



Investigating Estrogen and Progesterone Receptors in the Lacrimal Sacs of Individuals With and Without Chronic Dacryocystitis

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Abstract

Objectives: Chronic dacryocystitis is usually seen in middle-aged or older women, suggesting that decreased estrogen and progesterone serum levels may be a causative factor in the disease pathology. However, the occurrence of the disease in premenopausal females and males suggests that there may be more to the explanation than the level of female sex hormones. The purpose of the present study was to investigate estrogen and progesterone receptor positivity in the lacrimal sacs of individuals with and without chronic dacryocystitis.

Methods: The study group included 50 female and 20 male patients diagnosed with chronic dacryocystitis. Lacrimal sac samples were taken during a dacryocystorhinostomy. The control group comprised 29 cadavers with no evidence of lacrimal system pathology in the health records. The samples were obtained transconjunctivally. Lacrimal sac samples from both groups were stained with the estrogen and progesterone receptor protein antigen. Fisher's exact test and a chi-square test were used to compare the receptor positivity results of premenopausal and postmenopausal women, and samples of those with dacryocystitis and cadaver sacs without the disease.

Results: In the control group, estrogen receptor positivity was observed in the samples of 2 premenopausal females. In the study group, estrogen receptor positivity was seen in 4 premenopausal females. There was no significant difference in estrogen receptor positivity between the premenopausal and postmenopausal female groups ($p=0.41$). A similar result was not established between the premenopausal and postmenopausal females in case group ($p=0.056$). No comparison was made of the progesterone receptor because only 1 example of progesterone receptor positivity was found in a premenopausal female in the dacryocystitis group.

Conclusion: Estrogen receptor positivity did not seem to be a factor in chronic dacryocystitis physiopathology.

Keywords: Dacryocystitis, estrogen receptor, inflammation, lacrimal sac, progesterone receptor.

Introduction

Chronic dacryocystitis is a long-lasting, non-infectious inflammation of the lacrimal sac that leads to epiphora (1). It is more common in females than males (2), which may be due, at least in part, to the anatomically narrower nasolacrimal duct in females (3). The exact pathophysiology is not clear.

Age seems an important factor, since most chronic dacryocystitis patients are middle-aged, although young individuals may also be affected. A lack of the estrogen hormone may be a cause and explain the presence of the disease in some males, (4) but this does not explain the presence of chronic dacryocystitis in premenopausal females. The presence or

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absence of the estrogen receptor in the lacrimal sac, rather than the hormone, may be a factor in the development of chronic dacryocystitis. The goal of the present study was to investigate and compare the presence of estrogen and progesterone receptors in the lacrimal sacs of individuals with and without chronic dacryocystitis.

Methods

This case-control study was reviewed and approved by the Local Ethics Committees. Informed consent was obtained from all of the participating patients. For the case group, 50 female patients (26 premenopausal and 24 postmenopausal) and 20 male patients who had experienced eye tearing for a long period of time were enrolled. A complete ophthalmic examination was performed, followed by a Jones I test and lacrimal irrigation test. External dacryocystorhinostomy was performed using the Dupuy-Dutemps-Bourguet technique. A lacrimal sac tissue sample approximately 3x4 mm in size was removed from each patient.

The control group comprised 20 female (10 premenopausal and 10 postmenopausal) and 9 male cadavers. These individuals did not have any known previous lacrimal disease and were at least 18 years of age. Specimens of the lacrimal sac were obtained using a transconjunctival approach.

The tissue taken from both groups was fixated in buffered formalin solution, then dehydrated with alcohol and embedded in paraffin. The tissue sections were prepared for pathological examination: A portion of the sections was stained with hematoxylin and eosin dye, and microwave antigen retrieval was performed for the remainder, followed by a streptavidin-biotin application to reveal the estrogen and progesterone receptors (Dako Omnis; Acilent, Santa Clara, CA, USA). The results were grouped as estrogen receptor-positive (Fig. 1) or -negative and progesterone receptor-positive (Fig. 2) or -negative. The hematoxylin and eosin stain samples were examined for signs of inflammation (Fig. 3). The case and con-

rol groups were divided into groups of males and females. The female group was further divided into premenopausal and postmenopausal individuals. The results were compared using the Fisher's exact Chi-square test.

Results

The mean age of the patients in the control group was 47.64 ± 16.019 years and the mean age of the patients in the case group was 50.53 ± 4.571 years. The mean age of the men and the premenopausal and postmenopausal women in both the control and the case groups is provided in Table 1.

The positive and negative stain results are shown in Table 2 for the case group and in Table 3 for the control group.

Progesterone receptor positivity was found in only 1 premenopausal female in the case group. Estrogen receptor positivity was found in 1 lacrimal sac of a male in the control group; the remainder were estrogen receptor-negative. No estrogen receptor staining positivity was found between the case and control group. In the case group specimens, various levels of fibrosis and vascular and lymphocytic proliferation were observed.

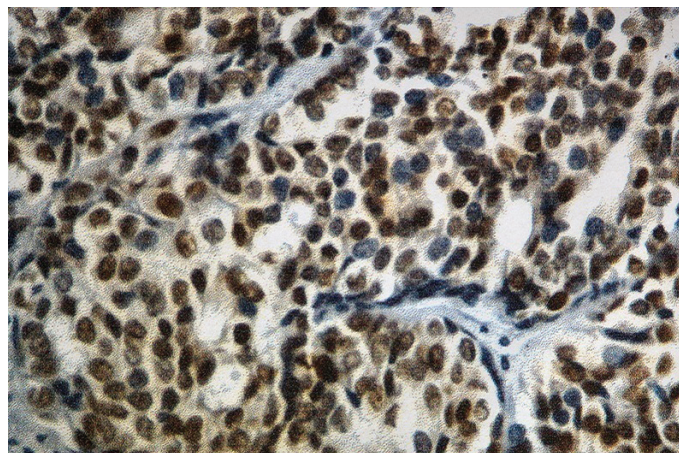


Figure 2. Progesterone receptor positivity in the lacrimal sac of a premenopausal female (Dako Omnis; Acilent, Santa Clara, CA, USA).

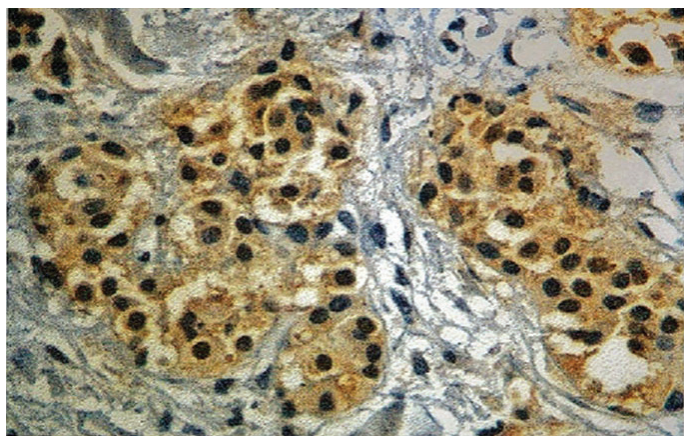


Figure 1. Estrogen receptor positivity in the lacrimal sac of a premenopausal female (Dako Omnis; Acilent, Santa Clara, CA, USA)

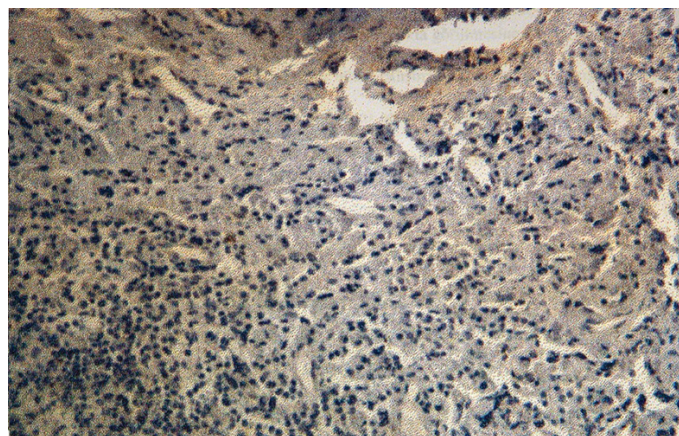


Figure 3. Inflammation and fibrosis in a lacrimal sac (hematoxylin and eosin).

Table 1. Mean ages and ranges of both groups premenopausal, postmenopausal females and males

	Case group	Control group
Premenopausal	33.125±4.988 (27-40)	50.533±14.57(27-82)
Postmenopausal	57.833±7.802 (49-72)	31.00±6.74 (23-38)
Males	50.533±14.571 (27-82)	31.00±6.74 (23-38)

Table 2. Results of lacrimal sac tissue staining for estrogen receptors in the case group females

	Positive staining	Negative staining
Premenopausals	4	22
Postmeopausals	0	24

Table 3. Results of lacrimal sac tissue staining for estrogen receptors in the control group females

	Positive staining	Negative staining
Premenopausals	2	8
Postmeopausals	0	10

Discussion

Chronic dacryocystitis is commonly seen in middle-aged women (5). The mean age of the cases in our study was 47.64±16.019 years, which was similar to the results of Yang and Majidaee (6). The age range was also similar. But as noted here and in previous research, the disease can also occur in younger individuals. In the pathology sections, we observed established fibrosis and various degrees of lymphocyte and plasmocyte infiltration in the sac wall of the chronic dacryocystitis patients, similar to the findings of Mauriello et al. (7-9).

Inflammatory infiltrates may be due to autoimmune disease (10). Estrogen may affect the immune system; for example, hormones may be related to Schögren's syndrome (11). Furthermore, it has been established that estrogen has an influence on prolonged cell activity in rheumatoid arthritis and systemic lupus erythematosus (12). The uveitis rat model conducted by Buggage et al. (13) demonstrated that estrogen could be useful in the pre-treatment of uveitis. The study also demonstrated a regulatory effect of estrogen in inflammation.

In menopause, the monocyte level in human blood increases; however, the level of estrogen-receptors in peripheral monocytes decreases (14). This suggests that estrogen may affect monocytes, but the roles of sex hormones roles in immunity are not yet well understood, considering that our receptor-positive cases were premenopausal females, not postmenopausal.

During the menstrual cycle, changes occur in the corneal thickness, the volume of lacrimal tears, and the velocity of tears through the nasolacrimal duct (15). Tear production increases during menstruation, and with additional factors, this may enhance stasis and consequently result in infection. However, this does not explain disease in postmenopausal and male cases.

Studies have examined estrogen receptors in ocular and periocular structures. An experimental study by Wickham et al, (16) conducted with male and female rats, mice, hamsters, and guinea pigs, found sex steroid receptors and mRNA in the ocular structures of all of these animals. There are estradiol receptors in the human nasal mucosa, oral, parotid glands, and submandibular glands (17). We found only 1 example of research about estrogen receptors in the human lacrimal sac. Gupta et al. (18) performed a dacryocystorhinostomy on 20 individuals with dacryocystitis and examination of the tissue did not reveal estrogen and progesterone receptor positivity. The diagnostic method used was similar to that of our study and the results appear to support our findings. It was interesting for us to found estrogen receptor positivity in only premenopausal females, but this weakens our theory for the other receptors. Only 1 lacrimal sac tissue sample of a premenopausal female in the case group stained positively for the progesterone receptor; thus, we could not perform a statistical analysis for that hormone receptor.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Involved in design and conduct of the study (OB); preparation and review of the study (HB); data collection (HHU); and statistical analysis (YK).

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