Acquired Nasolacrimal Duct Obstruction: Clinical and Histological Findings of 275 Cases

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Research Article

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Abstract

Background: Acquired nasolacrimal duct obstruction is a blockage of the lacrimal outflow system usually caused by a local non-specific inflammation of the lacrimal sac and the nasolacrimal duct. However, cases exist where the primary nasolacrimal system obstruction was caused by malignancies.

Our aim was to investigate lacrimal sac pathologies in patients with acquired nasolacrimal duct obstruction and compare its clinical manifestations.

Methods: The retrospective clinical study included 275 cases with acquired nasolacrimal duct obstruction who underwent external dacryocystorhinostomy and lacrimal sac biopsy. Cases were classified into tumor or non-specific pathology groups subdivided according to the level of inflammation. Histological and clinical data were analyzed.

Results: Three tumors (1.1%) (adenoid cystic carcinoma, eccrine spiradenoma and small B cell lymphoma) were diagnosed. Chronic non-granulomatous inflammation was the most common histological finding, corresponding to 194 cases (70.5%). Other 81 (29.5%) were subacute, chronic forms of non-granulomatous inflammation, tumor and fibrosis cases. Epiphora with continuous purulent discharge was the most common clinical sign reported by 144 (52.4%) patients, two (0.7%) patients had a palpable mass near the medial canthal tendon, which were identified as an eccrine spiradenoma and small B cell lymphoma. There was no significant difference in the clinical symptoms, its' duration or case history between the non-specific pathology and the tumor groups ($p = 0.292$).

Conclusions: Chronic non-granulomatous inflammation of the lacrimal sac was the most frequent etiology of acquired nasolacrimal duct obstruction. There were no associations between the histological findings and clinical presentation. The authors recommend a lacrimal sac biopsy only in cases when a tumor is clinically suspected.

Background

Acquired nasolacrimal duct obstruction (ANDO) is a common disease of the lacrimal passages that is most frequently caused by local non-specific inflammation of the lacrimal sac and the nasolacrimal duct, resulting in occlusive fibrosis [1–2]. The clinical symptoms include permanent lacrimation that is aggravated by exposure to sun, wind, or cold.

Secondary causes of ANDO include neoplasia of the lacrimal sac, inflammatory diseases, specific infections, mechanical obstruction, and trauma [3]. Most frequently, tumors of the lacrimal sac are malignant and arise from the squamous cell or glandular epithelium [4]. Bloody discharge from a lacrimal duct and the presence of a palpable mass in the area of a lacrimal sac are suggestive of a malignant tumor. However, up to 40% of all nasolacrimal duct tumors may be undiagnosed and confused with primary ANDO and/or chronic dacryocystitis [5–7].

According to some authors, to ensure the timely diagnosis of tumors involving the lacrimal drainage system, a routine biopsy and histopathological examination of the lacrimal sac should be performed for all patients undergoing dacryocystorhinostomy (DCR) [4, 8–10]. However, other researchers only recommend selected biopsies in cases when there is clinical or intraoperative suspicion of a tumor because unsuspected tumors causing ANDO are relatively rare, with an incidence ranging from 0–7.1% [11–14].

Methods

This retrospective interventional clinical study was carried out at the Center of Eye Diseases of Vilnius University Hospital Santaros Klinikos from January 1, 2010 to January 1, 2021. Histological and clinical data from the patients who underwent external DCR surgery due to ANDO were analyzed. Patients with previous nasolacrimal duct trauma were excluded. The study was conducted on the basis of the Declaration of Helsinki with the approval of the institutional bioethical committee. Informed consent was obtained from the participants.

The diagnosis of ANDO was confirmed by probing and irrigating the lacrimal drainage system. Each patient's demographic and clinical data (presenting symptoms, duration of the symptoms), as well as disease history (episodes of acute dacryocystitis, previous surgeries of nasolacrimal system), were recorded. In total, 275 external DCR were performed by three surgeons (A. M., A. R., and J. A.) using an external approach with an osteotome or bone drill, followed by canalicular silicon intubation.

Biopsy specimens were obtained from the medial-posterior wall of the lacrimal sac after full visualization of the internal sac structures, and they were preserved in a 10% formalin solution. Histological specimens were prepared from paraffin blocks and stained with hematoxylin/eosin. The specimens were also submitted to histochemical staining with Alcian blue and immunohistochemical staining with antibodies against the cytokeratins AE1/AE3 (Dako), CK5 (XM26, Novocastra), p63 (4A4, Dako), and Ber-Ep4 (Dako), as well as CD117 (c-kit p145, Dako) and CD43 (DF-T1, Dako). All the tumors found in this study were stained for Ki67 (MIB-1, Dako) to determine the proliferative index. All histopathological findings were allocated to either a non-specific pathology or a tumor group. The specimens with non-specific pathology were further divided into groups of chronic, acute, or subacute inflammation or fibrosis on the basis of the presence of elements of an active inflammatory process (Table 1, Fig. 1).

Data were analyzed using R commander software (R programme software version 3.1.2, CRAN Project). Fisher's Exact Test was used to compare clinical data between histological groups. The $p < 0.05$ was considered statistically significant.

Table 1
The histopathological categories of the non-specific pathology group

Group 1	Chronic inflammation	Lacrimal sac wall infiltrated with lymphocytes and plasmocytes (Fig. 1A).
Group 2	Acute inflammation	Tissue infiltration with/by granulocytes (Fig. 1B).
Group 3	Subacute inflammation	Infiltration of tissue by mixed granulocytes, plasmocytes and lymphocytes (Fig. 1C).
Group 4	Fibrosis	Fibrous tissue without inflammatory infiltration; calcification (Fig. 1D).

Results

A total of 258 patients (275 cases of DCR) were enrolled in the study and had their clinical and pathological findings analyzed. The study participants included 189 (73,3%) females and 69 (26,7%) males. The mean age of the patients were 69.7 years (SD 13.1, range 25–98).

Histopathological analysis revealed three (1.1%) specific pathologies: adenoid cystic carcinoma, eccrine spiradenoma and small B cell lymphoma. A total of 218 (79.2%) of the cases showed non-specific inflammation, and 54 (19.6%) demonstrated non-inflammatory fibrotic changes. Chronic non-granulomatous inflammation was the most common finding and was detected in 194 (70.5%) of the specimens (Table 2).

Table 2
The results of histological analysis

Non-specific pathology			Specific pathology
Cases (%)			Cases (%)
118 (98.3)			3 (1.1)
Non-granulomatous inflammation		Fibrosis	Tumor
218 (79.2)		54 (19.6)	3 (1.1)
Chronic	Acute	Subacute	
194 (70.5)	14 (5.1)	10 (3.6)	

Permanent lacrimation was observed in 213 (77.5%) of the cases, with a median duration of 24 (median; IQR 48.0) months. Purulent discharge was documented in 169 (61,5%) of the cases and lasted for 12 (median; IQR 20.4) months. A total of 144 (52.4%) of the patients complained of both epiphora and continuous purulent discharge, while 69 (25.1%) reported only epiphora, and 25 (9.1%) reported only

purulent discharge. The overall median duration of the symptoms was 12 (median; IQR 21) months. In 2 cases, a palpable mass in the region of the lacrimal sac was observed, and after histological analysis, it appeared to be an eccrine spiradenoma and small B cell lymphoma.

3 patients received repeated external DCR for the same eye and 10 for the other eye. An external incision had been performed for 3 patients on the same eye and for 1 patient on the contralateral eye before the study due to acute dacryocystitis or lacrimal sac abscesses.

No significant difference was found in the clinical symptoms between the cases with non-specific histological findings and those with tumors ($p = 0.292$) (Table 3).

Table 3
The clinical symptoms of the histological groups

	Lacrimation	Purulent discharge	Previous ipsilateral DCR	Previous contralateral DCR
Cases (%)				
Chronic inflammation	153/194 (78.9)	120/194 (61.9)	5/194 (2.6)	15/194 (7.7)
Acute inflammation	13/14 (92.9)	11/14 (78.6)	0/14 (0)	0/14 (0)
Subacute inflammation	8/10 (80.0)	7/10 (70.0)	0/10 (0)	1/10 (10.0)
Fibrosis	37/54 (68.5)	29/54 (53.7)	3/54 (5.56)	4/54 (7.4)
Tumor	2/3 (66.7)	2/3 (66.7)	0/3 (0)	0/3 (0)

% - Percentage of all cases of the histological group

The histological groups did not differ significantly in the duration of the symptoms ($p = 0.331$). The median duration of symptoms was longer in the tumor group. Lacrimation lasted 30 (IQR 12) months than in the non-specific pathology group 24 (IQR 48) months, though the difference was not significant. Purulation lasted 18 (IQR 12) months than in the non-specific pathology group 24 (IQR 20.4) months, though the difference was not significant. In all the patients with tumors, there was no history of preceding acute dacryocystitis or external DCR. However, the differences in the history of lacrimal pathology between the tumor group and the non-pathological group were not statistically significant.

Three cases of tumors in this study are described below.

Case 1

An 84-year-old woman presented with tearing and purulent discharge associated with a solid palpable mass below the medial canthal tendon lasting for two years. The neoplastic process was suspected.

Magnetic resonance imaging revealed a 16 x 18 x 16 mm mass in the region of the upper nasolacrimal duct with intensive non-homogeneous contrast accumulation and no signs of local invasion. A biopsy of the lacrimal sac confirmed the diagnosis of the eccrine spiradenoma. Histological analysis showed vascularized masses of compact solid and trabecular microcystic structures composed of cuboidal and cylindrical cells with clear cytoplasm and polymorphic nuclei with a Ki67 proliferative index of 4% (Fig. 2: A, B) and negative staining for S100 and CD43.

Case 2

A 65-year-old woman complained of epiphora lasting for 15 years and recent symptoms of itching and swelling of the eyelids. The patient had a history of bilateral maxillary sinus surgery due to sinusitis 20 years earlier. Histological analysis revealed the adenoid cystic carcinoma. The tumor was verified by histochemical and immunohistochemical methods, demonstrating that the lumens of the glands and cribriform structures composed of epithelial cells had Alcian blue-positive mucins and that the epithelial cells were positive for CD117 (90%), CD43 (10%), and the cytokeratins AE1/AE3, CK5, p63, and Ber-Ep4 (Fig. 2: C, D). The Ki67 proliferative index was 30%, and the tumor was negative for synaptophysin.

Case 3

An 82-year-old woman complained of epiphora lasting for 2 years and purulent discharge lasting for 1 year. Half a year ago she noticed a solid mass in the region of the lacrimal sac. During the observation solid mass 10 x 6 mm with the fluctuation was observed. Histological analysis revealed small B cell lymphoma with the spread to tear sac tissues (Fig. 3). Immunophenotype: CD20/CD23/CD5 +, Cyclin D1/CD10/Bcl6(-), Ki67 proliferative activity 15%.

Discussion

The major histologically identified cause of ANDO is non-specific chronic inflammation resulting in a blockage of the lacrimal outflow system. In our study, ANDO was associated with non-specific histological changes in 79.2% of the cases and most often showed a chronic non-granulomatous inflammation. These findings are consistent with those reported in other series. Some studies report no specific histologic features were found in 98% of the ANDO cases [4, 13]. In a study by other authors, chronic inflammation was diagnosed in 95% of specimens, and fibrosis was detected in 3.8% [12]. Other authors reported non-specific pathology in 96.49% of cases [10].

Previous studies have demonstrated that secondary causes, including primary or secondary tumors, tumor-like lesions, inflammatory diseases, and mechanical obstruction of the lacrimal drainage system represent the etiology of ANDO in 0–14.3% of cases [8, 9, 11, 12, 14, 15]. In our study, three specific histological findings associated with ANDO were identified after histopathological analysis of the lacrimal sac wall. They included three neoplastic lesions - an adenoid cystic carcinoma, an eccrine spiradenoma and one small B cell lymphoma case. The prevalence of ANDO caused by neoplastic lesions was 1.1%, which is similar to other studies, although it is lower than 8.2% of the cases of ANDO

by other authors [4, 9, 10]. One possible explanation for the difference is that their specimens may have been selected using laboratory findings but not surgical records [9]. Ecrine spiradenomas are rare benign sweat gland tumors, and few cases involving the eyelids have been described [16, 17]. This type of tumor is specific for skin adnexa; therefore, it could be interpreted as a skin tumor with ANDO. The patient with spiradenoma in our study did not complain of pain, which is common for this type of tumor [17]. Lacrimal sac adenoid cystic carcinoma is a rare malignant tumor that can be lethal [18]. Lacrimal sac lymphomas are rare and malignant tumors, that often are left misdiagnosed. They present with symptoms of dacryocystitis and epiphora. There are reports which describe 3 lacrimal sac Leukaemia/Small-Cell Lymphocytic Lymphoma cases [19]. Some authors found only 3 cases of adenocarcinoma among 74 malignant lacrimal sac tumors, and others reported 4 adenocarcinomas among 115 lacrimal sac neoplasms [5, 6]. According to previous studies, positivity for CD117 and CD43 is a sensitive and relatively specific marker of adenoid cystic carcinoma, as demonstrated in our study [20, 21].

Due to neoplastic causes, ANDO is reported to be relatively rare; however, overlooking this potentially lethal etiology can delay diagnosis until an advanced stage [6, 7, 22]. Our study demonstrated that the common clinical symptoms of ANDO, such as epiphora and purulence, did not allow for differentiation between the neoplastic lesions and non-specific etiology, however, a specific sign solid palpable mass helped to suspect the tumor in spiradenoma and small B cell lymphoma cases. Most of the primary tumors of the lacrimal sac are malignant, with mortality as high as 37.5%; thus, prompt diagnosis is important for effective treatment [6, 10]. In a study was made an analysis of 82 cases of dacryocystic tumors showed that primary diagnosis of dacryocystitis was established in 5% of patients; in 55% of patients, diagnosis was confirmed only when the tumor had already invaded the adjacent tissues, and in 18% of patients, the tumor was diagnosed when distant metastases were already present [6]. Another study examined 22 clinical cases of lacrimal sac tumors and found that in 27% of cases, the primary diagnosis was incorrect, and the patients were previously treated for dacryocystitis [7].

Considering the low frequency of cases with this specific etiology, many researchers advocate biopsy of the lacrimal sac wall only when anamnestic, clinical, or intraoperative suspicion is present [4, 8–10]. However, this approach can potentially delay the diagnosis. In a Stage 1 tumor described by some authors, no palpable masses of the lacrimal sac were found, and no symptoms of ANDO were observed [6]. However, according to other authors, only 0.5% of 1294 cases were unsuspected when the specific pathologies of ANDO were diagnosed [14].

In our study, there was no significant difference in the disease history, clinical symptoms, or symptom duration between the cases of ANDO with specific and non-specific pathology or among the histological groups of non-specific inflammation, suggesting that the clinical context does not improve the identification of the cause of ANDO, and a biopsy is required. However, in the cases of eccrine spiradenoma and small B cell lymphoma, the palpation of a hard, subcutaneous mass and the intraoperative appearance of the tissues of the lacrimal sac led us to suspect a neoplastic disease. We did not observe a bloody discharge in any of the cases, as described [23, 24]. No suspicious clinical symptoms or intra-operative observations were noted in the adenocarcinoma of lacrimal sac. On the

basis that only one case of preoperatively unsuspected malignant neoplasia were diagnosed histologically out of 275 specimens, the authors of this study recommend the selective biopsy of the lacrimal sac when there is clinical or intraoperative suspicion of a tumor.

The first limitation of the study is the number of cases. Larger sample size could make it possible to more accurately evaluate the frequencies of the secondary changes of ANDO and its associations with the clinical appearance. An insufficient sample size and biopsy specimens only from the medial-posterior wall of the lacrimal sac could be the reason why we did not find any specific inflammatory changes such as sarcoidosis or Wegener granulomatosis in our patients, as described in other studies [9, 10, 14]. Additionally, a larger sample size may have revealed a difference in the symptom duration between tumor group and the non-specific pathology group. Second limitation would be that data on the lacrimal system irrigation would add value to this study by improving the preoperative evaluation of the patients.

The authors conclude that chronic non-granulomatous inflammation of the lacrimal sac wall was the most frequent histological findings in cases associated with ANDO; however, three cases of tumors were diagnosed, and two of them were potentially lethal. The complaints of the patients were non-specific, and no associations between the histological findings, clinical presentation, and history of the disease were observed. Because the rate of malignant neoplasia was low, the authors support that a lacrimal sac biopsy is indicated only in the clinically or intraoperatively suspicious cases of ANDO.

List Of Abbreviations

ANDO: acquired nasolacrimal duct obstruction; DCR: dacryocystorhinostomy.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from patient for publication of this case report and accompanying images.

Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AM interpreted data, drafted the manuscript, coordinated data collection. DP coordinated data collection and analysis. AK coordinated data collection and analysis. RJ interpreted data and drafted the manuscript. AR contributed to data acquisition. AC coordinated data collection. JB interpreted data. RSA coordinated data collection and analysis. All authors discussed the results and contributed to the final manuscript. All authors have read and approved the manuscript.

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Figures

Figure 1

Hematoxylin/eosin (H/E) staining of the specimens. A Chronic inflammation: dense infiltration of plasmacytes (arrows) with some lymphocytes (short arrows in the lower right part) under a desquamated epithelium. H/E. B Acute inflammation: necrotic debris with some epithelium (in the center), granulocytes (below; short arrows), and calcification granules (arrow in the upper part). H/E. C Active chronic inflammation: mixed inflammation (plasmacytes – arrows, lymphocytes – short arrows, granulocytes – arrowheads) in the subepithelial stroma and some intraepithelial granulocytes (stars).

H/E. D Fibrosis: fibrotic tissue with calcification (arrow) in the center without any inflammatory cells.
H/E.

Figure 2

Tumor histological findings. A. Eccrine spiradenoma. Magnified image of a hematoxylin/eosin (H/E) stained tissue. B. The epithelial cell Ki67 proliferative index of the eccrine spiradenoma was 4%. C. Adenoid cystic carcinoma. Magnified image of a H/E stained tissue with a secretion in the ductal structure lumens. D. Adenoid cystic carcinoma cells were positive for CD117.

Figure 3

Chronic lymphocytic leukaemia / small lymphocytic lymphoma. A-B tear sac tissue section illustrating a diffuse and focally nodular pattern of lymphocytic infiltration composed of small and round lymphocytes, with distinct clumped chromatin. (H/E). Immunophenotype: CD20+ (C), CD5+ (D), CD23+ (E), Ki67 proliferative activity <15% (F).