

Corneal pyogenic granuloma secondary to toxic epidermal necrolysis syndrome

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Abstract

A 30-year man was referred to our institution for progressive bilateral keratoconjunctivitis following toxic epidermal necrolysis. Slit-lamp examination showed an elevated, red, vascularized lesion covering the entire cornea. The lesion was removed by superficial lamellar keratectomy. The histopathological findings confirmed the diagnosis of corneal pyogenic granuloma. These uncommon lesions usually develop in adults after minor trauma or surgery. To our knowledge, this is the first reported case of corneal pyogenic granuloma related to toxic epidermal necrolysis.

Keywords: Corneal pyogenic granuloma; necrolysis; keratoconjunctivitis

Introduction

Pyogenic granuloma (PG) is an exuberant proliferation of granulation tissue that typically develops after minor trauma or surgery. This tissue is similar to that seen in association with wound healing¹. Corneal pyogenic granuloma (CPG) can rarely complicate corneal surgeries and there is one report following penetrating keratoplasty². CPG is rare, only few cases have been reported. The avascular nature of the cornea may explain the rarity of pyogenic granuloma at this site³. PG have been reported in many sites⁴ including the eyelid skin, conjunctiva, limbus, lacrimal puncta, acquired anophthalmic orbits and veins of ocular adnexa¹⁵. A constant clinical finding of these reported corneal lesions is either an epithelial defect in the presence of corneal neovascularization and ocular surface disease or mechanical irritation⁶.

We report here a case of CPG that occurred 12 years after toxic epidermal necrolysis induced by oral carbamazepine.

Case report

A 30-year-old man from Morocco was referred to our institution in 2012 with bilateral progressive fibrotic keratoconjunctivitis developed

following toxic epidermal necrolysis in 2005, caused by carbamazepine.

On presentation, visual acuity was hand motion perception in the right eye and finger counting in the left eye. Slit-lamp examination of both eyes showed superior and inferior symblephara, fluorescein-positive corneal epithelial defects, stromal scarring, loss of visible palisades of Vogt, both superficial and deep vascularization, and stage-3 limbal stem cell deficiency (Fig. 1). Anterior chamber examination and fundus were unremarkable. Spectral domain optical coherence tomography (SD-OCT) showed abnormal corneal and limbal epithelium (Fig. 1).

Despite topical cyclosporine and oral mycophenolate mofetyl, the patient underwent progressive worsening of the ocular surface condition with increased vascularization and stromal thinning in both eyes.

Five years later, slit-lamp examination revealed a solitary red elevated vascularized lesion covering the entire cornea of the right eye (Fig. 2). SD-OCT showed a hyperreflective elevated lesion, with irregular edges, well demarcated from adjacent limbal tissue (Fig. 2). A corneal tumor was suspected. It was surgically removed by superficial lamellar keratectomy combined with amniotic membrane transplantation.

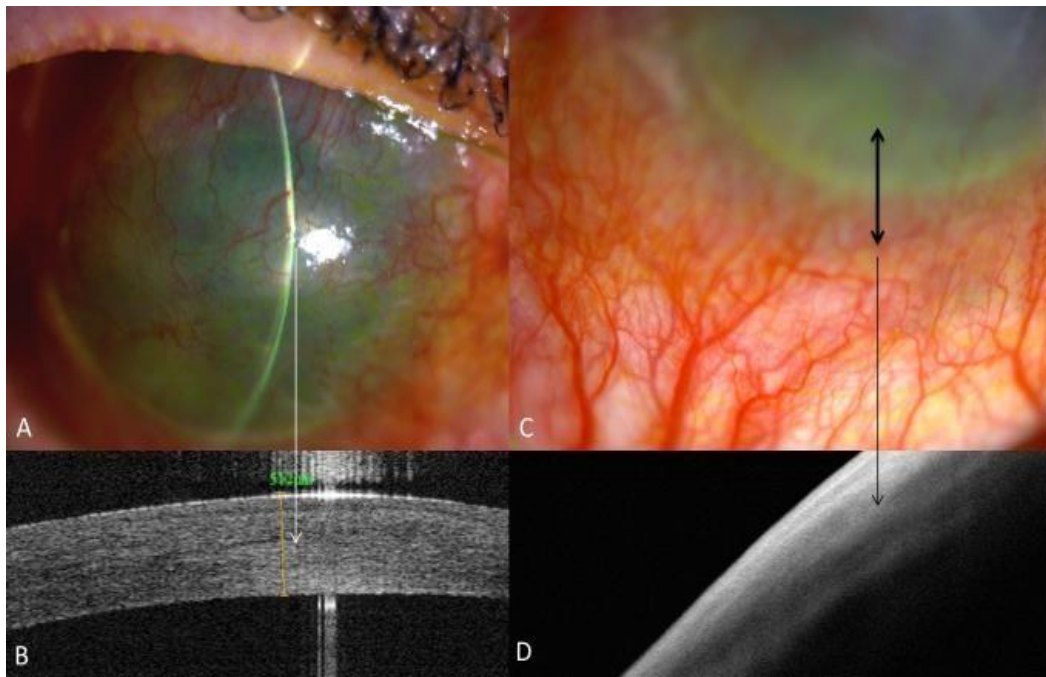


Figure 1. Slit-lamp (A, C) and spectral domain optical coherence tomography (B, D) of the right eye in 2002.

Slit-lamp images show superficial corneal vascularization and opacification of the whole cornea associated with absence of visible palisades of Vogt related to advanced limbal stem cell deficiency. OCT

images show hyperreflective and irregular epithelium and loss of normal limbal niche structures featuring flat hyperreflective limbal epithelium.

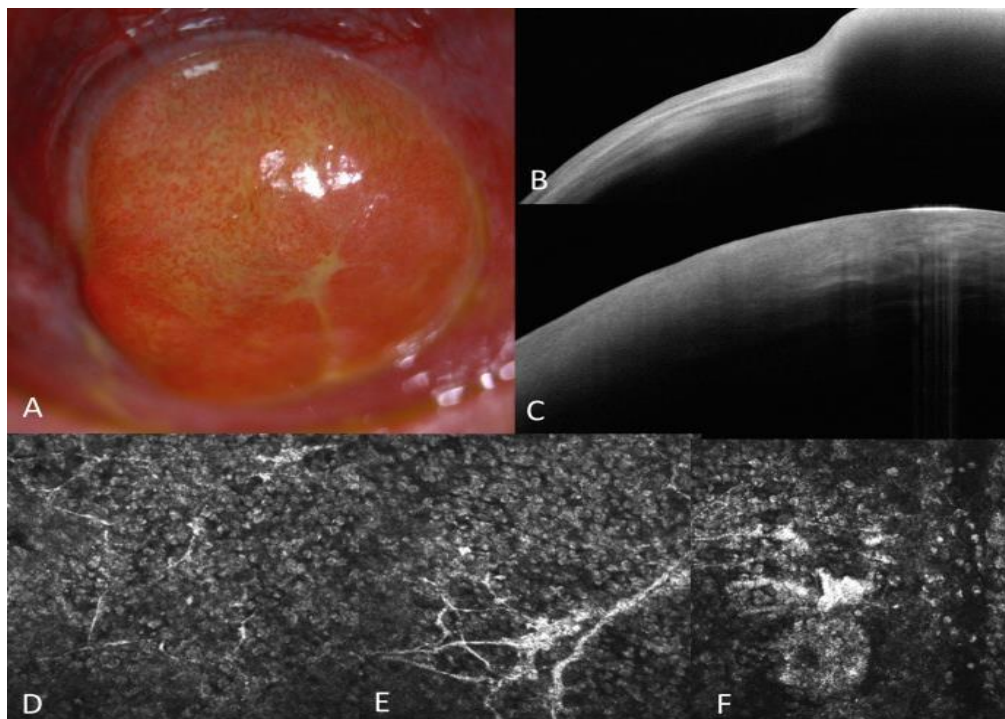


Figure 2. Slit-lamp (A), spectral domain optical coherence tomography (limbus, B; central cornea, C), and in vivo confocal microscopy (D-F) of the right eye in 2017. Red elevated vascularized lesion covering the whole corneal surface (A) featuring thickened hyperreflective epithelium on OCT scans (B, C). IVCN shows abnormal epithelial cells with bright nuclei (D-F).

Histopathologic Findings

Macroscopically, the excisional red mass measured 5 x 4mm.

Microscopic examination revealed a non-specific pyogenic granuloma featuring neovessels within an edematous chorion and lymphoplasmacytic inflammatory elements with no fibrous reaction (negative staining for epithelial membrane antigen). The inflammatory infiltrate included B-lymphocytes and plasmocytes in addition to rare histiocytes. The lesion was strongly vascularized with positive staining for CD34. Alpha smooth muscle actin staining was negative showing the absence of myofibroblast proliferation. **Discussion**

Pyogenic granuloma (PG) is a common benign vascular lesion. PG in humans was first described in 1897⁷ by Poncet and Dor as “human botryomycosis”. It was thought at this time the lesion was due to a fungal infection, whereas others later thought it was due to pyogenic bacterial infection, usually *Staphylococcus aureus*⁸. In 1925, Michelson⁹ suggested that the term PG should include “all sharply circumscribed granulation tissue growths occurring on cutaneous or mucous membrane surfaces and having the appearance of a tumor”. Although misnamed, the term PG has persisted in the medical literature. In fact, the term is a misnomer; the lesion is not typically pyogenic, unless there is secondary infection. A PG contains neither the inflammatory exudate of polymorphonuclear leukocytes with the resulting tissue proteolysis which is characteristic of a pyogenic reaction, nor the typical epithelioid giant cell reaction characteristic of granulomatous inflammation¹⁰. A PG is actually a vasoproliferative inflammatory response composed of granulation tissue. This tissue is the healing response that occurs following inflammation and it is characterized by the presence of fibroblast proliferation, small capillary-like channels that may leak fluid and thereby contribute to the edematous nature of the healing tissue, and scattered inflammatory cells. The cellular infiltrate usually consists of varying amounts of neutrophils, lymphocytes, plasma cells and other mononuclear elements¹¹.

The common sites of its occurrence are the skin of the face, the extremities and mucosal surfaces of the oral cavity. They can also occur at the limbus or on the bulbar conjunctiva, simulating a pterygium¹². A CPG is a relatively rare entity.

The occurrence of CPG was first reported by Minckler¹³ who reported a case which was misdiagnosed as conjunctival squamous cell carcinoma and after enucleation confirmed the diagnostic of CPG.

The typical presentation of the CPG is a rapidly growing lump which, on slit lamp examination, appears as well circumscribed, smooth surfaced or rough irregular surfaced, red, sessile and highly vascularized mass^{5,44}. The shape of the lesion varied from a mushroom-like contour with a narrow base to a broad based attachment with the base as broad as the body⁸.

Our patient had a similar clinical presentation with a rapid course and a presentation within one month of the onset of the growth¹⁵. The solitary red elevated fleshy vascularized lesion covered the entire cornea of the right eye.

CPG commonly grows at the sites of pre-existing corneal trauma, infectious corneal ulcer, or surgery. Most authors consider this lesion to be a secondary reaction to these underlying processes^{16,17}. Cameron and Mahmood have described an epithelial defect preceding the development of a CPG in over half their patients⁸. They suggest the lesion resulted from delayed wound healing of the epithelial defect in the presence of corneal vascularization and an ocular surface disease or chronic irritant. Our patient developed his lesion in less than 3 months.

The histopathological findings of our case were consistent with the common histopathological findings of CPG showing an excessive proliferation of granulation tissue with mononuclear cell infiltration^{5,44}.

An exuberant granulation tissue lesion results from the delayed healing of the epithelial defect in the presence of corneal vascularization and an ocular surface disease or chronic irritant⁸.

OCT images showed hyperreflective and irregular epithelium and loss of normal limbal niche structures featuring flat hyperreflective limbal epithelium and IVCN showed abnormal epithelial cells with bright nuclei.

CPG is very unusual and can occasionally lead to difficult differential diagnosis of corneal masses. The differential diagnoses include anterior segment choristoma, vascular hamartoma, viral papilloma⁴ or squamous cell carcinoma (SCC). CPG can be mistaken for a SCC resulting in inappropriate enucleation^{12,13}. The history and clinical findings help for distinguish the lesions. The age of onset, history of prior trauma, infection or inflammation, rapid growth and the clinical appearance will often point to the correct diagnosis. CPG are typically preceded by a persistent epithelial defect. SCC is a slower growing lesion and has contact with the limbus with typical corneal extensions. It is generally not as vascular in appearance and the color is not as red as that observed with CPG. Histopathology of the tumor will confirm the diagnosis.

The first treatment of CPG consists in treating the ocular surface disease then remove chronic epithelial defects by medical or surgical methods¹⁸. Topical steroids may cause some shrinkage of corneal blood vessels as well as decrease the exudative response of the inflammatory reaction. If there is no response treatment of CPG is mainly surgical, which is excision. After surgical excision of the mass, the cornea may heal with scarring, especially if there is an underlying inflammatory process like our case. In such a condition, patients may benefit from optical keratoplasty. An appropriate clinical management of a patient with a CPG begins with the accurate recognition of the lesion to avoid unnecessarily aggressive treatment. Padadopoulos related a case of a spontaneous resolution³.

Despite its rarity, pyogenic granuloma should be considered in any patient with a fleshy, vascularized, elevated, rapidly growing corneal mass, especially in the setting of corneal infection preceded by a history of accidental and surgical trauma or persistent corneal defect. An excisional biopsy should be performed to make a definite diagnosis.

To our knowledge, this is the first case reported with an association between CPG and toxic epidermal necrolysis.

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