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# Clinical and Imaging Features of Lacrimal Gland Involvement in Granulomatosis with Polyangiitis

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***Purpose:*** Lacrimal gland involvement in granulomatosis with polyangiitis (GPA) commonly accompanies orbital disease, but occasionally may be the sole presentation preceding any other organ manifestation or systemic disease. Diagnosis of orbital GPA, especially in patients with lacrimal involvement as the initial presentation, can be difficult because of nonspecific clinical features and lack of diagnostic specificity on histologic and antineutrophilic cytoplasmic antibody (ANCA) testing. Orbital GPA can be associated with a high morbidity from potential visual loss or rapid progression of latent systemic disease, making early diagnosis important. The purpose of this study was to describe the clinical and imaging features of patients with lacrimal gland involvement secondary to GPA and to compare them with those of other orbital inflammatory conditions in the lacrimal gland fossa.

***Design:*** Retrospective, noninterventional comparative case series.

***Participants:*** Two hundred forty-seven patients who had undergone orbital biopsy over a 21-year period were identified from the Institute of Ophthalmology Pathology database. Sixty-nine patients were found to have orbital inflammatory disease with lacrimal gland involvement, of whom 7 had a final diagnosis of GPA.

***Methods:*** Clinical and imaging features of patients with GPA were analyzed and compared with those of the non-GPA group.

***Main Outcome Measures:*** Features associated with GPA.

***Results:*** The median age at presentation for GPA patients was 30 years (mean ± standard deviation, 36.7±16.7 years; range, 14–57 years). The interval from presentation to definitive diagnosis of GPA ranged from 3 to 20 months (mean, 12.1 months; median, 12 months). Sinonasal involvement was demonstrated in 43% and bony changes were demonstrated in 29% of patients with GPA. A higher proportion of patients with GPA demonstrated sinonasal involvement ($P = 0.011$) and bony destruction ($P = 0.048$) compared with non-GPA patients.

***Conclusions:*** Associated sinonasal involvement and bony changes on imaging are highly suggestive of GPA and should prompt a full diagnostic workup. A high index of suspicion should be maintained, with repeated ANCA testing, biopsy, and imaging where indicated, especially in the younger age group. *Ophthalmology 2015;■:1–5 © 2015 by the American Academy of Ophthalmology.*

Granulomatosis with polyangiitis (GPA), traditionally referred to as Wegener's granulomatosis, is one of the more common antineutrophil cytoplasm antibody (ANCA)–associated vasculitides, characterized by vasculitis mainly affecting the upper and lower respiratory tracts as well as the renal system. However, it can involve any organ system with variable clinical presentation and course of disease. A limited form of GPA involving the head and neck region has been recognized[1,2] that lacks renal involvement[3] and may not progress to systemic disease. Orbital involvement occurs in 45% of patients with GPA during the course of the disease and in 16% of patients can be the presenting feature.[4] Although lacrimal gland involvement often accompanies orbital GPA, isolated lacrimal gland involvement occasionally may be the initial presenting feature, preceding any orbital or systemic manifestation.[5–8]

Diagnosis of orbital GPA, especially in patients with lacrimal involvement as the presentation, can be difficult because of nonspecific clinical features and lack of diagnostic sensitivity on ANCA testing. The histologic picture often can be confusing and may be missed particularly in partially treated disease. In orbital GPA, the classic triad of vasculitis, tissue necrosis, and granulomatous inflammation was seen in only 50% of orbital biopsies.[9]

Serologic testing often demonstrates negative results in the early stages and in the limited form of the disease; whereas 90% of patients with generalized GPA demonstrate positive ANCA results, only 47% with limited disease show positive ANCA results and only 32% show positive cytoplasmic ANCA results.[10] In addition, GPA can have a wide range of imaging characteristics,[11] making it difficult to distinguish from other orbital inflammatory conditions, especially if lacrimal gland



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Table 1. Patient Demographics

| Demographics | Granulomatosis with Polyangiitis | Dacryoadenitis | Sarcoidosis | Idiopathic Orbital Inflammatory Disease |
|---|---|---|---|---|
| Mean age (yrs) | 36.7 | 52.1 | 36.1 | 47.5 |
| Male-to-female ratio | 3:4 | 7:25 | 2:13 | 12:13 |

involvement is the chief presentation. The purpose of the study was to describe the clinical and imaging features of patients with lacrimal gland involvement secondary to GPA at presentation and to compare them with those of other orbital inflammatory conditions in the lacrimal fossa.

## Methods

Ethical approval was granted by the Moorfields and Whittington Research Ethics Committee for a retrospective noninterventional study of patients who had undergone an orbital biopsy over a 21-year period from 1988 to 2009 at Moorfields Eye Hospital and had their results analyzed at the University College London Institute of Pathology. Clinical records were reviewed to obtain details on patient demographics, clinical and imaging features, ANCA status, final clinical diagnosis, treatment, and follow-up interval.

Of the 247 patients who underwent orbital and adnexal biopsy (including lacrimal gland) for orbital inflammatory conditions as in our recent report,[12] a subgroup of 69 patients had mainly lacrimal gland involvement and complete imaging results. Patients were grouped according to their final diagnoses, which were based on a constellation of clinical, laboratory, and histopathologic features. Available imaging data were reviewed by a neuroradiologist (I.D.) for the features that were analyzed: orbital involvement including laterality, involvement of lacrimal gland and adjacent orbital structures, sinonasal involvement (opacification of sinuses, mucosal thickening, bony changes of the sinus walls, and turbinates), bony destruction (nasal septum, nasal cavity, turbinates, and orbital walls), and extraorbital extension. Comparison between groups was performed using the Fisher exact test and comparison of means was performed using an unpaired Student $t$ test, with statistical significance defined as $P < 0.05$.

## Results

Complete clinical and imaging results were available for 69 patients undergoing biopsy for orbital inflammatory conditions with lacrimal gland involvement: GPA accounted for 10%, and non-GPA causes included nonspecific dacryoadenitis (42%), idiopathic inflammatory orbital inflammation (29%), and sarcoidosis (19%). The median age at presentation for GPA patients was 30 years (mean age ± standard deviation, 36.7±16.7 years; range, 14−57 years), and the male-to-female ratio was 3:4. The mean age at presentation was younger than in patients with nonspecific dacryoadenitis, but similar to that of patients with sarcoidosis and idiopathic orbital inflammatory disease (Table 1).

In GPA, the main presenting symptoms were nonspecific lid swelling (88%), orbital pain (71%), proptosis, and limitation of extraocular movements with diplopia (43%). There was a trend toward more pain as compared with patients with sarcoidosis and dacryoadenitis, but this was not significant when compared with non-GPA patients as a whole. Sinonasal symptoms were not always present at presentation (only in 14%) to differentiate from other lacrimal gland inflammation. Ocular inflammation such as scleritis or uveitis was not seen (Table 2).

All 7 patients underwent computed tomography, 3 patients underwent magnetic resonance imaging, and sequential imaging was available in 4 of 7 patients. One patient had bilateral involvement at presentation, with 4 eventually progressing to bilateral involvement on imaging. Associated orbital masses or orbital soft tissue infiltrate were demonstrated in 57% (with the remaining 43% having isolated lacrimal gland involvement), sinonasal involvement was demonstrated in 29%, and bony erosion was demonstrated in 14% at presentation (Table 3). Initial sinonasal involvement included subtotal opacification of the maxillary and ethmoid sinuses and inflammatory mucosal changes, which were noncontiguous with the orbital disease. On subsequent imaging, nasal septal destruction (Fig 1; n = 1) and bony scalloping of the orbital roof (Fig 2; n = 1) were demonstrated in different patients; the former progressed to extensive sinonasal disease with clinically evident collapse of nose bridge. In 3 of 4 of patients with an orbital mass, the lacrimal gland eventually was indistinguishable from the associated masses, and one showed encasement of the optic nerve behind the globe (Fig 3). Two patients underwent extension of the mass into the orbital apex, resulting in compressive optic neuropathy and visual loss. A higher proportion of patients with GPA demonstrated sinonasal ($P = 0.011$) and bony ($P = 0.048$) involvement as compared with non-GPA patients.

The interval from presentation to definitive diagnosis of GPA ranged from 3 to 20 months (mean, 12.1 months; median, 12 months), and the mean follow-up interval was 10.5 months (range, 1−25 months; median, 10 months). Six of 7 patients demonstrated positive ANCA results at presentation, with the remaining patient

Table 2. Presenting Features of Inflammatory Lacrimal Gland Lesions

| Clinical Features | Granulomatosis with Polyangiitis | Dacryoadenitis | Sarcoidosis | Idiopathic Orbital Inflammatory Disease |
|---|---|---|---|---|
| Lid swelling | 88% (6/7) | 96% (28/29) | 92% (12/13) | 90% (18/20) |
| Pain | 71% (5/7) | 34% (10/29) | 23% (3/13) | 60% (12/10) |
| Proptosis | 43% (3/7) | 34% (10/29) | 38% (5/13) | 85% (17/20) |
| Limitation of EOM | 43% (3/7) | 17% (5/29) | 23% (3/13) | 85% (17/20) |
| Sinonasal symptoms | 14% (1/7) | 3.4% (1/29) | 0 | 10% (2/20) |

EOM = extraocular movement.