Ocular pyoderma gangrenosum: A systematic review

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Background: Pyoderma gangrenosum (PG) is a rare, ulcerative cutaneous disorder. Ophthalmic involvement in PG is atypical, but can have devastating consequences.

Objective: We sought to characterize ocular PG to allow for earlier diagnosis and therapy. To our knowledge, this is the first systematic review summarizing this clinical variant.

Methods: A systematic review was conducted using PubMed and Web of Science. Data were extracted and studies were qualitatively assessed and analyzed.

Results: We identified all 34 cases of PG involving the eye and periorbital area, and categorized them into 4 different subtypes. Common presenting signs include ulceration, peripheral ulcerative keratitis, and decreased visual acuity. Although it is often difficult to biopsy ocular PG, histologic features are nonspecific. Combined therapy using corticosteroids and further surgical reconstruction as needed is the mainstay of treatment. Cases of the eye/orbit in particular should be treated aggressively, as these are more likely to relapse compared with cases of the periorbital area.

Limitations: Use of case reports, paucity of ocular PG cases, and heterogeneity of studies are limitations.

Conclusion: PG should be considered in the differential diagnosis of ulceration of ocular/periocular tissues. An aggressive, early, multimodal treatment strategy should be used to prevent relapse, especially in cases of the eye/orbit. (J Am Acad Dermatol 2017;76:512-8.)

Key words: extracutaneous; eye; inflammation; neutrophilic dermatoses; ocular; periorbital; pyoderma gangrenosum.

Pyoderma gangrenosum (PG) is a rare ulcerating neutrophilic dermatosis that affects 3 to 10 patients per million.[1] A classic PG lesion is a papule or pustule that extends peripherally to form a deep erythematous ulcer with a violaceous border.[2,3] There are no pathognomonic clinical or histologic findings of PG, making this a challenging skin condition to diagnose and treat.

PG lesions may occur anywhere on the body, however the ulcers are most commonly found on the trunk and lower extremities.[4,5] Ophthalmic involvement in PG is atypical, however it can result in devastating visual consequences. The key characteristics of this clinical variant have yet to be recognized. We conducted a systematic review of the literature to further a better understanding of the clinical features, histologic findings, and treatment strategies of ocular PG.

METHODS

Search strategy

A comprehensive literature search was conducted using PubMed and Web of Science to identify all case reports and case series describing PG of the ocular region. Search terms used were: "pyoderma gangrenosum" and "eye" or "eyelid" or "orbit" or "periorbital" or "ocular" or "periocular." Citations from all

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publications were reviewed to identify other pertinent articles. A flow chart of the study selection process is shown in Fig 1.

Inclusion and exclusion criteria

Articles were not excluded based on date. Publications that were not in English were excluded. Both authors assessed the validity of all included cases.

Data retrieval

Case details were obtained from selected articles and data were collected by means of a spreadsheet.

Data analysis

Statistical analyses were performed using GraphPad Prism 6 (GraphPad Software, San Diego, CA). Not all articles presented complete data; therefore analysis was conducted using data from the remaining complete reports.

CAPSULE SUMMARY

- Ocular pyoderma gangrenosum is a rare clinical variant.
- We identified 4 clinical subtypes of ocular pyoderma gangrenosum.
- Diagnosis of ocular pyoderma gangrenosum is difficult and commonly delayed. Early, multimodal treatment should be used to prevent long-term visual deficits.

RESULTS

Our systematic review resulted in the final selection of 29 articles, which describe 34 cases of ocular PG.[6-34]

Classification of ocular involvement

Ocular PG has variable clinical presentations; cases of PG may be cutaneous involving the periocular tissue or even extracutaneous involving the eye itself. We have classified the reviewed cases into 4 categories: cutaneous periocular PG, cutaneous periocular PG with orbital involvement, extracutaneous orbital/scleral PG, and ocular diseases associated with PG (Table I).

Patient demographics

Patient demographics of the 34 cases of ocular PG are outlined in Fig 2. Patient age ranged from 27 to 90 years, with a mean age of 58 (SD 16.3) years. It is known that PG has a slight predilection for females[4,35]; in our patient cohort the male:female ratio was 1:1.2.

Clinical features

Ocular PG was most commonly unilateral, and the right (38%) and left (47%) sides were almost equally affected. Sixteen patients had additional lesions in secondary locations.

Four clinical subtypes of PG have been reported in the literature: ulcerative, bullous, pustular, and vegetative.[1,36] Ulcerative PG is known to be the most common subtype of PG,[3] which was also true in our study. In fact, the most common presenting sign of ocular PG was ulceration, which was described in 18 cases (Table II). Two cases had vegetative PG, also known as superficial granulomatous PG. Other clinical features and presenting signs are summarized in Table II.

PG often occurs at sites of trauma, a concept known as pathergy.[37,38] This was evident in 5 cases of ocular PG; 4 of these cases developed PG after a surgical procedure and the fifth case initially developed PG after minor trauma and then again after reconstructive surgery.

Systemic disease associations

Inflammatory bowel disease (IBD), myeloproliferative disorders, and rheumatoid arthritis are all common comorbidities described in 50% to 70% of classic PG cases.[4,5,35,39-41] Close to 45% of ocular PG cases were associated with an underlying disease (Table III). Interestingly, 15% had diabetes mellitus reinforcing the newly suggested potential association with metabolic syndrome.[4,42,43] In addition, 41% of patients had a history of PG or recurrent ulcers, which is not surprising because PG has a high rate of relapse.[44]

Histopathology

Histologic findings were fairly consistent across cases. Much like classic PG, the most common finding was neutrophil infiltration/acute inflammatory infiltrate, which was reported in all 4 subtypes of ocular PG. Necrosis, dermal abscesses, and chronic inflammatory infiltrate were also described.

Diagnosis and treatment

PG is notoriously difficult to diagnose, primarily because of nonspecific clinical and histopathological features. Ocular PG is no different; of the 19 cases that reported time from onset to diagnosis, only 1 case was diagnosed within 1 week. Eight cases were diagnosed between 1 week and 1 month, 4 cases between 1 month and 1 year, 4 cases between 1 and 5 years, and 2 cases after more than 5 years. A wide array of differential diagnoses were considered including cellulitis, endophthalmitis, abscess, benign keratosis, stye, chalazion, granulomatous polyangiitis, and cancer.