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Case report

Conjunctivitis as a manifestation of Wegener's Granulomatosis

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Abstract

Purpose: To report a case of prolonged conjunctivitis as the manifestation of Granulomatosis with polyangiitis (GPA).
Methods: A 37-year-old man presented with prolonged conjunctivitis which had persisted for one month. He was taking medication for his conjunctivitis without any response. A slit-lamp examination revealed conjunctivitis and scleritis in the right eye. Conjunctivitis, 360-degree peripheral corneal thinning, corneal perforation, and scleritis were seen in the left eye.
Results: Emergency penetrating keratoplasty was performed to treat the patient's corneal perforation. After a consultation with the Internal Medicine Department, the patient was suspected of having GPA with positive cytoplasmic anti-neutrophil cytoplasmic antibodies (C-ANCA). Functional endoscopic sinus surgery was performed to treat right maxillary sinusitis, and a biopsy of the maxillary sinus mucosa was obtained. The pathology report showed granuloma and vasculitis with severe acute and chronic inflammation and few eosinophils; thus, the diagnosis was confirmed.
Conclusion: Because prolonged conjunctivitis occurs only rarely in association with systemic disease, ophthalmologists should be aware of this potential, particularly in patients with GPA.

Keywords: Granulomatosis with polyangiitis; Prolonged conjunctivitis; Scleritis; Keratitis

Introduction

Conjunctiva is a translucent mucous membrane covering the anterior part of the sclera and inside of the eyelids. Conjunctivitis is an inflammation or infection of the conjunctiva and is manifested by irritation, itching, foreign body sensation, and watering or discharge.[1,2] The most common causes of conjunctivitis are infections and allergies.[1,3]

Although conjunctivitis infrequently causes permanent visual loss and is a self-limited condition (resolved within 2–5 days in 65% of patients), it can be associated with a systemic disease.[2,3] Differentiating primary conjunctivitis from conjunctivitis secondary to a systemic disease is important.[1,3] Prolonged conjunctivitis can be associated with other conditions such as scleritis or peripheral ulcerative keratitis (PUK). Early recognition and treatment can preserve the eye and the patient's life.[3] Granulomatosis with polyangiitis (GPA), previously known as Wegener's Granulomatosis (WG), is a rare granulomatous vasculitis with incidence of ten cases per million of population. It affects the upper and lower airways and kidneys.[4] Ophthalmic manifestations are common in the disease (up to 58% of patients).[5] Cases of eyelid and conjunctival involvement as the initial manifestations of the disease are rare.[6]

Conflicts of interest: None of the authors has conflict of interest with the submission.

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Case report

A 37-year-old man presented to the ophthalmology emergency room of Khalili Hospital, Shiraz, Iran, an ophthalmology center affiliated with Shiraz University of Medical Sciences, with complaints of itching, foreign body sensation, and tearing. His physical examination was normal except for conjunctival injection and mucopurulent discharge of both eyes. The patient also complained of a 2-year nasal stuffiness, with cough and sputum in his past medical history. He was diagnosed with chronic bronchitis, and a nasal spray was recommended for him. During this time, he also had history of polyarthralgia (not associated arthritis). He was treated for conjunctivitis with topical Levofloxacin and Lotemax and was followed with no significant findings in ophthalmologic examination for about one month. Suddenly, the patient developed ocular pain, photophobia, and decreased visual acuity in left eye after one month. Physical examination of the patient's head and neck revealed crust on the nasal septum. Visual acuities were 9/10 in the right eye and light perception in the left eye. An ophthalmological examination revealed severe meibomian gland dysfunction (MGD) in the eyelid, conjunctivitis and scleritis in the right eye (Fig. 1), and MGD, conjunctivitis, 360-degree peripheral corneal thinning, corneal perforation, and scleritis in the left eye (Fig. 2). The fundus examination appeared unremarkable in both eyes. Due to corneal perforation, emergency penetrating keratoplasty was planned for the patient. Informed consent was obtained, and the procedure was performed. During surgery, the conjunctiva appeared hemorrhagic, like conjunctival necrosis. Due to the scleritis, both a corneal and a scleral graft were performed.

For a definitive diagnosis, the patient consulted with the Internal Medicine Department. A complete blood count showed leukocytosis, thrombocytosis, an erythrocyte sedimentation rate of 108, CRP of 70 mg/L, and a rheumatoid factor of 64 µl/ml. Immunologic tests revealed the patient was positive for cytoplasmic anti-neutrophil cytoplasmic antibodies (C-ANCA), and thus a diagnosis of WG was suspected.

A computed tomography (CT) scan of the orbit showed enlargement of the lacrimal glands. A paranasal sinus CT scan revealed sinusitis of the right maxillary sinus (Fig. 3). A spiral chest CT scan showed multiple caveating lesions in the lower lobe of the right lung. Due to right maxillary sinusitis, functional endoscopic sinus surgery was performed, and a biopsy was obtained from the maxillary sinus mucosa. The specimens were dried and fixed in 10% neutral-buffered formalin. Histopathological examination showed granuloma and vasculitis with severe acute and chronic inflammation and few eosinophils (Fig. 4a and b). The finding of granuloma was diagnostic for WG. The patient was started on oral cyclophosphamide and intravenous (IV) methylprednisolone pulse therapy followed by oral therapy.

The patient was followed during the postoperative period. After one month, the patient's visual acuity was hand motion, and the slit-lamp examination revealed severe MGD, cicatrization, scleromalacia, and corneal graft rejection. He was referred to his rheumatology clinic for intensification of the medications and advised to have periodic checkups for his systemic disorder.

Discussion

Conjunctivitis is a benign and self-limited condition. It is most commonly infectious and is usually resolved within two weeks.[3] In prolonged cases, association of a systemic disease such as vasculitis should be considered as a differential diagnosis.

In their large study on 158 patients, Hoffman et al found that about 52% of patients with Wegener present with ophthalmic

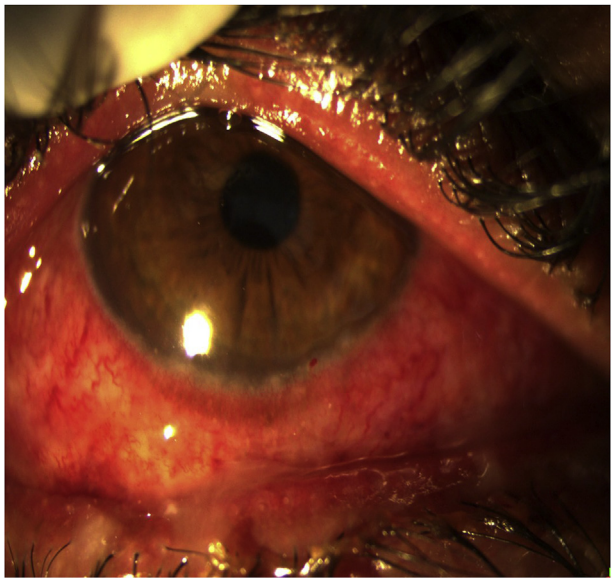

Fig. 1. Slit photography shows conjunctivitis and scleritis and severe meibomian gland dysfunction.

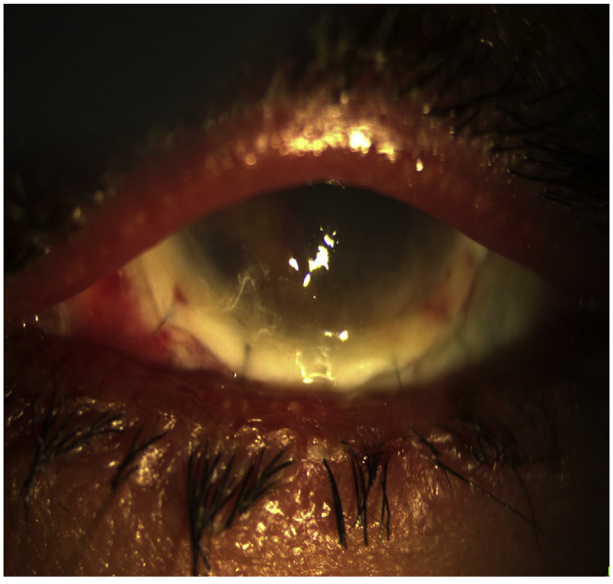

Fig. 2. Slit photography of left eye after penetrating keratoplasty shows conjunctivitis and scleritis.

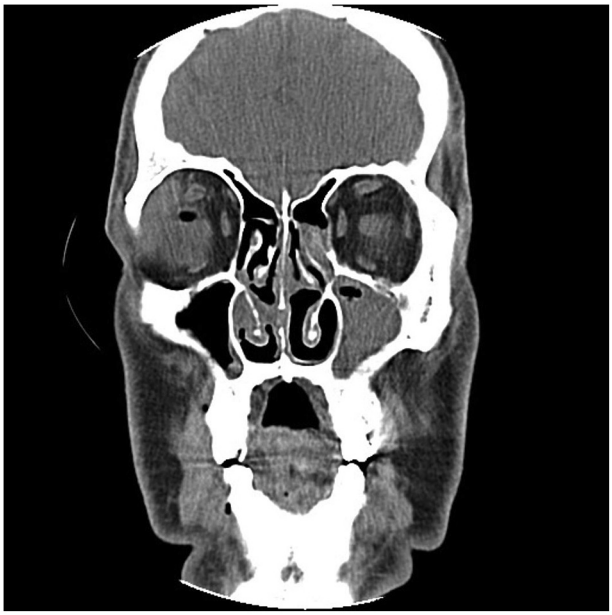

Fig. 3. Paranasal sinus computed tomography (CT) scan shows right maxillary sinusitis.

manifestations in their disease course.[7] Bullen et al reported that patients with GPA can present with various ophthalmologic manifestations. The most common manifestations are orbital disease (18/140, 15%) followed by scleral (7%), episcleral (3.5%), corneal (8%), and nasolacrimal (7%) abnormalities.[5,8] Conjunctivitis in GPA may be ulcerative and necrotic and can cause cicatricial changes in the ocular surface.[9,10] Areas of necrosis, active fibrovascular changes, and fibrovascular scars can be seen with tarsal conjunctivitis.[11] Tarsal conjunctivitis can be associated with nasolacrimal duct obstruction and subglottic stenosis.[5,11] Robinson et al reported conjunctivitis in 16% of Wegener patients.[11]

The patient in this case study presented with prolonged conjunctivitis and eyelid involvement as a manifestation of GPA and then gradually progressive PUK and scleritis leading to scleromalacia. Keratitis is an ocular manifestation of GPA that can present as an isolated event or in the presence of scleritis. Keratitis in GPA is associated with the presence of an autoantibody specific against cytokeratin-3.[5] It manifests as interstitial and PUK.[12] In the condition of PUK with scleritis, one important differential diagnosis is GPA.[13]

The patient in this case also gradually developed bilateral necrotizing scleritis. Scleritis typically presents with red eye without pain or visual impairment and is usually self-limited in the absence of GPA. In its presence, however, ocular pain and redness can occur.[14] Scleritis is an inflammatory condition characterized by hyperemia, discoloration, and edema of the sclera.[15,16] Although Hoffman et al, found that scleritis is the most common ocular manifestation reported at the time of GPA onset (about 10% of cases), and it is third most common manifestation overall. In 40% of cases, scleritis can be associated with systemic diseases such as rheumatoid arthritis, GPA, or relapsing polychondritis.[7,17] Notably, GPA must be considered as a differential diagnosis in conditions with bilateral necrotizing scleritis.[17]

Ophthalmic manifestations of GPA which have been reported to date include proptosis, dacryocystitis, chalazion, trichiasis, eyelid ulceration and fistula formation, tarsal-conjunctival disease, corneal involvement (interstitial keratitis or PUK), uveitis, retinitis, Horner's syndrome, cranial nerve palsies (III, IV, or VI), cavernous sinus thrombosis, compressive optic neuropathy, papilledema, anterior ischemic optic neuropathy, bilateral optic neuritis, optic atrophy, extraocular muscle involvement (superior oblique myositis), orbital pseudotumor, primary orbital vasculitis, orbital bone destruction, orbital cellulitis, lacrimal gland enlargement, dacryoadenitis, nasolacrimal duct obstruction, blepharitis, lid edema, ptosis, eyelid granuloma, xanthelasma, subconjunctival hemorrhage, episcleritis, pars planitis, keratitis sicca, exposure keratopathy, pannus, corneal granuloma, steroid-associated cataract, choroidal granuloma, ciliary granuloma, choroidal folds, macular edema, retinal epithelial pigmentary changes, retinitis with cotton-wool spots, acute retinal necrosis, exudative retinal detachment, retinal artery occlusion, and retinal vein occlusion.[4,8,11,16,18–47]These complications are listed in Table 1.

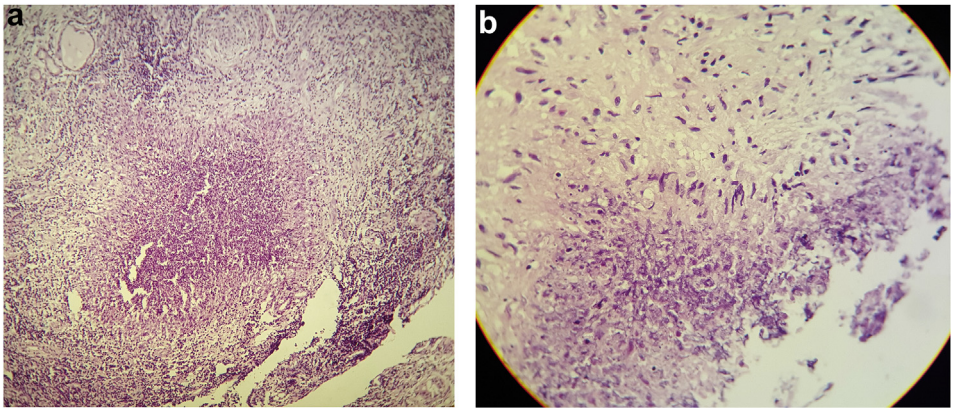

Fig. 4. a: Patchy area of necrosis with severe inflammatory reaction, H&E stain (×100). b: Necrotizing granuloma with palisaded epithelioid histiocytes, H&E stain (×400).

Table 1
Ocular complications that have been reported for Granulomatosis with polyangiitis (GPA).

Authors	Ophthalmic manifestation
Cocho et al[16]	Scleritis
Molina-sócola FE et al[18]	Proptosis
Ghanem RC et al[19]	Dacrocystitis,
Ismaei AR et al[20]	Chalazion
Jordan DR et al[4]	Trichiasis
Cassells-Brown et al[21]	Eyelid ulceration and fistula formation
Robinson et al[11]	Tarsal-conjunctival disease
Messmer et al[22]	Corneal involvement (interstitial keratitis or peripheral ulcerative keratitis)
Bullen et al[8]	Uveitis
Bullen et al[8]	Retinitis
Nishino et al[23]	Horner syndrome
Khurma et al[26]	Cranial nerve palsies (III, IV, or VI)
Robin et al[24]	Cavernous sinus thrombosis
Aakalu et al[25]	Compressive optic neuropathy
Bullen et al[8]	Papilledema
Khurma et al[26]	Anterior ischemic optic neuropathy
Monteiro et al[27]	Bilateral optic neuritis
Haynes et al[28]	Optic atrophy
Salam et al[29]	Extraocular muscle involvement (Superior Oblique Myositis)
Wardyne et al[30]	Orbital pseudotumor
Haynes et al[28]	Primary orbital vasculitis
Koyama et al[31]	Orbital bone destruction
Danda et al[32]	Orbital cellulitis
Danda et al[32]	Lacrimal gland enlargement
Kiratli et al[33]	Dacryoadenitis
Ghanem et al[19]	Nasolacrimal duct obstruction
Martinez Del Pero et al[34]	Blepharitis
Fechner et al[35]	Lid edema
Wardyn et al[30]	Ptosis
Lamprecht et al[36]	Eyelid granuloma
Hello et al[37]	Xanthelasma
Cheung et al[38]	Subconjunctival hemorrhage
Specks et al[39]	Episcleritis
Bullen et al[8]	Pars planitis
Stavrou et al[40]	Keratitis sicca
Bhatia et al[41]	Exposure keratopathy
Bullen et al[8]	Pannus
Fauci et al[42]	Corneal granuloma
Hoffman et al[7]	Steroid associated cataract
Proia et al[43]	Choroidal granuloma
Kamei et al[44]	Ciliary granuloma
Stavrou et al[40]	Choroidal folds
Onal et al[45]	Macular edema
Bullen et al[8]	Retinal epithelial pigmentary changes
Bullen et al[8]	Retinitis with cotton-wool spots
Stavrou et al[40]	Acute retinal necrosis
Robin et al[24]	Exudative retinal detachment
Costello et al[46]	Retinal artery occlusion
Wang et al[47]	Retinal vein occlusion

In conclusion, prolonged conjunctivitis can be rarely seen in systemic diseases such as GPA. A delay in diagnosis may result in blindness and death. Ophthalmologists should be aware of these conditions in differentiating between various possible origins of conjunctivitis and a high index of suspicion for GPA especially when it presents as a prolonged unresponsive disease and any associated signs of PUK or scleritis. Information about the presence of other systemic symptoms, especially sinonasal disease, arthralgia, arthritis, rashes, and constitutional symptoms, may aid in diagnosing GPA.

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