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Evaluvation of Risk Factors and Management Options in Patients with Peripheral Ulcerative Keratitis A Clinical Prospective Study

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ABSTRACT
To assess the clinical scenarios of peripheral ulcerative keratitis in systemic associations, risk factors, screening methods, complications and treatment. To study the clinical profile of the cases based on various etiological factors. This is a 2 years [November 2021 to November 2023] hospital based prospective clinical study conducted in the Department of ophthalmology, AC Subba Reddy Govt Medical college and Hospital Nellore. A number of 80 patients are included in the study after fulfilling the inclusion and exclusion criteria. Among 80 patients, a total number of 105 eyes were recruited for end point observation of these patients, 30 cases were bilateral, 50 cases had unilateral disease and Males were more commonly affected. The mean age of presentation is 62.73+11.76 years. Mooren's ulcer [24%] was found to be common followed by Rheumatoid arthritis [7%], Infection [6%] and granulomatous polyangiitis [2%]. PUK occurred following intraocular surgeries at the same site in 12.2% of cases.

INTRODUCTION

Peripheral ulcerative keratitis Is an ulcerative inflammation of the cornea that is usually associated with any systemic or local autoimmune disease and it is considered as potentially life-threatening condition as it may precede or follow an autoimmune disease. The need of this study aims at varied etiology of peripheral ulcerative keratitis and regarding specific treatment protocol. Early diagnosis and treatment are important because peripheral ulcerative keratitis can be a window to occult potentially lethal systemic disease.

MATERIALS AND METHODS

Study Protocol: Hospital based prospective study conducted at dept of ophthalmology, ggh, nellore.

Duration of Study: 24 months

Sample Size: Total 80 patients were included after fulfilling the inclusion and exclusion criteria.

Inclusion Criteria: patients with ulcer with in 2mm from the limbus with epithelial defect and stromal thinning. Both males and females of age 20-65 years. Patient who is willing to give consent and come for follow up visits.

Exclusion Criteria: Patient with conjunctivitis and scleritis, Demarcation by grey line from central cornea with intact epithelium, Age<20years, Pregnant women. Patient selection was based on inclusion and exclusion criteria. Any crescent shaped destructive inflammation within 2mm of limbus along with epithelial defect, stromal infiltration, degradation or thinning were included in the study. Patient details such as age, gender, history was collected. The area of epithelial defect, stromal thinning, ulcer depth, infiltration and vascularisations were measured in clock hours. Patients were carefully examined for scleritis, anterior chamber inflammation at presentation and during follow ups. Associated findings such as meibomitis, squamous blepharitis, climactic droplet keratopathy and pterygium were recorded. Corneal scrapings sent for smear Gram's stain and KOH wet mount. Culture was done in blood agar and Sabourad's dextrose agar to rule out infective etiology.

Routine blood investigations include total count, differential count, Erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], Rheumatoid factor [RF] and Mantoux test. Anti nuclear antibodies used to confirm collagen vascular diseases like rheumatoid arthritis and Granulomatosis polyangiitis. Based on the etiology and severity, cases were managed medically or surgically according to the clinician's judgement. Cases with impending or actual perforation and treatment failure with medication were managed surgically. Patients were started on topical antibiotic and steroid combination or plain steroid like 1% prednisolone acetate. On resolution the topical steroids were tapered over a period of three weeks. Surgical management includes conjunctival resection, tissue adhesives and patch grafts.

RESULTS AND DISCUSSIONS

We present an observational, prospective study of 110 eyes of 80 patients who are diagnosed with peripheral ulcerative keratitis. In our present study over a period of 24 months Demographic pattern resembled that of previous studies with mean age of presentation as 60.1. There could be a delay in referral to the tertiary eye care as they were referred only when unresponsive to topical therapy[1]. The most common etiology for PUK is Mooren's ulcer [24%] similar to another study done in India by Sharma *et al*[31.5%][1].The presenting complaint of pain is outstanding in Mooren's ulcer out of proportion to inflammation[3]. Kuriacose ET suggested the Hookworm infection associated with Mooren's ulcer[4,5] In the management of Mooren's ulcer the role of monoclonal antibodies were explained in causal relationship with associated Hepatitis C virus infection[6]. In cases of

Fig. 1: Laterality

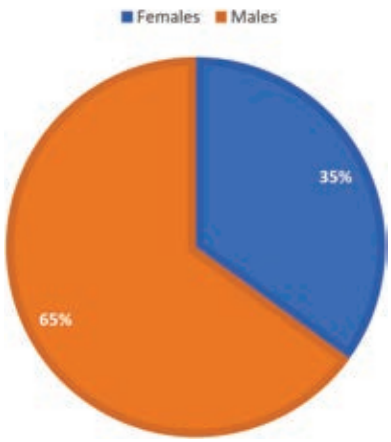

Fig. 2:Gender Distribution

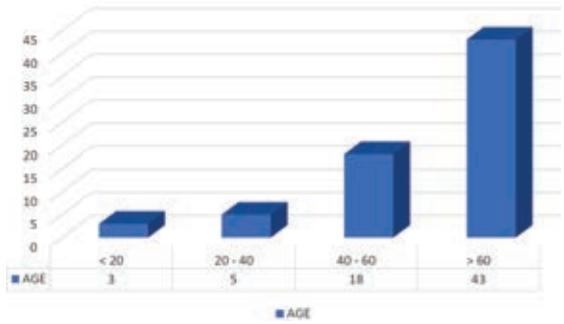

Fig. 3:Age Distribution

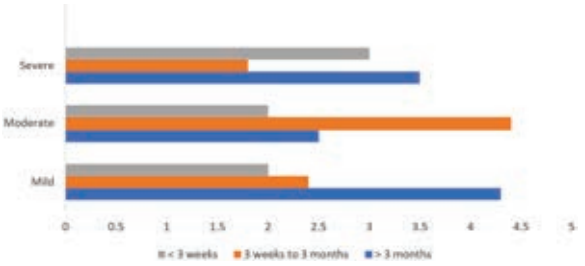

Fig. 4:Time of Presentation

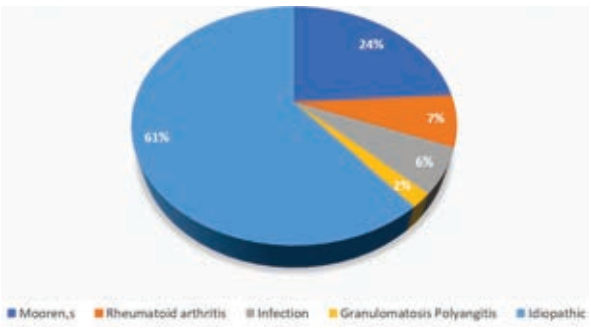

Fig. 5:Etiology

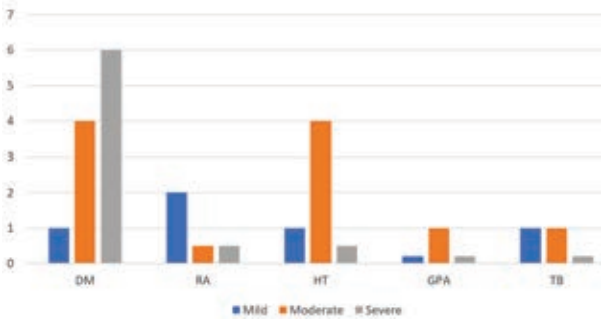

Fig. 6:Chart Title

Table 1: In this table Grade and our study

	p-value for pre and post treatment visual acuity	
Grade	**Our Study**	**SHARMA *et al.***
Mild	0.038	0.085
Moderate	< 0.001	0.160
Severe	0.029	0.01

Table 2: In this table Medical Management Only

Medical Management Only	Our Study	SHARMA *et al.*
Mild	100%	100%
Moderate	94.44%	100%
Severe	82.15%	50%

Table 3: In this table Laterality and No. of cases

Laterality	No. of cases
Bilateral	30(37%)
Unilateral	50(63%)

Table 4: This table telling about grade number of percentage and total

	n%		
Grade	**Male**	**Female**	**Total**
Mild	7 (33.34%)	14 (66.67%)	21 (100%)
Moderate	31 (79.48%)	8 (20.51%)	39 (100%)
Severe	14 (70.00%)	6 (30.0%)	20 (100%)

Table 5: In this table Management, Mild, Moderate and Severe

	n (%)		
Management	**Mild**	**Moderate**	**Severe**
Topical steroid+ Antibiotic only	27 (96.42)	48 (88.89)	21 (75,00)
Bandage contact lens	-	1 (1.85)	1 (3.57)
Methotrexate	1 (3.57)	1(1.85)	-
Cyclophosphamide	-	1 (1.85)	-
Tacrolimus	-	-	1 (3.57)
Patch Graft	-		1 (3.57)
Conjunctival resection	-	3 (5.56)	4 (14.28)
Total	28 (100)	54 (100)	28 (100)

systemic lupus erythematosis [SLE] and Disciod lupus erythematosis[DLE], the primary corneal consequence is superficial punctate keratitis, skin biopsy can be used to make the diagnosis and systemic medication works effectively to treat keratitis[6].In cases of Microscopic polyangiitis and churg-Strauss syndrome, visual disorders like PUK, uveitis, Episcleritis, Ischemic optic neuropathy and cranial nerve palsies may co exist though ocular involvement is uncommon[6]. Antineutrophil cytoplasmic antibodies [p-ANCA] against myeloperoxidase are present in 75% of MPA patients[7] Apart from autoimmune mechanisms of both cell-and humoral-mediated, other pathways like hypersensitive responses to external antigens, circulating immune complexes, reacting to corneal antigens are involved in the pathogenesis of PUK[8]. The role of activated Matrix metalloproteinase [MMP], which exhibits specificity for type 1 collagen has been implicated as a causative agent of PUK[9]. In many other studies Rheumatoid arthritis had been the most common etiology[9].Granulomatosis polyangiitis [GPA] was diagnosed in a patient showed positive to c-ANCA with initial presentation was peripheral ulcerative keratitis[10]. Tauber *et al.* stated that patients with Rheumatoid arthritis and PUK developed necrotising scleritis [70%] over a period of 14 years[12] and 34% of non-infectious PUK cases were caused by RA[12], while Foster et al stated that mortality rate of patients of RA with necrotising scleritis with or without PUK reduced

from 52-5% when started on cytotoxic immunosuppressant therapy[11]. The above table states that our study shows significant visual acuity improvement in moderate cases differing from the previous studies where severe cases had improved visual outcomes[1].

The above table shows that more cases of severe category were managed medically in our Study in comparison to Sharma et al where nearly 50% of them required surgical treatment[1]. In this prospective study, 110 eyes of 80 patients were recruited. Out of these patients, 5 patients lost follow up. Hence 105 eyes were recruited for end point observation. Of these patients, 30 cases were bilateral, 50 patients had unilateral disease. Males were more commonly affected with PUK than females. The male to female ratio is 3:1. This shows that female had lesser incidence of PUK and also presented with a milder form than men. The above results shows that patients with severe form shows slightly later presentation. This could be because the disease progressed to a severe form by the time when they reached the tertiary eye care center.

Etiological Classification[1,2,3]: Ocular infections -streptococcus, staphylococcus, Herpes zoster, Herpes simplex, Fungal pathogens. Systemic infections-varicella zoster, Gonococcal arthritis, Dengue fever, Leishmaniasis. Non infectitious ocular conditions-Mooren's ulcer, Traumatic, post surgical, siccas syndrome, Neuroparalytic keratitis. Non infectitious systemic conditions Rheumatoid arthritis, Polyarteritis nodosa, Systemic lupus erythematosus, Sjogren's syndrome, Rosacea, Steven-Johnson's syndrome, Psoriasis. Others, Leukemia, Porphyria. Mooren's ulcer [24%] was found to be common etiology followed by Rheumatoid arthritis [7%]. Infection 6%] and Granulomatosis polyangiitis[2%],PUK occured following intraocular surgeries at the same site in 12.2% of eyes. Regarding the systemic history it was found that Diabetes mellitus was present in 21.74% of cases. Rheumatoid arthritis was present in 7.25% of cases.

Modes of Treatment[13]**:**
Aim of Management of Puk:

- Identifying the etiology
- Facilitating epithelial wound repair
- Check ulceration and support repair

Role of Tissue Adhesives[14]**:** Application of tissue adhesive like isobutyl cyanoacrylate in an eye with stromal ulceration or impending perforation will prevent further ulceration and support the stroma through the period of neovascularization and repair. The mechanism of action is believed to be through the exclusion of inflammatory cells from the ulcerating stroma.

Role of Anti Inflammatory Agents[15]**:** Topical corticosteroids are useful in early therapy whereas systemic corticosteroids are helpful in cases of PUK associated with Relapsing polychondritis, Rheumatoid arthritis and SLE. Messmer and Foster observed that cytotoxic immunosuppressive agents are very successful in treating patients resistant to systemic corticosteroids[6]. In PUK patients with Rheumatoid arthritis not associated with systemic vasculitis cyclosporine is the first drug of choice. In cases of systemic vasculitis with severe inflammatory eye disease, more strong immunosuppressive agents like cytotoxic [cyclophosphamide] or indomitability [Methotrexate] are used. Most of the patients were successfully managed with topical steroid and antibiotics in the mild [96.42%] and moderate [88.89%] form of disease. The severe form of disease required more of surgical treatment in comparison to the other forms.

Complications: Complicated cataract 44% [22/50 eyes] was the most common complication observed followed by Anterior uveitis in 10% [5/50 eyes], Glaucoma in 7% of cases. Perforation occurred in most cases of Mooren's ulcer [66.7%], Nodular scleritis in 3% of cases.

Summary: This is a prospective study on clinical profile of peripheral ulcerative keratitis of various etiologies was conducted over a period of 24 months. In our study most common cause of PUK is Mooren's ulcer followed by Rheumatoid arthritis.

PUK should be regarded as a vision and globe-integrity threatening disease. Biological therapy like conjunctival resection along with patch grafts plays a vital role in addition to medical therapy with steroids and immunosuppressive agents in patients with autoimmune diseases.

CONCLUSION

PUK is an ophthalmic emergency as the patient is at risk of corneal perforation and blindness. A multidisciplinary approach is mandatory for better work up of investigations related to confirmation of etiology. There has been delay in patients reaching the tertiary eye care center which is more observed in most of the severe cases. Hence, earlier the referral to a tertiary eye care center, better the management outcomes.

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