CASE REPORT

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Bilateral lacrimal caruncle lesions

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ABSTRACT

A 65-year-old man was referred to our hospital for the treatment of a lesion on the medial lacrimal canthus of both eyes. He had a history of perinuclear anti-neutrophil cytoplasmic antibodies, i.e., pANCA-positive interstitial pneumonia. Orbital magnetic resonance imaging excluded space occupying lesions, and laboratory testing excluded thyroid-related diseases. The masses were excised, and histopathological examinations showed sebaceous gland hyperplasia and inflammatory changes around the gland. In addition, the specimen from the left eye showed a retention cyst possibly caused by an infection. It was also possible that the use of steroid was involved in the development of the lesions. A relationship between the ANCA and the lesions was not completely eliminated.

Key Words: lacrimal caruncle, perinuclear anti-neutrophil cytoplasmic antibodies (pANCA), interstitial pneumonia, inflammation, sebaceous gland

INTRODUCTION

The lacrimal caruncle, or caruncula lacrimalis, is a small, pink, globular nodule at the medial canthus of the eye, and it consists of skin, hair follicles, sebaceous glands, sweat glands, and accessory lacrimal tissue.[1)] Lesions of the caruncle are rare, and the lesions developing from the caruncle are very diverse making their clinical diagnosis very difficult. The lesions can be neoplasms,[2-4)] inflammation-related,[2-4)] or cysts,[4,5)] and these are derived from the different tissues making up the caruncles. Lesions of the lacrimal caruncles can also be associated with systemic abnormalities, e.g., hyperthyroidism,[6)] lymphomas,[5)] and neurofibroma.[7)] The vast majority of lesions of the caruncle are benign but if malignant they can be fatal.

The caruncles do not have direct effects on visual function, thus they seldom attract interest even from ophthalmologists. We have examined a patient with a mass on the caruncle of both eyes, and they were initially suspected to be related to perinuclear anti-neutrophil cytoplasmic antibodies (pANCA).

The aim of this report is to describe the lesions on the lacrimal caruncle of both eyes possibly associated with ANCA-positivity and/or the use of steroid.

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CASE REPORT

A 64-year-old man had a pulmonary shadow detected at his annual physical examination. One year later, he developed a productive cough, and he consulted a physician. His laboratory tests showed a high level (30.1 U/ml) of myeloperoxidase anti-neutrophil cytoplasmic antibodies (MPO-ANCA) suggesting the presence of an autoimmune disorder, e.g., microscopic polyangiitis. The level of Krebs von den Lungen-6 (KL-6) was also high at 1480 U/ml, and a lung biopsy with the video-associated thoracic surgical technique was performed. Histopathological examination of the biopsy specimen showed the usual interstitial pneumonia pattern. His laboratory data did not indicate renal involvement. Taken together, a diagnosis of perinuclear ANCA (p-ANCA) positive interstitial pneumonia was made, and prednisolone was started.

Six months after the diagnosis and treatment, the patient noticed a mass at the medial canthus of both eyes, and he was referred to our hospital. He did not report any ocular symptoms including epiphora. Our examination showed that his decimal best-corrected visual acuity was 0.16 in the left eye, and the reduction was due to an earlier diagnosis of polypoidal choroidal vasculopathy which had been treated by photodynamic therapy.

The size of the mass was 10 mm × 4 mm in the right eye and 10 mm × 6 mm in the left eye. The surface was whitish and smooth with a papilloma-like extrusion on top of the mass of the left eye. (Fig. 1a-d). Magnetic resonance imaging showed no intraorbital lesions or metastasis, and the extraocular muscles were normal. Laboratory tests showed that the levels of serum thyroid hormones and thyroid-related antibodies were within normal limits, i.e., free T3, 2.97 pg/ml;

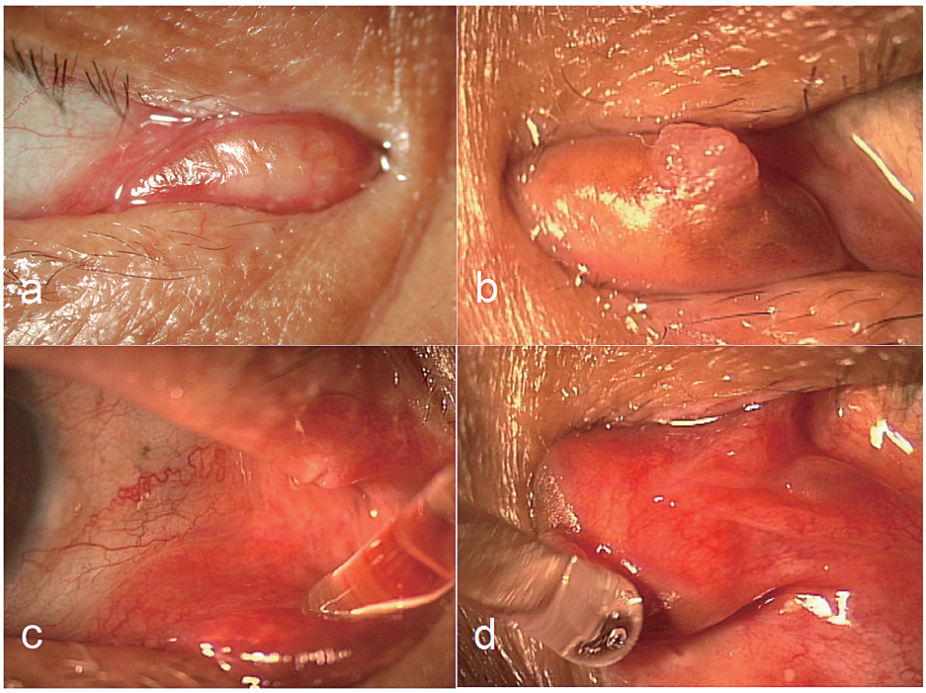

Fig. 1 Clinical appearance of the lacrimal caruncles of a 65-year-old patient.
a: Appearance of a whitish caruncle of the right eye before surgery.
b: Appearance of the left caruncle with a papillomatous tumor on the surface.
c: and d: Root of the caruncle of the right eye (c) and left eye (d).

free T4, 1.18 ng/dl; thyroid stimulating hormone, 1.14 μU/ml; anti-thyroid stimulating hormone receptor antibody, 0.7%; and anti-thyroid peroxidase antibody, 0.3 IU/l.

The masses were totally excised, and histopathological examinations of both specimens showed abnormal dilations of the tubular tissues surrounded by inflammatory lymphocytes (Fig. 2a). The specimen from the left eye contained sulfur granules and neutrophils. The lumens of the tubes were lined with nonkeratinizing squamous epithelial cells with goblet cells (Fig. 2b). The sebaceous glands were hyperplastic with lymphocytic infiltration around the glands and edematous. The epithelium had a thick basal cell layer (Figs. 2c and 2d). No vasculitis, giant

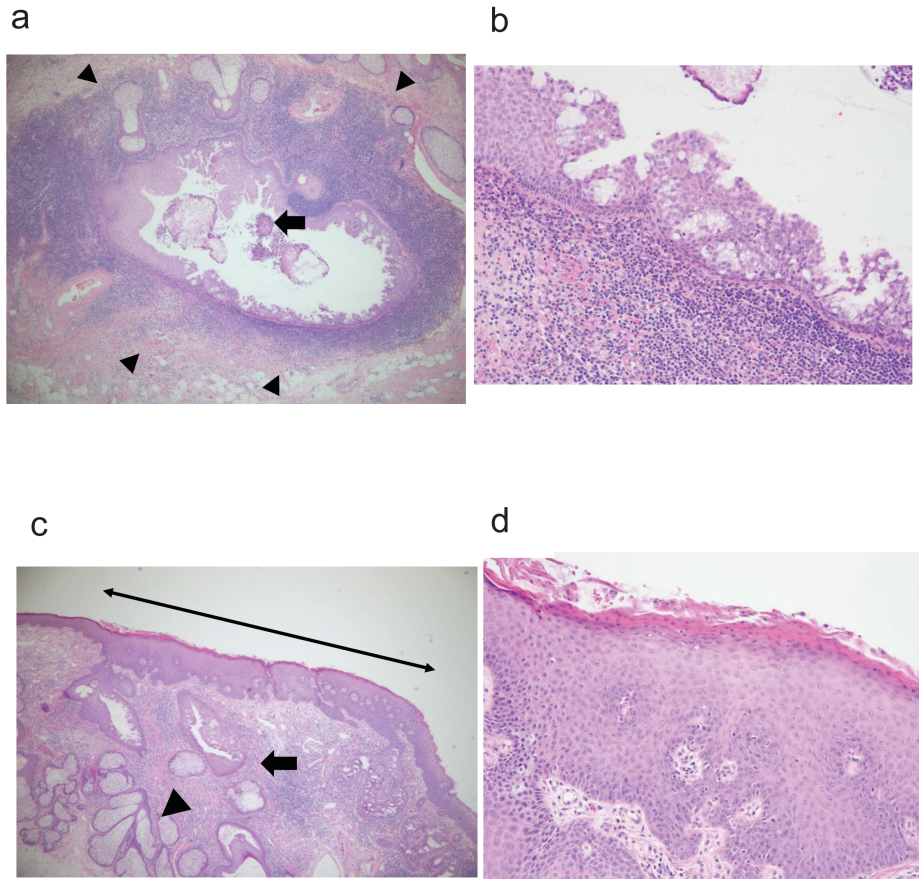

Fig. 2 Histopathology of excised caruncular tissues.
a: Left eye. Central duct of left eye with a thick wall (arrowheads) containing sulfur granules in the cavity (arrow). The sebaceous gland surrounds the duct. Lymphocytes have proliferated and infiltrated into the wall. Hematoxylin-eosin, original magnification, ×40.
b: Left eye. Epithelium of the dilated duct (arrow) is hyperplastic with a mixture of squamous cells and glandular cells with lymphocytes surrounding the wall. Hematoxylin-eosin, original magnification, ×200.
c: Right eye. Lacrimal caruncle with epithelial hypertrophy (long arrow). This specimen also shows the sebaceous gland (arrow head) and its duct with a thick wall with lymphocytic migration (arrow). Hematoxylin-eosin, original magnification, ×40.
d: Right eye. Epithelial hypertrophy with basal cell proliferation. Hematoxylin-eosin, original magnification, ×200.

cell, or granulomatous tissue was found. The diagnosis made by the pathologist was lacrimal caruncle inflammation with hyperplasia of the sebaceous gland and dilation of the tubes for both eyes with an infected retention cyst in the left eye.

The patient was followed for 4 years, and no recurrences occurred. The patient was satisfied with the cosmetic results.

DISCUSSION

Earlier studies have shown that lacrimal caruncle lesions can be due to inflammation,[2-4] neoplasms or pseudoneoplasms,[2-4] and cysts.[4,5] Bilateral inflammation of the caruncles can also be an antecedent sign of systemic diseases such as thyroid ophthalmopathy.[6]

In our case, histopathology showed bilateral lacrimal caruncle hyperplasia and inflammation although the interorbital histology was slightly different. Sebaceous gland hyperplasia and the dilation of the sebaceous ducts were more obvious in the right eye. The periductal inflammation and edema were similar in both eyes, however an infected retention cyst was seen only in the left eye.

These findings suggested that the inflammatory lesions were probably caused by systemic mechanisms with the MPO-ANCA antibodies as the most likely suspect. Otherwise, simultaneous bilateral infection or ductal obstruction due to the hyperplasia of the sebaceous gland which might have been caused by the systemic use of steroids[8-10] may be the reason of the inflammation.

The ANCA antibodies can cause granulomatous inflammation and vascular destruction. One of the more common forms of the disease is known as granulomatosis with polyangiitis (GPA), traditionally referred to as Wegener's granulomatosis, which is known to be related to PR3-ANCA.

In this case, the detected ANCA was an MPO-ANCA and the lung biopsy did not show any relationship to GPA. However, both ANCAs can be associated with ocular alterations. Multiple authors have reported on MPO-ANCA associated ocular symptoms; e.g., scleritis, uveitis, peripheral keratitis,[11] ischemic optic neuropathy,[12] orbital pseudotumor,[13] and choroidal tumor.[14] Masuda *et al.*[14] reported that the biopsy specimen of the choroidal tumor showed the necrotizing vasculitis and granulomatous inflammation. Thus, MPO-ANCA could cause GPA-like granulomatous changes. Harper[15] reported that 43% of patients who were diagnosed with ANCA-positive vasculitis later had ocular involvements as the first clinical sign. According to the report, among their patient group who had only ocular symptoms at the first visit, 64% were cANCA positive and 36% were pANCA positive.

It is also known that there are limited and localized forms of GPA.[16] In the same report by Harper,[15] they say that the diagnosis of ANCA-related ocular signs could be made if the tissue had more than three of the following pathological findings even without ANCA positivity; granulomatous inflammation, collagen necrosis, plasma cells, vasculitis, eosinophils, neutrophils, and nuclear dust.

As for GPA diagnosis, Kalina *et al*. reported[17] that there were marked differences between orbital biopsy and nasal biopsy of the same GPA case with the nasal biopsies showing more extensive inflammation, vasculitis, and necrosis than the orbital specimens. Thus, the presence of even mild inflammation in an orbital biopsy cannot exclude an ANCA-related ocular lesion when the ANCA serologic test results are positive. Although we did not find positive evidence for angiitis, we could not completely eliminate the idea that the lesions in our patient were ANCA-associated.

In this case, interstitial pneumonia was not diagnosed with GPA, and his laboratory data did not reveal PR3-ANCA, and we did not find positive evidence of any of these, however, we

considered inflammation due to ANCA because of the above mentioned reasons. The ANCA-specific findings might be resolved after the use of steroids.

The cyst in the left eye contained sulfur granules which indicated that the inflammation around the cyst may have been caused by an infection, possibly secondary to the use of the immunosuppressant. The sebaceous gland hyperplasia may have been due to the use of corticosteroids because it has been reported that corticosteroids reduce the androgen secretion and this enhances the proliferation of the cells of the sebaceous glands.[8-10] However, the sebaceous gland hyperplasia and obstruction of ducts could not be the only explanation for the inflammation around the ducts and the swollen caruncles. Thus, we cannot state conclusively that the swollen caruncles were caused by the use of steroids.

In conclusion, the lesions on the caruncles were probably caused by inflammation in association with serological pANCA positivity. By recognizing this symptom as one of the ANCA-associated conditions, and if the orbital lesion is treated when the condition is confined, we will be able to prevent this local disease from progressing to a fatal systemic condition.

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Conflict of interest: none

REFERENCES

1) Duke-Elder S. The anatomy of the visual system. In:The anatomy of the visual system., edited by Duke-Elder S. 557–558, 1961, C.O. Mosby Co St. Louis.
2) Santos A, Gomez-Leal A. Lesions of the lacrimal caruncle. Clinicopathologic features. *Ophthalmology,* 1994; 101: 943–949.
3) Solari HP, Ventura MP, Orellana ME, Novais GA, Cheema DP, Burnier MN, Jr. Histopathological study of lesions of the caruncle: a 15-year single center review. *Diagn Pathol,* 2009; 4: 29–32.
4) Shields CL, Shields JA, White D, Augsburger JJ. Types and frequency of lesions of the caruncle. *Am J Ophthalmol,* 1986; 102: 771–778.
5) Levy J, Ilsar M, Deckel Y, Maly A, Pe'er J. Lesions of the caruncle: a description of 42 cases and a review of the literature. *Eye (Lond),* 2009; 23: 1004–1018.
6) Mourits MP, Prummel MF, Wiersinga WM, Koornneef L. Clinical activity score as a guide in the management of patients with Graves' ophthalmopathy [see comments] [published erratum appears in Clin Endocrinol (Oxf) 1997 Nov; 47(5): 632]. *Clinical Endocrinology,* 1997; 47: 9–14.
7) Freedman KA, Tran RM. Neurofibroma involving the caruncle. *Arch Ophthalmol,* 2004; 122: 294–295.
8) Khandwala HM, Vassilopoulou-Sellin R, Logethetis CJ, Friend KE. Corticosteroid-induced inhibition of adrenal androgen production in selected patients with prostate cancer. *Endocr Pract,* 2001; 7: 11–15.
9) Pochi PE. Acne: endocrinologic aspects. *Cutis,* 1982; 30: 212–7, 219.
10) Zouboulis CC, Boschnakow A. Chronological ageing and photoageing of the human sebaceous gland. *Clin Exp Dermatol,* 2001; 26: 600–607.
11) Matsuo T. Eye manifestations in patients with perinuclear antineutrophil cytoplasmic antibody-associated vasculitis: case series and literature review. *Jpn J Ophthalmol,* 2007; 51: 131–138.
12) Shichinohe N, Shinmei Y, Nitta T, Chin S, Yamada Y, Kase M. Arteritic anterior ischemic optic neuropathy with positive myeloperoxidase antineutrophil cytoplasmic antibody. *Jpn J Ophthalmol,* 2010; 54: 344–348.
13) Ogasawara T, Kasamatsu N, Haga T, Kobayashi T, Shibata M, Hashizume I. [A case of Wegener's granulomatosis with orbital inflammatory pseudotumor]. *Nihon Kokyuki Gakkai Zasshi,* 2009; 47: 308–313.
14) Masuda T, Izumi Y, Takeshita H, Kawahara C, Tsuji Y, Kurohama H, *et al*. Granulomatosis with polyangiitis presenting as a choroidal tumor. *Case Rep Rheumatol,* 2015; 2015: 271823.

15) Harper SL, Letko E, Samson CM, Zafirakis P, Sangwan V, Nguyen Q, *et al*. Wegener's granulomatosis: the relationship between ocular and systemic disease. *J Rheumatol,* 2001; 28: 1025–1032.
16) Carrington CB, Liebow A. Limited forms of angiitis and granulomatosis of Wegener's type. *Am J Med,* 1966; 41: 497–527.
17) Kalina PH, Lie JT, Campbell RJ, Garrity JA. Diagnostic value and limitations of orbital biopsy in Wegener's granulomatosis. *Ophthalmology,* 1992; 99: 120–124.