Original Article

Assessment of the Relationship between Primary Nasolacrimal Duct Obstruction and Nasal Mucosal Goblet Cells

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ABSTRACT

Background and Objectives: **Primary acquired nasolacrimal duct obstruction (PANDO) is a common ocular problem. Clinical presentation can range from simple tearing to a life-threatening condition. The exact pathophysiology of obstruction is not completely understood. In this study, the relationship between PANDO and nasal mucosal goblet cells was investigated.**

Materials & Methods: **In this case-control study, 15 subsequent patients with PANDO were enrolled. Patients were operated with endoscopic dacryocyctorhinostomy. A small piece of nasal mucosal biopsy sample was obtained from inferior turbinate. The samples were prepared and stained for mucin. Goblet cells were counted in the specimens. The results were compared with the nasal mucosa of 15 normal persons who were underwent rhinoplasty surgery as control group. Data were analyzed by SPSS version 16 software and were assessed using t-test, analysis of variance, and Pearson correlation test.**

Results: **In patients group, 13 cases (86.7%) were female and 2 cases (13.3%) were male. The mean age was 42.4±14.3 years (range, 23-68 years). In control group, 9 persons (60%) were female and 6 persons (40%) were male. The mean age was 35.5±12.1 (range, 19-58 years) (*P*>0.05). All patients had epiphora, and 66.7% of patients had purulent discharge. Duration of symptoms ranged from 1 year to 12 years. The number of goblet cells of the nasal mucosa in patient group was significantly higher than the control group (*P*<0.001). Inflammation was not related to goblet cell numbers**

Conclusion: **According to findings of this study, goblet cells have important role in inflammatory process and perhaps obstruction in nasolacrimal duct.**

Keywords: Goblet cell, Lacrimal Duct Obstructions, Inflammations

Introduction

Primary nasolacrimal duct obstruction (PANDO) is actually the most common acquired nasolacrimal duct (NLD) problems in adults. The disease may be expressed by chronic tearing (epiphora), purulent discharge or mild and recurrent conjunctivitis, chronic or acute dacryocystitis. Main stimulus of this process is yet unclear (1). The syndrome is more prevalent in adult white pre-menopausal females (2).Obviously any inflammation may cause narrowing of the duct and accumulation of cellular remnants and debris in the lumen. This vicious cycle may leads to continuous inflammation and congestion and finally evolution of permanent scar in nasolacrimal lumen and even if not treated properly may cause impending and potentially lethal orbital cellulitis (3). Pseudo-stratified columnar epithelium has covered posterior two third of the nasal cavity, but ciliated and non- ciliated columnar cells, goblet cells that producing mucin, and basal cells are the most important parts. The ratios of columnar cells to goblet cells are approximately 5/1. Goblet cells produce thick mucin that entrapped small debris and infected foreign bodies. The superficial parts of the mucin layer in the sino nasal cavities are produced by goblet cells and sub mucosal glandular cells indeed. The third part of the nasal mucosa is the olfactory epithelium (4,5). External and endoscopic Dacryocystorhinostomy (DCR) is the treatment of choice in these patients. The histopathologic presence of subepithelial scarring and shrinkage in nasal mucosa biopsy specimens was associated with longer time intervals between dacryocystitis and surgery as well as with less favorable postoperative outcomes, therefore the patients should undergo rather early surgery following the regression of acute inflammation(6).

In the study of Mauriello (1992) on 44 patients, the lacrimal sac and nasal mucosa adjacent to the osteotomy were examined histologically. Chronic inflammatory changes of the lacrimal sac and varying degrees of fibrosis were seen in most of the cases, and the pathology of the lacrimal sac and nasal mucosa was similar to that of the nasolacrimal duct in complete nasolacrimal duct obstruction (7). Increased numbers of goblet cells has reported in various diseases. Cystic fibrosis and chronic bronchitis are the examples for goblet cells metaplasia and hyperplasia and increased mucin secretion by goblet cells (8-10). Saetta *et al.* has demonstrated the role of goblet cells in functional obstruction in peripheral air ways (11). Nakaya *et al.* has demonstrated the role of goblet cells hyperplasia in nasal airways remodeling(12). There are few studies about the relationship between goblet cells and the degrees of nasal mucosal inflammation and the nasolacrimal duct obstruction in the literature. The aim of this study was to assess the relationship between PANDO and nasal mucosal goblet cells.

Materials and Methods

In this case control study, 15 consecutive cases with PANDO were enrolled. Coronal CT scanning of the nasal and paranasal sinuses was made in all the cases, and then they were examined by an ophthalmologist and an ear, nose, and throat specialist to ensure that the obstructions are mainly primary. The control group was selected from 15 healthy volunteers that have referred for cosmetic rhinoplasty without any evidence of nasolacrimal duct or sinonasal problems. The study was approved by the Shahed University Ethical Committee. A written informed consent was obtained from all participants before the study. Exclusion criteria were included, history of any surgery on nasolacrimal system or nasal cavity, history of traumatic orbital of facial fracture, presence of trichiasis or entropion, and NLD obstruction secondary to tumors, lithiasis, sarcoidosis or Wagner granulomatosis. Standard endoscopic DCR were performed in the cases and standard rhinoplasty surgery was made for the controls. Small pieces of nasal mucosal specimens were excised by endoscopic manner from inferior turbinate mucosa of both groups. Regarding the degrees of inflammation and the numbers of the goblet cells the specimens were stained by hematoxilin & eosine method and were examined by an expert pathologist with a binocular laboratory microscope (Zeiss Standard 20, Germany) and 400 x magnitudes,. The severities of inflammation were divided in 4 sub groups of, no, mild, moderate, and sever inflammation. The numbers of goblet cells were counted up in at least 10 fields and the mean numbers of the goblet cell count were calculated in each microscopic field.

The results of demographic Information about

age, sex, duration of disease, and site of obstruction (unilateral or bilateral) and Physical signs and symptoms, goblet cells count according to the pathologist reports, were rerecorded in an examination chart.

The needed information's about dependent and independent variants were collected. Data were analyzed by SPSS version 16, *t*- test, and analysis of variance. The findings were considered significant when *P* was ≤ 0.05.

Results

In demographic information age range of the cases were between 23-68 years (mean ± SD = 42.4 ± 14.3), and of the controls were 19-58 years (mean ± SD = 35.5 ± 12.1). Also regarding the sex distribution in the cases, 13 were female (86.7%) and 2 were male (13.3%) and in the controls 9 were female (60%) and 6 were male (40%). There were no significant differences between demographic information of the two groups. In clinical problems, 100% of the cases had epiphora, and other complaints were included swelling and redness over the lacrimal sac, burning,

pain, and intermittent purulent discharge. 12 cases had unilateral and 3 cases had bilateral NLD obstruction. Considering the age, sex, laterality, unilateral or bilateral obstruction and the numbers of goblet cells and their relationship with the pathogenesis of the NLD obstruction, the Pearson correlation, and the *t*- test was not significant. NLD obstruction were unilateral in %80 (12 cases) and bilateral in 20% (3 cases) of the patients, in addition the site of obstruction in 66.7% of the patients were in the left sided. Among 15 cases, DCR surgery was made on the left sided in 10 cases and on the right sided in 5 cases. The Duration of obstruction were between 1-12 years (mean ± SD =4.6 ± 2.9).

In addition to the mentioned signs and symptoms, according to the pathological reports, degrees of inflammation were divided in to 4 subgroups with, no, mild, moderate, and severe inflammation in the excised nasal mucosal specimens from inferior turbinate. The absolute and relative degrees of inflammation are listed in the Table-1. There were no significant differences between the degrees of inflammation in the cases and controls (*P*>0.05).

Table1: Absolute and relative Distribution of the degree of inflammation in the cases and controls

Groups	Cases		Controls	
Degree of inflammation	Absolute frequency	Relative frequency	Absolute frequency	Relative frequency
No	3	20	2	13.3
Mild	6	40	7	46.7
Moderate	4	26.7	4	26.7
Severe	2	13.3	2	13.3
Sum	15	100	15	100

There were no significant differences between the degrees of inflammation in the cases and controls (*P*>0.05).

The numbers of goblet cells in the cases and controls were classified according to their frequency in five groups by each five numbers interval. The relative and absolute frequencies of distribution of the goblet cells numbers in the pathologic specimens of the nasal mucosa of both groups are showed in Table-2. Higher grades of inflammation in the controls were

not accompanied by NLD obstruction while in the cases even in the lower grades of inflammation; significantly, higher numbers of goblet cells and NLD obstruction were encountered. Independent from the degrees of inflammation the mean numbers of the goblet cells in the cases were 12.2 and in the controls were 3.07, this difference was statistically significant by *t* test (*P*<0.001).

In the cases, mean numbers of goblet cell in male, were 17.5 ± 3.5 and in females were 11.38 ± 5.7, the

difference was not significant. In addition, there were no correlations between the numbers of goblet cells and the duration of NLD obstruction and the ages of the patients by Pearson correlation test (*P*>0.05). There were no significant differences between the mean numbers of goblet cells in unilateral (mean=3.2) or bilateral (mean=2.3) form of NLD obstruction by *t*-test (*P*>0.05). In addition, the mean numbers of goblet cells in the right sided (mean=4.4) or left sided (mean=2.4) nasal mucosa were not significantly different by *t*-test (*P*>0.05). Table 3 shows that although each degree increased in the severity of inflammation in all biopsy specimens was accompanied by means of an increased in the mean goblet cells count, but this finding was not statistically significant by variant analysis test.

Table 2- Absolute and relative Distribution of the goblet cell numbers in the cases and controls

Groups	Cases		Controls	
Frequency of goblet cells	Absolute frequency	Relative frequency	Absolute frequency	Relative frequency
0-4	1	6.7	10	66.7
5-9	4	26.7	3	20
10-14	4	26.7	2	13.3
15-19	5	33.3	0	0
20 or more	1	6,7	0	0
sum	15	100	15	100

Mean numbers of the goblet cells in the cases were 12.2 and in the controls were 3.07, this difference was statistically significant by *t* test (*P*<0.001).

Table 3: Mean distribution of goblet cells and degrees of inflammation

Degrees of inflammation	Frequency	Mean numbers of goblet cells	Standard deviation
No	3	8.6	1.1
Mild	6	9.6	6.2
Moderate	4	16	2.7
Severe	2	17.5	7.7

Although the mean numbers of goblet cells increased by the degrees of inflammation in the cases and controls but this finding was not significant by variance analysis test.

Discussion

The pathologic findings of this study showed that regardless of the degrees of inflammation, the numbers of goblet cells in the nasal mucosa of the patients with PANDO are significantly higher than the normal controls.

In parallel with many other studies, findings of this study also showed that the PANDO in adults is more frequent in female than in male (up to 2/1 or more) (13). In this study, the mean age of the cases were 42.4 years. The mean age range of the patients in the study of Lew, *et al.* was 44.8 years (14) and it was 57.4 years in the study of Hind *et al.* (6). In an evaluation of NLD obstruction performed by Mandal, *et al.* 2008, the obstruction was more frequent in females than in the males, and the left side was more frequently affected than the right side (15).

In another study in sub acute and acute Eustachian tube pathological reactions, especially tubal occlusion, and chronic diseases, such as active chronic otitis and in secretory otitis media, the goblet cell density were apparently increased (16). Larsen *et al.* pathologically noticed that there are marked differences in the distribution of epithelium and goblet cell density between anterior and posterior polyps and the goblet cell density was highest in hyperplastic pseudostratified epithelium, illustrating that the epithelium constantly changes under the influence of air current, contact with other polyps, infection, growth, and age of the polyp as well as other unknown factors (17). Petruson (1994) proved that the number of goblet cells in the normal mucosa in the paranasal sinuses is comparable

to that of the nasal mucosa and there are relatively few mucosal glands in the normal sinuses, but after induced infections, the number of goblet cells increases significantly (18). Shimizu *et al.* (1996) demonstrated that endotoxin, induces hypertrophic and metaplastic changes of goblet cells in rat nasal mucosal epithelium rather than a hyperplastic change, and this metaplasia is produced by direct conversion of nongranulated secretory cells into the goblet cells (19). Based on the study of Bedrger *et al.* a basal state of nasal goblet cell mucus secretion in non-stimulated healthy people was established (20). Furthermore, it was concluded that the enhancement in mucus discharge, from the inferior turbinate goblet cells of patients with perennial allergic rhinitis, was attributed to a non-hyperplastic increase of nasal goblet cell functional activity (20). Saetta *et al.* showed that the smokers with both symptoms of chronic bronchitis and chronic airflow limitation compared with non smokers, have an increased number of goblet cells and inflammatory cells in the epithelium of peripheral airways (21). Curran *et al.* have recommended anti mucus plaque new medications for the treatment of chronic airway diseases (22). The hyperplasia of goblet cells and increased number of gland openings are most prominent in the rhinitis medicamentosa with chronic hypertrophic rhinitis, this phenomenon may cause impairment of mucociliary transport and may be responsible for the nasal obstruction and posterior nasal drip (23). Based on pathologic evidence of the Sino-nasal mucosa, significant increased goblet cell count reflects the important role of these cells in the pathogenesis of nasal polyposis and systemic factors as much as local factors such as airflow and mucosal contact affect nasal polyposis and sufficient airflow decreased numbers of goblet cells (24). In parallel with these studies, Lei *et al.* demonstrated that long time minimal persistent inflammation in the allergic rhinitis of animal models resulted in some changes of tissue remodeling in nasal mucosa such as increased number of goblet cells and collagen deposition within the basement membrane of epithelium (25). Although these results are in parallel with the findings of the present study, none of them has simultaneously evaluated the effects of nasal mucosal inflammation in correlation with goblet cells count in NLD obstruction.

Moreover, an overview of theses studies shows that the cellular mechanisms including, inflammation, vascular congestion, and edema cause partial obstruction of the NLD. On the other hand, gradual accumulation of cellular debris in an underlying increased goblet cell numbers and mucin secretion leaded to increased inflammation by a vicious cycle in the NLD that may account as an important factor in permanent obstruction.

Conclusion

Due to especial cellular genome, the goblet cells can produce kinds of known mucins in different parts of the body and especially the nasal mucosa that has anatomically connected to the NLD. Therefore, potentially these cells may have an important effect in the occlusion of lacrimal system. Although the possible obstructive effect of this cells may excrete independent from the inflammatory process, but this may take place in parallel and/or coordination with the inflammation. Finally this question must be answered by further studies that weather the increased numbers of goblet cells are primary for NLD obstruction or are secondary to other factors such as decreased air flow rate or other inflammatory reactions?

Acknowledgments

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