PERIPHERAL ULCERATIVE KERATITIS (PUK)

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Peripheral Ulcerative keratitis is a potentially sight threatening disorder which usually begins with crescentic destructive inflammation at the corneal periphery and is associated with epithelial defect, presence of stromal inflammoatory cells, progressieve stromal melting, degradation & necrosis. It may sometimes lead to perforation.

Clinical features

Symptoms : Foreign body sensation, severe pain if there is associated scleritis, watering, photophobia, dimness of vision which is sometimes rapidly progressive PUK associated with moorens ulcer may also cause pain without scleral involvement.

Slit lamp examination : Reveals a crescent shaped destructive lesion at the juxtalimbal corneal stroma, associated with epithelial defect, stromal yellow-white infiltrates composed of inflammatory cells and varying degrees of corneal thinning. Typical "overhanging" adges are seen in Moorens ulcer. The anterior chamber should be examined for depth and inflammation. Presence of necrotizing scleritis indicated potentially lethal systemic disease.

Etiology

Unlike avascular central cornea the peripheral cornea derives part of its blood supply from the anterior conjectiva and deep episcleral blood vessels. These blood vessels are a source of immunocompetent cells. Some of the causes of PUK are.

Noninfectious conditions

- Local- Mooren ulcer, marginal keratitis blepharitis (eg. staphylococcal infection, rosacea), contact lens use, chemical injury to the eyes, trauma, surgery, neurotrophic and neuroparalytic causes, nutritional deficiencies, keratoconjunctivities sicca, Terrien marginal degeneration.
- Systemic - Rheumatoid Arthritis (RA), Systemic Lupus Erythromatous (SLE), Relapsing Polychondritis (RP), sarcoidosis, progressive systemic sclerosis (PSS), rosacea Wegners granulomatosis (WG), Polyarteritis Nodosa (PAN), giant cell arteritis (GCA), inflammoatory bowel disease, and metabolic and neoplastic condtions.

Infectious conditions

- Local - Herpes simplex keratitis, varicella-zoster keratitis, bacterial keratitis, fungal keratitis, and acanthamoeba species.
- Systemic-Shigella species, tuberculosis syphilis, hepatitis, C, HIV, gonococcus, salmonella species and bacillary dysentery. The incidence of Moorens is particularly high in areas where parasitic infestations are endemic

All the above mentioned causes lead to inflammotory reaction at the corneal periphery. Inflammation causes immun complex deposition, complement activation and further increase in vascular permeability. This an turn generates more chemotactic factors (C3a, C5a) for Neutrophils. Neutrophils thus recruited at the peripheral cornea liberate proteolytic and collagenolytic enzmes causing destruction of corneal stroma.

History

Systemic signs are sometimes helpful for diagnosis.

RA : typical swan neck deformity.

SLE : characteristic butterfly distribution of rashes

PSS : shiny and thickened skin effacement of skin margins, tautness of skin leading to sclerodactyly

WG : cavitary lung lesions

Sarcoidosis : enlarged mediastinal lymph nodes.

Patients with Mooren's ulceration have no

diagnosable systemic disorders and suffer from extreme ocular pain without any scleral involvement, marked photophobia and increased tearing. It is more a diagnosis of exclusion.

Differential diagnosis

- Marginal keratitis associated with blepharitis
- Dellen
- Furrow degenerationu
- Pellucid marginal degeneration

Lab Investigations

Complete blood count, ESR

Rheumatoid factor : +ve in 80% of patients with RA

Angiotensin converting enzyme : elevated in sarcoidosis

Antinuclear antibodies (ANA) : + ve in SLE & RA

Antibody to double-stranded DNA (anti-ds DNA); associated with SLE

Antibodies to small nuclear ribonucleoprotein-SM (anti-SM) : associated with SLE

Antibodies to small nuclear ribonucleoproteins-RNP (anti-RNP) : associated with SLE

Antineutrophil cytoplasmic antibodies (ANCA) : C-ANCA : 96% sensitivity for WG

Hepatitis B surface antigen (HBsAG) HBsAg + ve40% patients with PAN

Imaging Studies

- Chest x-ray and sinus CT scan to rule out WG, sarcoidosis, and tuberculosis
- Radiographic studies of affected joints.

Conjunctival biopsy

Biopsy of adjacent conjunctiva is not a standard diagnostic procedure but can be considered in cases with diagnostic dilemma when conjunctival resection is planned. It may show features of vaso occlution or granulomatous inflammation (in WG).

Treatment

Medical Management

Combination of local and systemic therapy. The local therapy helps the epithelium to heal whereas the systemic therapy will quiet down the underlying disease.

Certain collagenase inhibitors like topical 20% N-acetylcystiene or collagenase synthesis inhibitor like Medroxyprogesterone along with profuse preservative free lubricating drops help in reepithelialization of the cornea.

Aggressive topical steroids, topical cyclosporine A 2%, collagenase inhibitors or collagenase synthetase inhibitors have been used with varying results as adjunct therapy.

Treatment with topical corticosteroids may be harmful in a subset of vasculitic PUK because they inhibit new collagen production.

Systemic collagenase inhibitors like Tetracycline 250 mg qid or Doxycycline 100mg bid may slow progression.

Indication for Immunosupression

- PUK associated with lethal systemic vasculitic syndromes PAN, RA, SLE, PSS, Sjogren's syndrome, RP, Wegener's granulomatosis.
- PUK associated with necrotizing scleritis
- Bilateral and or progressive Mooren's ulcer.
- PUK unresponsive to agreessive conventional medical and surgical therapy.

Cyclophosphamide is the drug of choice for PUK associated with connective tissue disorders. Methotrexate, Azathioprine, Cyclosporine A are also effective. All these agents are to be used based on the clinical response and adverse effects.

Dosage and precautions

- Cyclophosphamide : 2 mg/kg / day orally; side effect bone marrow depression Monitor blood counts.
- Methotrexate : 7.5-12.5 mg/week oral/IM inj. Monitor CBC, LFT & Renal function

- Azathioprine : 1-3 mg/kg/day orally Monitor Absolute platelet count, LFT.

Usually oral prednisolone and an immunomodulatory agent such as Cyclophosphamide is initiated at the same time. It may take about 4 to 6 weeks for the immunomodulatory agent to take effect. Oral prednisolone is used in the interim period to stabilize the patient and control the active inflammatory process until the immunomodulatory agent takes effects. Prednisolone is subsequently tapered and the patient is maintained on the systemic immunomodulatory agent.

Systemic Infliximab/ Ritumimab (CD 20 antagogonists) are useful when patients cannot tolerate cyclophosphamide or methotrexate.

If local or systemic infections are suspected as a cause then appropriate antibiotic medications based on clinical signs of the disease or culture reports are used.

Surgical management

Conjunctival resection helps to remove the limbal source of collagenases and other factors causing progressive destruction of stroma.

Tissue adhesives (cyanoacrylate glue) and Bandage contact lens application combined with conjunctival resection are helpful in cases of impending perforation.

Tectonic procedures such as patch grafts full thickness or lamellar are done to maintain the integrity of the globe in cases of perforations. Elective reconstructive keratoplasty once the disease process is controlled. Amniotic membrane grafting can be done to promote healing Mooren's ulcer.

Follow up

Lifelong follow-up care is necessary even after complete resolution since relapses may occur. Many patients may require prolonged systemic steroid, nonsteroidal anti-inflammatory, and / or chemotherapeutic medications for the systemic disease despite a quiet eye.