Case Report

Recalcitrant bilateral shield ulcer in vernal keratoconjunctivitis

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Abstract

Allergic conjunctivitis is frequently encountered in general practice and in the specialist pediatric clinics. Though these cases are well managed in specialty allergy clinics yet a rare and severe manifestation in the form of bilateral shield ulcer can be potentially blinding and comes with management challenges. The pathobiology is driven by multiple inflammatory mediators which contribute to the recalcitrant nature of these noninfectious indolent ulcers. A seven-year-old boy presented with a recent onset photophobia with other characteristic ocular manifestations of vernal keratoconjunctivitis. Grade three shield ulcer in both the eyes was managed with both medical and surgical arms. Medical immunomodulation was achieved with topical steroids, topical immunomodulators along-with copious lubrication of the ulcer. Surgical intervention included a permanent tarsorraphy in the left eye and debridement of the plaques over the ulcer base in both the eyes. Aggressive follow-up and step wise management approach resulted in promising results without any recurrence.

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Introduction

Allergic conjunctivitis is a disease that is frequently encountered in general practice and in the specialist pediatric clinics. Multiple precipitating contributors including environmental, psychological, and genetic factors play a key role in its pathogenesis. Vernal keratoconjunctivitis (VKC) is a severe form of allergic conjunctivitis. This entity is well described in many eye institutions in tropics and temperate countries where the disease exacerbates with seasonal variations.[1] The severe complication in the form of shield ulcer can be potentially sight threatening to the eyes. This case highlights the management challenges faced in tackling the immune mediated pathobiology in one such rare case of bilateral shield ulcer in a seven year old boy.

Case presentation

He presented with a history of itching and redness in both eyes (OU) for past six months and developed a recent onset photophobia since last 15 days. He had no accompanying systemic allergies. His unaided visual acuity (VA) OU was 6/12 with no further improvement. There was marked papillary hyperplasia on the tarsal conjunctiva (Figure 1A), diffuse punctate epitheliopathy over bilateral corneas accompanied-with a thick ropy discharge. Shield ulcer was present OU. The ulcer in the left eye (OS) was larger (Figure 1A) and measured 4.5 mm x 3 mm. Right eye (OD) ulcer measured 2.5 mm x 2 mm. The diagnosis was VKC with shield ulcer OU. Fundus examination OU was unremarkable. Topical treatment that was initiated comprised of antihistaminic and mast-cell stabilizer eye drop (olopatidine 0.1%) administered thrice daily (TDS); topical dexamethasone (0.1 %) administered four times a day, topical tobramycin (0.3%, TDS) along-with carboxymethycellulose and hyaluronate as lubricants. Ulcer edges OS were scraped under slit lamp to hasten epithelialization. Although the symptoms reduced in ten days but the ulcer seemed recalcitrant to treatment (Figure 1A-B, 2A). Intraocular pressures (IOP) were 14 mm Hg- OD; 16 mm Hg-OS. Cyclosporine 0.05 % eye drop twice daily was added to accelerate the healing process. Lubricating eye drops at this stage were instilled on hourly basis. It had been one month and the signs of healing didn't seem to appear OU (Figure 1B, 2B). Subsequently lateral tarsorraphy was performed under general anesthesia OS in an attempt to augment undisturbed growth of the epithelium and prevent the evaporation of tears. It was ensured that all topical formulations were preservative free. Chloramphenicol eye drop was substituted for tobramycin. Fifteen days later a thick plaque seen over the ulcer OS was surgically debrided (Figure 1C-D). Over a span of two weeks this ulcer had started to become shallow however features of ocular surface instability were seen OU. Dexamethasone was substituted with a lower potency topical steroid in a lower strength (loteprednol 0.2%), administered TDS. A similar plaque was removed from the right eye (Figure 2C). The child was quite bothered by a specific burning sensation in his eyes although demonstrated a good response to treatment all this while. His conjunctiva seemed hyperemic. Therefore topical cyclosporine was changed to tacrolimus eye ointment (0.03%) instilled at a similar frequency as the latter causes less of burning and conjunctival hyperemia. Eventually, ulcer OU healed with scarring after a rigorous pharmacological immunomodulation over 12 weeks (Figure 1E, 2D). Refractive correction was advised for astigmatism (-1.00 diopter cylinders (DC) x 170°- OD, -1.25 DC x 180°- OS) . Maintenance therapy with tacrolimus eye ointment and lubricants was continued for nearly six weeks. Presently after one year (Figure 1F, 2E), he wears glasses, maintains his VA and is doing well.

Discussion

Multiple inflammatory mediators contribute to the pathogenesis of shield ulcer. The inflammatory cell infiltrate in the conjunctival tissue in patients with active VKC comprises of eosinophils, mast cells revealing membranous IgE staining, B lymphocytes, IgA+, IgG+ ,IgM+,and IgE+ plasma cells along-with T lymphocytes,

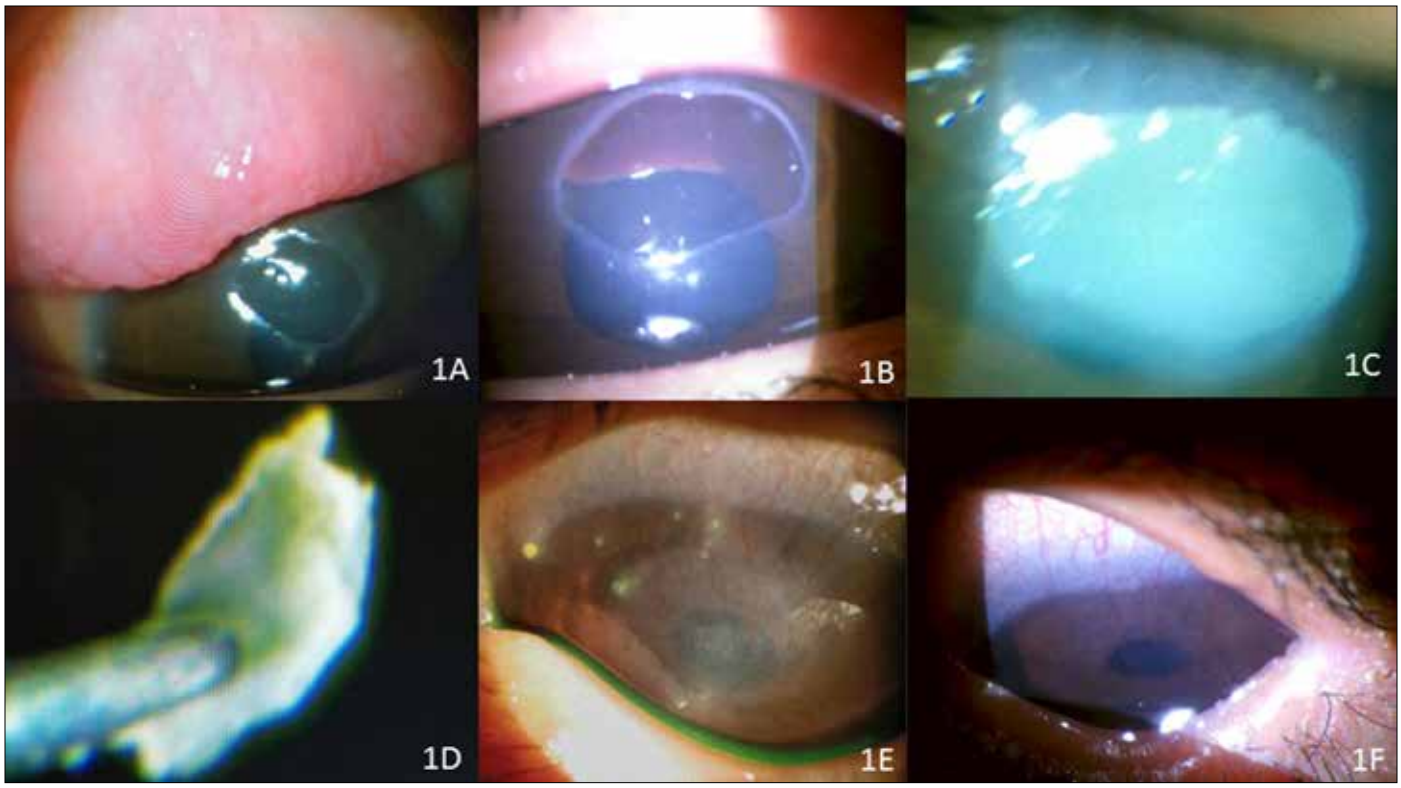

Figure 1: *(1A-F): Left eye had marked papillary hyperplasia and shield ulcer (Fig. 1A). Ulcer increased in size over one month (Fig. 1B). Plaque formed (Fig. 1C) and was removed (Fig. 1D). Ulcer healed forming a vascularized corneal opacity (Fig. 1E). Follow up after one year (Fig. 1F)*

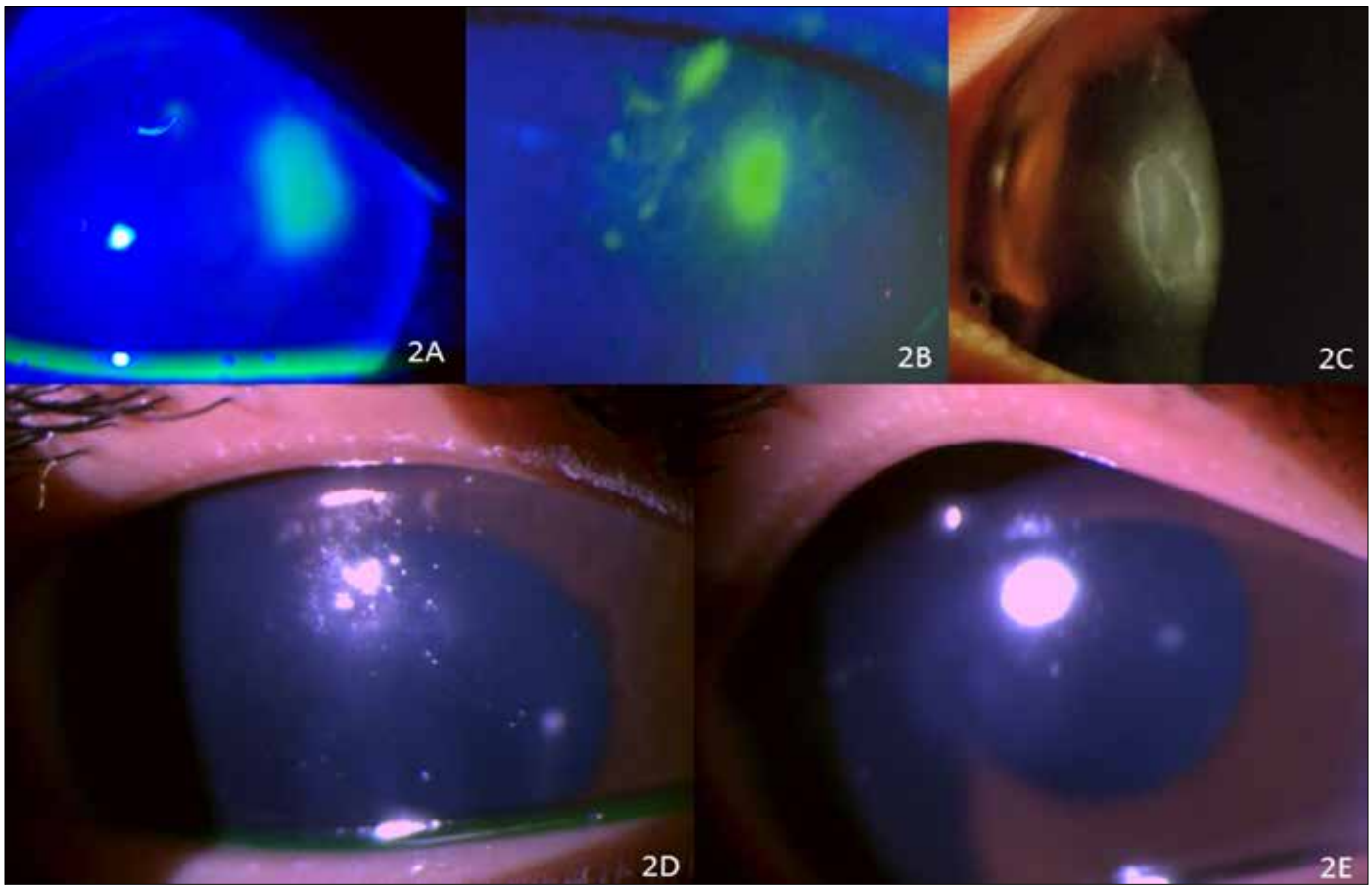

Figure 2: *(2A-E): Right eye shield ulcer on presentation (Fig. 2A). Ulcer increased in size over one month (Fig. 2B) and stained with fluorescein dye. Plaque formed and was removed (Fig. 2C). After plaque removal, ulcer healed (Fig. 2D). Follow up after one year (Fig. 2E).*

macrophages, dendritic cells.[2] The underlying molecular basis for the selective migration and accumulation of various inflammatory cells observed in VKC remains unclear till date.[3] VKC specimens have shown significantly increased expression of adhesion molecules responsible for selective recruitment of different leucocytes to inflammatory sites. A large proportion have negative results in the standard allergy diagnostic tests, confirming that the pathogenesis is not solely mediated by immunoglobulin E (IgE). Shield ulcer is observed in about 3 to 11% of patients suffering from VKC.1 Without treatment, a plaque forms over this ulcer comprising of fibrin and mucus deposits which hampers the re-epithelialization.[4] Grade three ulcer as in our patient needs surgical manipulation to remove the elevated plaque (Table 1).[5] Intra-operative optical coherence tomography (iOCT) has recently been popularized for providing continuous monitoring of the depth of dissection and allows for a safe and complete debridement of the shield ulcer with plaque.[6] The same may be beneficial in children who undergo general anesthesia for debridement of the ulcer and a careful and complete dissection may be achieved in the same sitting averting the need for subjecting the child to multiple sessions of general anesthesia. However medical management in all grades is indispensible. Topical steroids are needed for a short period to induce remission of the allergic crisis. Long term instillation of steroid has a risk of causing cataract, glaucoma and corneal complications.Immunomodulators have been used as substitutes for corticosteroids. Their potent anti-inflammatory action and fewer side effects are a boon for VKC patients needing long-term therapy. Despite a higher cost of long-term usage, topical cyclosporine (CsA) is a good alternative.[7] CsA acts by interfering with the activity and growth of T cells. It also affects mitochondrial activity in conjunctival cells by preventing the epithelial cell death.8 Nanomicellar formulations help create a clear aqueous solution of this drug and have shown significantly improved levels of tear production and stabilizing effects to maintain ocular surface integrity. Therefore it is used as a first line agent in VKC pharmacotherapy. Tacrolimus is a macrolide. It has similar mechanism of action like CsA but is 100 times more potent.[8] Studies show that corticosteroids, tacrolimus and other immunosuppressive drugs have similar efficacy in allergic crisis control and as a maintenance therapy for VKC.9 Tacrolimus also inhibits the release of histamine, prostaglandins and basophils. 0.03% ointment has showed promising clinical response with minimum side effects and ocular discomfort.[9,10,11] 0.03% tacrolimus eye ointment is very effective, safe, and well tolerated in the treatment of refractive cases of simple allergic conjunctivitis. It helps limit recurrences. Initiation of topical immunomodulators under the supervision of a pediatrician can be considered as first line therapy in children presenting with shield ulcer. Simultaneous administration of topical corticosteroid, artificial tears and immunomodulators combined with surgical intervention seems to enhance the therapeutic efficacy of each other and shows promising results.

Table 1: Grading of shield ulcer with management

Grade	Clinical features	Primary management	If initial therapy fails
1	Ulcer with a transparent base	Topical treatment • Steroids • Mast cell stabilizer • Antibiotics • Topical lubricants with/ without a Bandage contact lens	Modify treatment and frequency of eye drop instillation Surgery-scraping of base and margins if no response observed
2	Ulcer with a translucent base/ inflammatory deposits	Topical treatment as in grade 1, Corneal scraping if infective keratitis suspected	Modify treatment frequency Surgery: Debridement with/ without Amniotic membrane transplantation
3	Ulcer with elevated plaque	Surgery: Plaque removal with Amniotic membrane transplantation along with medical management as in grade 1	Repeat surgery

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