrolytes are related to the pathogenesis of dacryoliths.<sup>14</sup>

#### **Composition**

Previous studies about the composition of dacryoliths mainly focused on the chemical composition, types of included electrolytes, and the correlation of these electrolytes with the tear values. Some studies now report the results of histopathological examinations. In a study of Daxecker et al, histological and immunohistochemical examinations of dacryoliths revealed keratin antibodies; calcium, sulfur and some phosphorus were

determined as major constituents in the chemical analysis.<sup>24</sup> In another study that analyzed the composition of dacryoliths, Herzig et al<sup>7</sup> examined tear samples obtained from<sup>14</sup> patients with dacryoliths and compared them with seven normal patients with regard to calcium, phosphorus, and uric acid concentrations, tear to serum calcium ratios, and calcium-phosphate products. There was no significant difference between the two groups and thus there was no evidence of formation of dacryoliths due to abnormal tear electrolytes. One dacryolith was examined and shown to be consisting of ammonium and was related to the presence of bacteria in the media. The authors believed that dacryolith formation results from chronic obstruction and inflammation of the sac causing a build-up of various electrolytes, particularly calcium.

A standard classification of dacryoliths according to the composition is not determined up to now since it is not clear what kinds of dacryoliths exist in terms of chemical/histopathological composition. Some may be composed of amorphous inorganic material only and another far more frequent type composed of organic material with secretory product inclusions of epithelial cells, extruded cells and defense cells.<sup>13</sup>

In a recent study by Perry LJ<sup>25</sup>, two major forms of concretions were determined histopathologically: mucopeptide and bacterial. Mucopeptide concretions were found exclusively within the lacrimal sac, while bacterial concretions were found mainly in the canaliculus. A third category of "mixed" concretions with mucopeptide and bacterial characteristics was also defined in some specimen. Bacterial concretions consisted of large masses of filamentous, presumed *Actinomyces* organisms that were identified with the Grocott's methenamine silver stain. Mucopeptide concretions were generally devoid of cellular elements and were composed diffusely eosinophilic, acellular, periodic acid-Schiff-positive material. They were often colonized by small numbers of bacterial cocci and occasional fungi. All 3 types of concretions were found to predominate in women. Patients with bacterial concretions were reported to have dry eye symptoms frequently.

In recent years, investigators started to use atomic absorption spectrophotometry (AAS) for detection of organic-inorganic compounds in dacryoliths. Iliadelis et al demonstrated dacryoliths consisting almost entirely of organic proteins and, to a much lesser extent, of inorganic material.<sup>23,26</sup> AAS was used in another study, but this time, no inorganic compound was found in the structure, despite four types of unidentified organic materials in composition, and calcium staining was negative.<sup>17</sup> Polarized X-ray fluorescence spectrometry (XRF) is now determined as an alternative method for the analysis of inorganic elements in dacryoliths.<sup>27</sup> XRF analysis in the case report presenting this new method to the literature demonstrated calcium,

potassium, iron, titanium, manganese, and their oxidized forms (CaO, K<sub>2</sub>O, Fe<sub>2</sub>O<sub>3</sub>, TiO<sub>2</sub>, MnO) in the chemical composition of a dacryolith.

Another study about the organic composition of dacryoliths revealed parts of amorphous core proteins staining with alcian blue and reacting with antibodies to mucins and TFF peptides.<sup>13</sup> Moreover, the findings show that most dacryoliths contain single cells and cellular debris.<sup>13</sup> But it is not clear yet whether TFF peptides and mucins influence dacryolith formation or whether their secretion is only a secondary phenomenon. It is also unknown whether dacryolith formation occurs as a reaction to previous inflammation of the nasolacrimal duct or whether other factors such as drugs (perhaps some eye drops), changes in the hormonal status or immunomodulation (allergy) may lead to the initiation of dacryolith formation with recurrent dacryocystitis as a secondary phenomenon.<sup>13</sup>

Differences in the composition of dacryoliths with regard to mucins and defense cells may be explained by colonization with distinct bacteria.<sup>13</sup> Any type of specific bacterial growth is not determined in dacryoliths but fungal colonization (*Candida*, *Pityrosporum* spp. and *Aeromonas Hydrophila*) seems to occur in some cases.<sup>15,28,29</sup>

Recent studies investigate and compare the lacrimal fluid compounds in patients with dacryoliths and normal subjects. According to Lew et al,<sup>14</sup> lacrimal fluid from patients with dacryoliths contains a reduced amount of lysozyme and a lower calcium concentration than normal lacrimal fluid. Although no specific protein causing the condition was detected immunologically, a decrease in the total protein concentration with a low TPF4 protein denotes a large decrease in lysozyme concentration in the tear flow of PANDO/dacryolith patients. Inhibitors such as organic (glycoprotein, amino acid, citrate) and inorganic substances (pyrophosphate, diphosphate, magnesium) can be a decisive factor of stone formation. The loss of lysozyme may be a contributing factor of dacryolith formation due to a loss of its proteolytic effect and inhibition of bacterial growth. It is possible that lysozyme makes the tear flow lubricative without aggregation through the stenotic nasolacrimal pathway and inhibits stone growth on the matrix.<sup>14</sup>

As reported in the same study,<sup>14</sup> the tears from PANDO patients with dacryoliths were deficient in protein and not enriched in the common electrolytes K<sup>+</sup> and Cl<sup>-</sup> compared with those from PANDO patients without dacryoliths. Possible explanations for the formation of dacryoliths described in this study are as follows: The loss of proteins such as lysozyme may create a permissive environment for dacryoliths by the aggregation of organic substances and infection. Increased evaporation resulting in unstable concentrations of electrolyte substances may lead to crystal formation on the matrix.<sup>14</sup>

## Conclusion

Dacryoliths are concretions observed in any part of nasolacrimal system but most commonly in the lacrimal sac.<sup>6</sup> They are generally found incidentally in DCR surgeries, and can be described as a cause of PANDO. They are often underlying contributors in cases of intermittent or chronic dacryocystitis and the main complaint of the patient is usually recurrent epiphora with or without inflammation. In the literature, chemical analysis of the dacryoliths were reported to reveal calcium, magnesium, potassium, sulfur and some phosphorus.<sup>23,24</sup>

AAS investigations demonstrated dacryoliths consist almost entirely of organic proteins and, to a much lesser extent, of inorganic material.<sup>23,26</sup>

Further investigations about the organic and inorganic compounds of dacryoliths and the correlation of dacryolith chemicals to tear film minerals may lead to clarification of the pathogenesis of dacryoliths and to improve the treatments for nasolacrimal obstruction.

## Acknowledgements/Disclosure

There is no government or non-government support for the study. There isn't a financial support for this study, either.

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