

## Our Patient's Eyes are Red: Is It Just a Conjunctivitis or a Complex Disorder Like Ocular Cicatricial Pemphigoid? (Ocular Cicatricial Pemphigoid - Clinical Features for Diagnosis)

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**R**ed eye is a common presenting complaint in ambulatory practice. A small percentage of these patients need ophthalmological referral and treatment, although the vast majority can be treated by the primary care clinician.

**Ocular Cicatricial Pemphigoid** is a disease entity which often presents as a chronic conjunctivitis and can be diagnosed clinically and treated optimally to prevent blindness which would slowly ensue without treatment. It is hence necessary that we remain aware of this condition.

### Descriptive Case

A 31-year-old lady presented to our Out Patient Services at Taparia Institute of Ophthalmology, Bombay Hospital, Mumbai in 2015 with bilateral gradually progressive painless decrease of vision since past 13-15 years associated with multiple self-resolving oral ulcers with an increase in symptoms since past 3-4 years. She had been treated in the past initially as a routine Conjunctivitis and later as "Chronic Conjunctivitis" with various eye drops including ocular lubricants, antibiotics and steroids.

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On Examination, she was found to have (Fig 1 & 2)

1. Ankyloblepharon - which is a partial or complete adhesion of the edge of one eyelid to that of the other
2. Symblepharon - which is a partial or complete adhesion of the palpebral conjunctiva of the eyelid to the bulbar conjunctiva of the eyeball
3. Forniceal Foreshortening - which is shortening of the fornices mainly lower
4. Limbal Stem Cell Deficiency - which is a deficiency of the stem cells of the cornea present in the limbus which demarcates the conjunctival from the corneal epithelium causing a vascularised corneal scar with a visually significant cataract in both eyes.

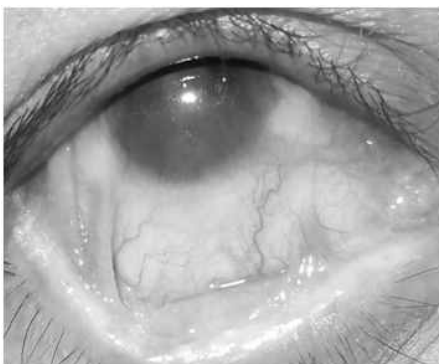
The above are classical clinical signs of "**Ocular Cicatricial Pemphigoid**".

Mucous membrane pemphigoid is a systemic disorder that primarily affects mucous membranes. When localised to the conjunctiva, it is known as ocular cicatricial pemphigoid, a potentially blinding disease.<sup>1</sup>

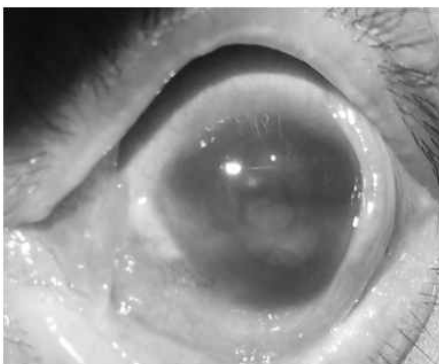
She had an old conjunctival biopsy report of 2004 with immunofluorescence showing a faint IgM positivity consistent with the current clinical diagnosis of Ocular Cicatricial Pemphigoid.

Ocular cicatricial pemphigoid is an

indication for systemic immunosuppressive treatment to achieve adequate remission. Immunosuppressive agents are selected with a "stepladder" approach, commencing with medications having the fewest side effects.<sup>1</sup>



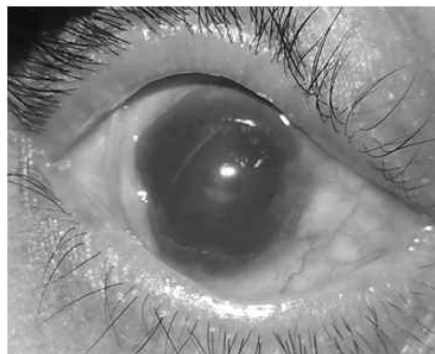
*Fig 1: Right Eye of a patient with Ocular Cicatricial Pemphigoid showing the classical clinical feature of "Forniceal foreshortening" i.e. obliteration of the fornices due to a conjunctival fold that bridges the gap between the palpebral and bulbar conjunctiva along with lid margin keratinisation.*



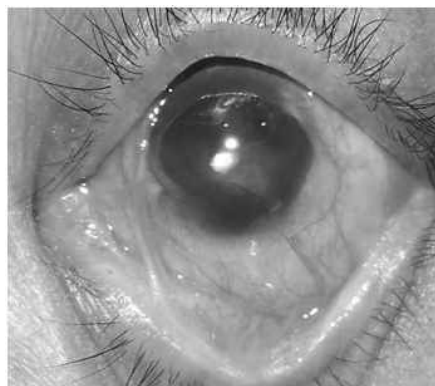
*Fig 2: Left Eye of the same patient with Ocular Cicatricial Pemphigoid showing a limbal stem cell deficiency causing conjunctivalisation of the cornea and resultant ocular surface disease.*

Our patient first underwent immunomodulation with Oral Azathioprine/Oral Methotrexate which were ineffective and with side effects and was thus shifted on to Intravenous Cyclophosphamide to achieve a good

control of surface inflammation without any side effects allowing an eventless cataract surgery with PCIOL implantation in both eyes. More than anything else currently she is working and supporting her family being stable on low dose Azathioprine. She has since been on our follow up and is doing well. (Figs. 3 & 4).



*Fig 3: Right Eye of the same patient with Ocular Cicatricial Pemphigoid after visual rehabilitation with cataract surgery under immunomodulatory cover*



*Fig 4: Left Eye of the same patient with Ocular Cicatricial Pemphigoid after visual rehabilitation with cataract surgery under immunomodulatory cover*

### **Discussion**

Red eye is a cardinal sign of inflammation which can result from many conditions which are listed as follows:

1. Conjunctivitis
2. Sub conjunctival haemorrhage
3. Ocular surface inflammation

consisting of dry eye diseases

4. Uveitis i.e. inflammation of uveal layer of eye
5. Acute congestive glaucoma

Other causes include Episcleritis and Scleritis and raccoon eyes in intra cranial bleed

Most of the patients presenting with red eye are of conjunctivitis and subconjunctival haemorrhage while small group of patients has uveitis, acute congestive glaucoma and ocular surface diseases. Entities like the commoner one can be treated conservatively whereas uncommon needs specialist eye care.

#### **Assessment Of A Red Eye In Primary Health Care**

1. Patient having conjunctivitis will generally present with unilateral complaints of redness watering and foreign body sensation which later on can involve the other eye. Generally, the vision is not affected in case of conjunctivitis except in severe form of adenoviral conjunctivitis in which patients develop sub-epithelial infiltrates resulting in diminution of vision.
2. Sub conjunctival haemorrhage presents as a painless redness which is mostly unilateral. Patients give a history of sudden onset redness or redness following any trivial trauma to eye and require monitoring of blood pressure or coagulation parameters.
3. Patients complaining of acute onset of redness associated with pain and diminution of vision generally need evaluation for uveitis, acute congestive glaucoma. Uveitis is inflammation of

uveal layer of eye which can involve anterior, middle or posterior part of eye. Acute anterior uveitis can present with redness, pain and diminution of vision. It is mostly unilateral. Acute congestive glaucoma presents as acute severe pain associated with redness and diminution of vision. It generally affects one eye but sometimes it can involve both eyes. Bilateral involvement is with acute congestive glaucoma and is classically seen as an adverse effect of Topiramate drug used for seizures. These patients complaining diminution of vision should be sent for ophthalmological opinion without any further delay.

4. Ocular surface diseases have a wide range of symptoms which are similar and thus, makes it, at times difficult even for an ophthalmologist to diagnose. Ocular Surface Diseases comprise severe Dry Eye Disease including limbal stem cell deficiency because of various causes including chemical burns, drug reactions like Stevens Johnson Syndrome require expert intervention. Simple Limbal Epithelial Transplantation (SLET) is a surgical technique first described by Sangwan et al in 2012 has shown to be an efficient and cost-effective surgical technique for the restoration of the ocular surface even in cases with severe burns and complete Limbal Stem Cell Transplantation.<sup>2,3</sup>

#### **Ocular Cicatricial Pemphigoid**

Ocular Cicatricial Pemphigoid, a debilitating ocular surface disorder is diagnosed clinically with or without

conjunctival biopsy. A negative biopsy on direct immunofluorescence does not preclude a diagnosis of ocular cicatricial pemphigoid.<sup>4</sup>

Severe symptoms incapacitate the patients making them dependent in day to day activities. Ocular cicatricial pemphigoid can cause blindness out of relentless, disease progression.

Aggressive use of immunomodulation with drugs like Methotrexate, Azathioprine, Cyclosporine and Cyclophosphamide help halt progression of disease and can achieve remission and a stable ocular surface (Figs. 5 & 6).



*Fig 5: Right Eye of another patient with Ocular Cicatricial Pemphigoid on pulses of Intravenous Cyclophosphamide. Seen in the picture is a healing Ocular surface disease with reversal of an impending corneal melt and a stabilising area of central corneal thinning along with the other features of ocular surface disease. Note the quiet and non-congested conjunctiva with pulses of Cyclophosphamide*

Patients of ocular cicatricial pemphigoid who require cataract surgery, can have surgery safely with no major intra- or postoperative complications.<sup>5</sup> In these patients, the surgical intervention itself is not associated with acute exacerbations of inflammation, if adequately immunomodulated, but

progression of disease may be noted in some cases over time.<sup>5</sup>



*Fig 6: Left Eye of the patient shown in Fig 3 above with Ocular Cicatricial Pemphigoid on pulses of Intravenous Cyclophosphamide. Seen in the picture against a quiet and non-congested conjunctiva with pulses of Cyclophosphamide - Stabilising Ocular Surface Disease in Ocular Cicatricial Pemphigoid with Cyclophosphamide.*

#### **Take Home Message**

1. Red Eyes due to common entities like Conjunctivitis can be treated conservatively at primary care level.
2. Uncommon ones such as those accompanied by pain, decrease of vision or those involving severe Dry Eyes including chemical burns, drug reactions like Stevens Johnson Syndrome and ocular surface inflammations like Ocular Cicatricial Pemphigoid require expert intervention.
3. Ocular Cicatricial Pemphigoid requires early aggressive care with immunomodulation, including drugs like Azathioprine and Cyclophosphamide and Biologics (where necessary), to prevent debility and blindness.
4. A knowledge of the clinical features of Ocular Cicatricial Pemphigoid

including Ankyloblepharon, Symblepharon, Forniceal Foreshortening in Chronic Conjunctivitis gives the primary care specialist an edge in being able to appropriately diagnose this disease and appropriately guide the care of the patient with an Ocular Inflammation Specialist.

#### References

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#### Thyroid cancer screening

Whether screening for a disease is beneficial or not is widely debated.

The USPSTF reviewed evidence for the benefits and harms of screening for and treatment of thyroid cancer, concluding that the harms outweigh the benefits. Benefits are small for various reasons. First thyroid cancer is fairly rare, at 3.4% of newly diagnosed cancer cases projected in the USA in 2017 and 0.3% of cancer deaths. Second observational studies of patients receiving surgery do not show survival benefits compared with those receiving surveillance. Finally, screening leads to increased incidence of thyroid cancer, but not decreased mortality.

This discrepancy occurs because tumours are often identified that are so small or slow growing that they would have remained asymptomatic; making treatment unnecessary. Harms from treatment, however, are moderate, including low blood calcium concentrations and vocal cord paralysis caused by surgical thyroid gland removal, as well as occurrence of a second cancer and salivary gland harms caused by radiotherapy.

Further investigation is needed since no direct studies have compared screening with no screening or immediate surgery with surveillance, and the benefit of screening in high-risk patients has not been studied.

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