OIUF THE OCULAR IMMUNOLOGY AND UVEITIS FOUNDATION

Dedicated to Eye Disease Cure and Education

Ocular Cicatricial Pemphigoid

Arash Maleki, MD; C. Stephen Foster, MD, FACS, FACR

May 2026

Ocular cicatricial pemphigoid (OCP), which affects the eyes, is classified as a variant of mucous membrane pemphigoid, a disorder that can affect all mucous membrane tissues in the body. The defining feature of OCP is the presence of bilateral, chronic, relapsing–remitting autoimmune conjunctivitis, which can lead to significant visual impairment due to conjunctival scarring and secondary corneal vascularization and opacification.

Incidence rates for this condition exhibit considerable variation, ranging from approximately 1/10000–1/60000. The age of onset is estimated to be approximately 60-80 years. It affects women at twice the rate of men but does not show any specific race preference. Inflammation in OCP results from systemic immune dysregulation and therefore requires systemic immunomodulatory therapy with immunosuppressive agents.

OCP initially presents with ocular surface irritation manifested by discomfort, dryness, and redness of the eyes. These findings may be more prominent in one eye. Many times, it is initially diagnosed and treated for conjunctivitis, blepharitis, or dry eye disease for a substantial period before receiving the correct diagnosis of OCP, which is a major reason for delayed diagnosis, poor prognosis, and complications. Therefore, it is critical to diagnose OCP in its early stages. Even trichiasis (misdirected lashes) without an identifiable etiology warrants consideration of OCP rather than simply mechanically removing the misdirected eyelashes. Given the association of OCP with mucus membrane pemphigoid (MMP), it is important providers ask about symptoms involving other mucous membrane sites. In later stages, fornix foreshortening, symblepharon (adhesion between two conjunctival surfaces), and a frozen globe (marked restriction of ocular movement) may occur (Foster staging system). Corneal vascularization and haze are the end results of the disease.

The differential diagnosis of OCP include infections (adenovirus conjunctivitis with its complications), allergic reactions (to medications, trauma, environment), other autoimmune diseases (IgA disease, lichen planus, discoid lupus, scleroderma, sarcoidosis, and ocular graft versus host disease, and miscellaneous conditions (radiation, trauma, ocular rosacea, conjunctivitis medicamentosa, chemical or thermal injury, and neoplasia).

Although the underlying cause is not completely clear, OCP is believed to involve the production of autoantibodies against components of the epithelial basement membrane complex. The diagnosis of OCP is based on the detection of these antibodies by immunofluorescence and immunoperoxidase staining of conjunctival biopsy specimens. However, the results can be false-negative in up to 5% of patients; therefore, negative results do not rule out the diagnosis of OCP.

Current evidence indicates that topical medications do not demonstrate sufficient efficacy in managing disease activity. Therefore, systemic immunomodulatory therapy is imperative for controlling the condition and preventing vision loss. Immunosuppressive agents are chosen using a step-up stepladder approach: starting with those having the fewest side effects and progressively moving to more potent drugs with greater side effects (e.g.; cyclophosphamide, biologic response modifier agents, and intravenous immunoglobulin [IVIg]). Additionally, step-down stepladder strategy with a transition to less potent immunosuppressive agents with fewer side effects from more potent agents after controlling the disease has also been discussed. Observational studies have indicated the effectiveness of dapsone, azathioprine, mycophenolate mofetil, rituximab, IVIg, and cyclophosphamide in the treatment of OCP.

It is important to note that any nonurgent ocular surgery (intraocular and eyelid) should be postponed until the patient has achieved remission of OCP for several months while receiving treatment.

Treatment of ocular cicatricial pemphigoid

Several medications have been used for this purpose. Evidence from observational studies supports the use of dapsone, azathioprine (AZA), mycophenolate (MMF), rituximab, intravenous immunoglobulin (IVIg), and oral/pulse cyclophosphamide for the treatment of OCP. Dapsone has been reported as a treatment for OCP; however, in our opinion, its clinical utility may be limited to very early or mild cases.

A step-up stepladder approach is an appropriate and effective strategy for treating patients with OCP. Initial management generally involves conventional immunomodulatory therapy, including antimetabolites—methotrexate (MTX), MMF, or AZA—administered alone or in combination, with possible addition of T-cell inhibitors such as CsA. However, in cases of disease refractory to these therapies, escalation to cytotoxic agents, biologic response–

modifiers, or other agents, including intravenous or oral cyclophosphamide, biologic agents such as rituximab, or IVIg is warranted. Additionally, the step-down stepladder approach, explored in limited studies for OCP, entails de-escalation to less potent therapies. Typically, a duration of one to three months is generally allowed for each medication to achieve its therapeutic effect.

In a study by Saw et al. treatment was initiated with MTX, dapsone, or sulfapyridine as monotherapy. Patients requiring escalation received AZA or MMF as second-line therapy, followed by a combination of oral cyclophosphamide and prednisone as third-line treatment, and IVIg as fourth-line therapy. Additionally, in recalcitrant and severe cases, combination therapy with rituximab and IVIg represents an effective and widely utilized treatment strategy.

In most recent years, subcutaneous repository corticotropin injection (RCI), has been employed in the treatment of ocular inflammatory diseases including OCP; however, it is primarily utilized as an adjunctive therapy rather than as monotherapy.