Isolated noncaseating granulomatous inflammation of the lacrimal sac masquerading as a malignancy

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Abstract:
Idiopathic orbital granulomatous inflammation has been reported before, but isolated involvement of the lacrimal sac is extremely rare. The authors report the case of granulomatous inflammation in a 47-year-old-female limited to the lacrimal sac, nasolacrimal duct (NLD), and adjacent inferior meatal mucosa without any identifiable cause. She presented with rapidly progressive swelling involving the left medial canthal region and a palpable, nontender, nonregurgitant firm mass lesion extending above the medial canthus. The lacrimal irrigation was patent, and imaging showed a heterogeneous mass lesion involving the lacrimal fossa and extending into the NLD. The clinical presentation was suggestive of malignancy arising from the lacrimal sac, but histopathological findings of noncaseating granulomas, multinucleated giant cells, and scattered lymphoplasmacytic infiltrate involving the lacrimal sac and inferior meatal mucosa were suggestive of granulomatous inflammation. Her immunological workup was negative. She responded to oral steroids with complete clinical resolution maintained till 9 months of follow-up.

Keywords:
Granulomatous inflammation, lacrimal sac, malignancy, sarcoidosis

INTRODUCTION

Inflammations involving the lacrimal sac are commonly nonspecific as seen in chronic dacryocystitis.1,2 Specific granulomatous inflammation of lacrimal sac accounts for 1%–2% of lacrimal sac biopsies performed during dacryocystorhinostomy surgery and is attributed mostly to systemic sarcoidosis and granulomatosis with polyangiitis (GPA).1,3 The clinical presentation is similar to any nasolacrimal duct (NLD) obstruction of nonspecific etiology and is usually diagnosed solely based on positive lacrimal sac biopsy in the presence of an identifiable systemic cause. Sarcoidosis constitutes the most common cause of specific granulomatous inflammations involving the lacrimal sac.4-6 The involvement of orbital and adnexal tissues has been reported in the association with systemic sarcoidosis or as a limited form of sarcoidosis.4 The diagnosis of idiopathic granulomatous orbital inflammation is of exclusion and is based upon the histological findings in the absence of any other clinical and systemic association or infectious etiology.4,7,8 To the best of the authors’ knowledge, idiopathic noncaseating granulomatous inflammation involving lacrimal sac mimicking a malignancy has not been reported. The authors report the rare case of lacrimal sac inflammation with emphasis on the existing lacunae in the literature. The patient consented for publishing the photographs, and this report adhered to the Tenets of Declaration of Helsinki and all its subsequent amendments.

CASE REPORT

A 47-year-old female presented with rapidly progressive swelling involving the medial canthal region of the left eye with mild bloodless epiphora of 2 weeks duration. Examination revealed a palpable, nontender, nonregurgitant firm mass lesion measuring 15 mm × 10 mm, extending above the medial canthus and adherent to the subcutaneous tissues [Figure 1a]. Lacrimal irrigation was patent without any blood-tinged discharge. The lacrimal sac was not distended. Imaging revealed a heterogeneous mass lesion involving the lacrimal fossa and extending into the NLD. The clinical presentation was suggestive of malignancy arising from the lacrimal sac, but histopathological findings of noncaseating granulomas, multinucleated giant cells, and scattered lymphoplasmacytic infiltrate involving the lacrimal sac and inferior meatal mucosa were suggestive of granulomatous inflammation. Her immunological workup was negative. She responded to oral steroids with complete clinical resolution maintained till 9 months of follow-up.

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reflux. Her vision was 6/6 with unremarkable anterior and posterior segments in both eyes. Computed tomography (CT) of the orbit showed a heterogeneous mass lesion located in the lacrimal fossa and extending into the NLD causing widening of its bony walls [Figure 1b and c]. There was no involvement of extraocular muscles or orbital tissues. Inferior meatal endoscopy revealed thickening of the nasolacrimal opening and surrounding inferior meatal mucosa without any identifiable mass lesion. In view of the rapidly enhancing mass lesion, short duration of history, firm lesion extending above the medial canthal tendon and the radiological findings, a clinical impression of a lacrimal sac malignancy was made. A large incisional biopsy (5 mm × 4 mm) was taken from both the medial canthal area and the inferior meatal mucosa (2 mm × 2 mm). Incisional biopsy from the mass lesion felt firm did not bleed much, and the overlying skin was uninvolved. Histological evaluation of the biopsy from the lacrimal sac area and nasal cavity showed the presence of scattered noncaseating granulomas in the mucosal layer composed of epithelioid cells, lymphoplasmacytic infiltrate surrounding the epithelioid cells, and scattered multinucleated giant cells without localized vasculitis [Figure 2]. Also noted was the chronic nonspecific inflammation in the submucosal layer of the lacrimal sac. The fibrosis was of mild degree without any lymphoid follicle formation. There were no fungal elements seen on Gomori methanamine silver stain, and Ziehl–Neelsen staining was negative for acid-fast bacilli. Complete blood count revealed anemia with elevated erythrocyte sedimentation rate. Extensive systemic investigations and workup were advised after the unsuspected histopathology findings. There was no evidence of pulmonary involvement (CT chest), and autoimmune workup (anti-neutrophilic cytoplasmic antibodies [ANCAs] [c-ANCA, p-ANCA], anti-nuclear antibodies, rheumatoid factor, Rho and La antibodies, and serum lysozyme) came back negative. Liver function test, renal function test, serum calcium, and urine analysis were normal. Serum angiotensin-converting enzyme (ACE) levels were unremarkable. Mantoux test was positive (had history of bacille Calmette-Guérin vaccination), but quantiFERON gold test was negative. In view of the negative extensive systemic workup, a diagnosis of idiopathic noncaseating inflammation involving lacrimal sac and contiguous nasal mucosa was made. The patient was started on tapering oral steroids (0.5 mg/kg), and the lesion resolved completely without any evidence of recurrence at 9 months' follow-up [Figure 1d]. The patient is being routinely monitored.

**Discussion**

Involvement of lacrimal sac in patients with systemic sarcoidosis is rare, and isolated lacrimal sac involvement is even rarer. The current case had noncaseating granulomatous inflammation on tissue biopsy but in the absence of any clinical or investigative evidence of any systemic or local causes, such as sarcoidosis, systemic vasculitis, foreign body, orbital trauma, and infection, the diagnosis of isolated idiopathic noncaseating granulomatous inflammation was made. Many of such cases when located in the orbit are labeled as probable sarcoidosis or solitary orbital sarcoid but the diagnostic criteria for such nomenclature is unclear. Another interesting finding is of patent lacrimal irrigation despite extensive involvement of lacrimal sac and NLD, which could be due to the uninvolved lumen of the lacrimal system.

Granulomatous inflammations involving lacrimal sac are very rarely reported, and the possibilities include sarcoidosis, eosinophilic angiocentric fibrosis, GPA, and pyogenic granuloma. The negative c-ANCA and p-ANCA, no tissue or systemic eosinophilia, negative autoimmune workup, and no other organ involvement with normal serum ACE and

![Figure 1](image1.png)

**Figure 1:** (a) Clinical photograph showing a mass lesion located at the left lacrimal medial canthus. (b and c) Computed tomography of orbit (axial cuts) show a heterogeneous well-defined lesion situated at lacrimal fossa adjacent to nasal bone, and widening of bony nasolacrimal duct with erosion of its posteromedial plate and maxillary sinus mucosal thickening. (d) One week after surgery, the lesion has resolved completely

![Figure 2](image2.png)

**Figure 2:** (a) Photomicrograph (×10) of the lacrimal sac biopsy shows multiple granulomas with scattered multinucleated giant cells (marked with arrow), epithelioid cells and lymphocytes. Higher magnification (×40) of the nasal (b) and lacrimal sac mucosa (c) show scattered epithelioid cells admixed with lymphocytes. (d) Negative Ziehl–Neelsen staining for acid-fast bacilli
CT chest ruled out specific etiologies for the current case. Idiopathic form of granulomatous lacrimal sac inflammation has not been reported before, and such cases in the orbit are believed to be either a limited orbital sarcoid or granulomatous orbital pseudotumor or as a separate entity “idiopathic granulomatous inflammation.”[9] The idiopathic form of orbital granulomatous inflammation can occur as an isolated condition with unilateral involvement and is considered to behave as any other orbital pseudotumor.[7,8] Surgical debulking of the orbital and lacrimal gland mass alone resolved the inflammation completely in 57% (4/7) of patients in a series of 7 patients diagnosed with idiopathic granulomatous inflammation.[9] One case having extensive orbital involvement in their series recurred following oral steroids and was managed successfully with radiotherapy. The majority of the mass lesions resolved spontaneously following biopsy, which has been observed in both sarcoidosis and idiopathic granulomatous inflammation, as also in the present case. However, the presence of lymphocytic rim around granulomas make sarcoidosis unlikely.[6,8]

Malignancy was the provisional diagnosis before biopsy since the lesion was rapidly growing, painless, nonregurgitant, extended above the medial canthus and had no signs of inflammation. The radiological findings of mass in the lacrimal sac fossa extending into the NLD and its dilatation extended above the medial canthus and had no signs of inflammation. The radiological findings of mass in the lacrimal sac fossa extending into the NLD and its dilatation. The role of routine nasolacrimal sac biopsy during endoscopic dacryocystorhinostomy. Laryngoscope 2020;130:1214-7. The role of routine nasolacrimal sac biopsy during endoscopic dacryocystorhinostomy. Laryngoscope 2020;130:1214-7.

Table 1: Summary of published cases of sarcoidosis involving lacrimal sac

| Author/Year    | Number of cases | Age/ gender | Presenting complaints                                      | Systemic involvement                        | Treatment                                      | Follow-up (months) | Recurrence |
|----------------|-----------------|-------------|-----------------------------------------------------------|---------------------------------------------|-----------------------------------------------|--------------------|------------|
| FSher/1971     | 1               | 41/male     | Epiphora, Acute dacryocystitis                             | Pulmonary, cervical lymphadenopathy         | Systemic antibiotics                          | 6                  | -          |
| Harris/1981    | 2               | 57/female   | Epiphora, Acute dacryocystitis                             | Nose, generalized lymphadenopathy           | Systemic steroids                             | 6                  | Uveitis    |
| Vasquez/1988   | 1               | 51/female   | Epiphora, Acute dacryocystitis                             | No                                          | DCR                                           | 18                 | -          |
| Kay/2002       | 1               | 37/male     | Epiphora, Acute dacryocystitis                             | Pulmonary                                   | Endoscopic DCR                                | NA                 | -          |
| Murphy/2013    | 1               | 34/male     | Epiphora, Purulent discharge                               | Nose and skin                               | DCR with silicone stent with ethmoidectomy   | NA                 | -          |
| Prabhakaran/2007 | 2             | 44/female   | Epiphora, Acute dacryocystitis                             | Pulmonary                                   | Debulking oral steroids                       | 9                  | -          |

DCR: Dacryocystorhinostomy, NA: Not applicable

Table 1 provides the summary of published articles on sarcoid involvement of the lacrimal system. Two cases that did not have elevated serum ACE levels had positive X-rays for hilar adenopathy.[4] In view of extensively negative systemic workup and the histopathology, a diagnosis of idiopathic noncaseating granulomatous inflammation of lacrimal sac would be more appropriate in the present case rather than a probable sarcoidosis, although it cannot be completely ruled out. Whether elevated ACE levels in isolated lacrimal sac sarcoid involvement should be labeled, as sarcoidosis is unclear in the literature. The limited involvement of one organ without any other systemic manifestation has been reported as extrapulmonary sarcoidosis involving lacrimal sac alone.[12] The criteria for orbital and adnexal sarcoidosis should be crisply formulated to avoid the misdiagnosis of such cases under the rubric of sarcoidosis. Reporting of similar cases would provide more insights and further our understanding.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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