PERIPHERAL ULCERATIVE KERATITIS

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INTRODUCTION

The unique anatomic and immunologic characteristics of the peripheral cornea predispose it to disorders which normally do not involve the central cornea. Because of it proximity and contiguity with the sclera, episclera and conjunctiva, conditions affecting these structures including infections, hypersensitivity disorders, mass lesions and degenerations may secondarily spread to involve the limbus and peripheral cornea[1]. Unlike the avascular central cornea, the limbus and peripheral cornea obtain part of their nutrient supply from the anterior conjunctival and deep episclera vessels which extend 0.5 mm into the clear cornea[2]. Accompanying these vessels are subconjunctival lymphatics which drain into the regional lymph nodes, providing access to the affarent arm of the corneal immunologic reactions. The presence of this limbal vasculature allows for limited diffusion of some molecules such as immunoglobulins and complement components into the cornea. IgA and IgG are found in similar concentrations in the peripheral and central cornea, but there is more IgM in the periphery probably because its larger size restricts diffusion into the central cornea. Both IgM and IgG fix complement via the classical pathway. C1, the recognition unit of this pathway is more concentrated in the peripheral cornea. It might be expected that antigen-antibody complexes, may activate complement more effectively in the peripheral than in the central cornea. The resultant attraction of inflammatory cells including neutrophils and macrophages may release proteolytic and collagenolytic enzymes that cause destruction of the peripheral cornea. Langerhans cells, the dendritic antigen presenting cells are distributed most abundantly in the conjunctiva and peripheral cornea, with very few detected in the central cornea. In addition to antigen presentation, these cells may be capable of inflammatory mediator secretion and may thus contribute to peripheral corneal ulceration[3]. Histologically, the peripheral cornea also contains a reservoir of inflammatory cells including neutrophils, eosinophils, lymphocytes, plasma cells and mast cells[2]. The presence of blood vessels, lymphatic channels, antibodies, complement components, Langerhan's cells and inflammatory cells account for the predilection of the peripheral cornea to be more susceptible to alteration in a wide variety of infectious and non-infectious systemic and local diseases, leading to a clinical entity termed Peripheral Ulcerative Keratitis (PUK).

Definition

Peripheral ulcerative keratitis refers to a crescent shaped destructive inflammation of the juxtalimbal corneal stroma associated with an epithelial defect, presence of stromal inflammatory cells, and stromal degradation[4]. The ulceration may progress both centrally and circumferentially, relentlessly, unresponsive to topical or conservative local therapy. The conjunctiva, episclera and/or sclera are usually inflamed. Vascularized corneal pannus is absent in the active phase[5]. The signs of resolution of active PUK include resolution of the conjunctival inflammation, epithelialization of the corneal surface with residual corneal thinning and a vascularized scar. Whatever the etiology, PUK is always a local destructive process mediated by the final pathway of collagenolytic and proteolytic enzymes released from neutrophils and/or macrophages[6]. The end result is peripheral corneal stromal degradation.(Fig 1)

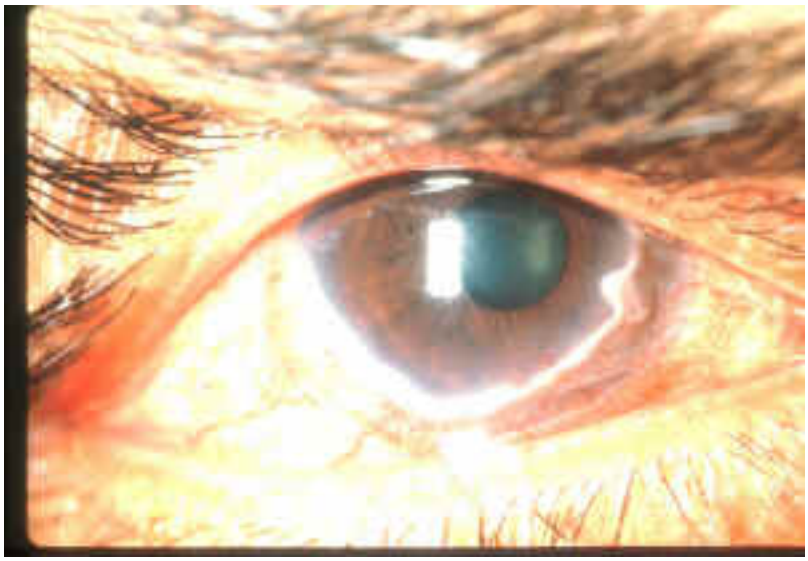


Figure 1

CLINICAL FEATURES

Patients with PUK frequently present with pain, tearing and photophobia. In contrast, patients with non-inflammatory peripheral thinning disorders such as Pellucid or Terrien's marginal degeneration are usually asymptomatic except for decreased vision. Visual acuity may be decreased in patients with PUK if there is central corneal involvement or significant astigmatism. On slit lamp biomicroscopy, one finds variable degrees of stromal loss or thinning adjacent to the limbus. As in all true ulceration, there is an epithelial defect with an underlying subepithelial inflammatory infiltrate. Non-ulcerative peripheral corneal thinning such as Terrien's degeneration will have intact epithelium.

The conjunctiva and episclera are usually inflamed. Associated scleritis, especially the necrotizing form, is a highly significant finding because its presence signals an underlying systemic vasculitic process. In the appropriate clinical setting, the detection of scleritis may rule out Mooren's ulcer, which classically has no associated scleritis.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses of PUK are extensive and include infectious and noninfectious causes subgrouped into four categories (Table 1)[7] a) ocular infections b) non-infectious ocular inflammations c) systemic infections and, d) systemic non-infections. At the onset, one must rule out Collagen Vascular Diseases (CVD) and Sjogren's syndrome. The corneal thinning caused by these conditions has different courses and requires different treatment. Vasculitides/ CVD are responsible for approximately one half of the non-infectious causes of PUK[8]. Associated necrotizing scleritis is frequently evident. The onset of PUK in patients with connective tissue disease such as rheumatoid arthritis, relapsing polychondritis or systemic lupus erythematosus may herald the presence of a potentially lethal systemic vasculitis that requires systemic immunosuppresive therapy. PUK may be the presenting sign of systemic necrotizing vasculitis in patients with Wegener's granulomatosis, polyarteritis nodosa, microscospic polyangiitis or Churg Strauss syndrome. Sjogren's syndrome is an uncommon cause of non-inflammatory peripheral corneal thinning.

Mooren's ulceration may be distinguished from PUK associated with collagen vascular disease by the extreme pain, the absence of scleritis, the typical overhanging central corneal edge and lack of associated systemic diseases. Any microbe, including bacteria (Fig 2), viruses, fungi and

parasites may cause peripheral ulceration. PUK may also occur as a result of lid abnormalities and dermatologic disorders such as rosacea. Both systemic and local malignancies including leukemia, sebaceous and squamous cell carcinoma may, though rarely, cause PUK

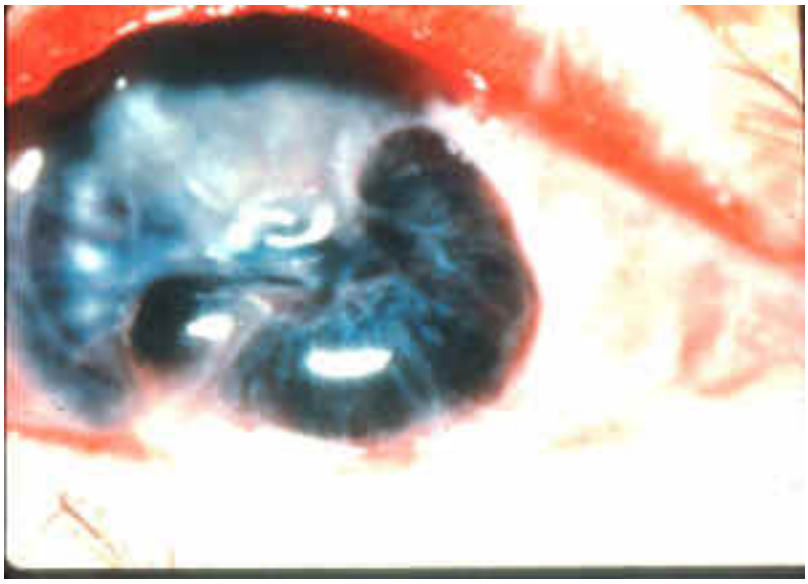


Figure 2

Diagnosis

A thorough history encompassing the chief complaint, past history, family history, past and present therapy and review of systems (table 2)[6], is extremely important and may provide useful clues to the underlying etiology of PUK. Physical examination of the head and neck, extremities and skin may reveal significant signs or guide the physician to the possible diagnosis (table 3)[6]. For example the presence of saddle nose deformity and/or auricular pinnae deformity can be signs of relapsing polychondritis. Loss of facial expression or a tight skin may suggest the diagnosis of scleroderma. Facial telangiectasias can be signs of acne rosacea or scleroderma. Facial rashes or ulcer may implicate any vasculitic syndrome.

There are no set diagnostic tests for PUK. The findings of history, review of systems and physical examination should guide the testing to be ordered. Typical investigations may include: CBC, ESR, CRP, alpha-1-acid glycoprotein, properdin factor B, cryoglobulins, C_{1q}binding assay, Raji cell assay, hepatitis B & C antibodies, rheumatoid factors, ANA's, ANCA, anti type 2 collagen antibody and Urinalysis. Table 4,[6] shows other tests that may be useful based on the suspected diagnosis. Chest X rays are of diagnostic significance in tuberculosis, sarcoidosis and Wegener's granulomatosis. Sinus films showing mucosal thickening and/or destruction of bony walls can be helpful in the diagnosis of Wegener's granulomatosis.. Appropriate cultures and corneal scrapping should be done to exclude infectious etiologies.

Biopsy of the bulbar conjunctiva adjacent to the ulcerating cornea should be considered, especially in suspected autoimmune associated PUK. Available modalities for studying the specimens include light and electron microscopy, immunoprobes and Polymerase chain reaction (PCR).

The combination of clinical data, test results and biopsy findings can lead to better diagnostic prediction. In addition, biopsy findings may be helpful in deciding a specific therapy. Because PUK may be the presenting manifestation of an occult systemic vasculitic disease and may proceed detectable extra-ocular manifestations by several years, the finding in ocular tissue of a necrotizing vasculitis provides justification for a systemic immunomodulating agent. Vasculitis

manifesting as neutrophil invasion of the vessel wall with fibrinoid necrosis on light microscopy may be associated with a systemic vasculitic process such as PAN, SLE, PSS, relapsing polychondritis, Sjogren's syndrome, Wegener's granulomatosis and allergic angiitis of Churg-Strauss syndrome. Its absence in a patient clinically suspected of having Mooren's ulcer, may clinch the diagnosis. Granulomas are usually found in patients with Wegener's granulomatosis, Giant cell arteritis and Churg-Strauss, and is absent in polyarteritis nodosa.

THERAPY

A combination of local and systemic therapy may be indicated in autoimmune mediated or vasculitic PUK. 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. Local surgical therapy such as conjunctival resection, ulcer debridement, application of tissue adhesive to the ulcer bed and to a small rim of surrounding normal cornea and sclera, and application of continuous wear bandage soft contact lens can be used to delay the disease process while the patient is being immunosuppressed. The indications for the use of systemic immunomodulatory agents including methotrexate, cyclophosphamide, cyclosporine and azathroprine are[6]: (1) PUK associated with potentially lethal systemic vasculitic syndromes such as PAN, RA, SLE, PSS, Sjogren's syndrome, RP, Wegener's granulomatosis, allergic angiitis of Churg-Strauss, and giant cell arteritis. (2) PUK associated with necrotizing scleritis and vasculitis is found by histopathologic analysis of ocular tissue. (3) Bilateral and / or progressive Mooren's ulcer. (4) PUK unresponsive to aggressive conventional medical and surgical therapy. A combination of oral prednisone and an immunomodulatory agent such as methotrexate is usually initiated at the same time. It may take about 4 to 6weeks for the immunomodulatory agents to take effect. Oral prednisone is used in the interim to stabilize the patient and control the active inflammatory process until the immunomodulatory agent takes effect. Prednisone is subsequently tapered and the patient maintained on the systemic immunomodulatory agent. If the initial combination of therapy is ineffective after several months, the patient will be switched to a different agent such as cyclophosphamide. The methotrexate is stopped and the oral prednisone increased in the crossover period. In patients with PUK associated with Wegener's granulomatosis and polyarteritis nodosa, cyclophosphamide at a daily dosage of 2mg/Kg orally together with corticosteroids (1mg/Kg) may be the initial therapy of choice. Oral cyclosporine is more effective in intra-ocular inflammation and is rarely used in PUK. Treatment of patients with nonautoimmune associated PUK such as rosacea may include systemic doxycycline or minocycline, lid hygiene and lubrication, and metronidazale for the dermatologic findings.

CASE EXAMPLES

HSV and VZV

Both HSV and VZV can cause PUK in the absence of dermatologic findings. Normally this is a consequence of production of limbal vasculitis. Culture of corneal scrapings might be negative. The microbes may be detected within the biopsied limbal conjunctiva vessels by immunoprobing. Treatment with topical steroids and systemic antiviral agent is normally effective.

Staphylococcal Marginal Keratitis

These local hypersensitivity responses to microbial antigens may represent the most common form of peripheral cornea infiltrates and ulceration often in association with longstanding Staphylococcal blepharoconjunctivitis. Usually the infiltrates are separated from the limbus by a distinct lucid interval of clear, noninvolved cornea. The direction of spread of the lesion is concentric with the limbus, rather than centrally or peripherally. In the early phase, the epithelium

overlying the infiltrate is intact. If the lesions are left untreated, epithelial breakdown and eventual ulceration occurs. The natural course of the lesion however is benign, and healing usually occurs in 2 to 4 weeks. Vascularized corneal pannus directed to the ulcer site may bridged the lucid interval after healing. The lesions may occur recur if the blepharitis is not properly treated.

Microbial culture of the lid margins will yield Staphylococcus aureus in the majority of cases. Corneal cultures of the ulcer are negative for bacteria. Gram and Giemsa stains of the corneal scrapings usually show neutrophils but no bacteria. Treatments of the acute lesions with mild topical steroids usually cause rapid resolutions of symptoms. A combination of lid hygiene and topical antibodies is used to treat the blepharitis and prevent recurrences.

Mooren's ulcer

Mooren's ulcer is a chronic unilateral or bilateral, idiopathic painful ulceration and thinning of the peripheral not associated with scleritis. The ulceration begins as grayish infiltration in the perilimbal cornea usually in the interpalpebral fissure. Loss of epithelium follows within a few days to form a marginal ulcer. Characteristically the central wall of the ulcer is undermined leading to an overhanging advancing edge of an epithelial effect (**Figure 3**). It is a diagnosis of exclusion, since many conditions can present somewhat similarly.

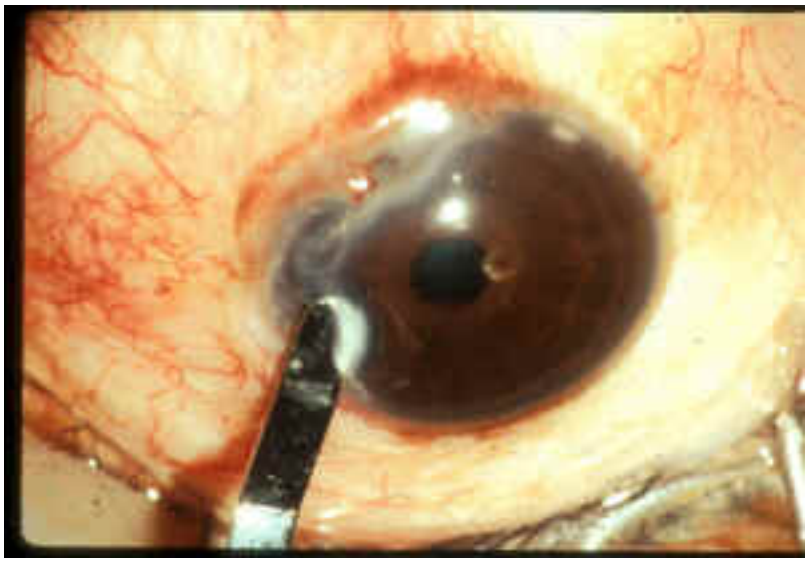


Figure 3

The ulceration first spreads circumferentially and then centrally, ultimately subsiding after the entire cornea has been involved typically over a period of 4 to 18 months. The pain also disappears with healing and vascularization. Spontaneous or traumatic perforation may occur. Patients with Mooren's ulceration have no diagnosable systemic disorders and suffer from extreme ocular pain, marked photophobia and increased tearing. Severe visual loss due to irregular astigmatism may be present.

Treatment might involve initial aggressive topical steroid therapy with prophylactic antibiotics, followed by conjunctival resection, ulcer debridement, application of tissue adhesive to thinned areas with soft contact lens application and subsequent treatment with predinosolone phosphate 1% four times daily. Bilateral or progressive Mooren's ulcer usually requires systemic immunomodulatory therapy to control the progressive corneal destruction.

Terrien's Marginal Degeneration

This is a slowly progressive cause of marginal corneal thinning more common in males, and can occur in all age groups, including children. It is usually painless, with only minor or no episodes of acute inflammation and the corneal epithelium remains intact. The thinning usually begins superiorly, (**Figure 4**) and progresses circumferentially but minimally centrally. Associated lipid deposition at the edge of fine superficial vessels may be evident. The cornea can become extremely thin and perforate with minor trauma. Decreased vision may result from severe against the rule astigmatism. Management might require surgical intervention.

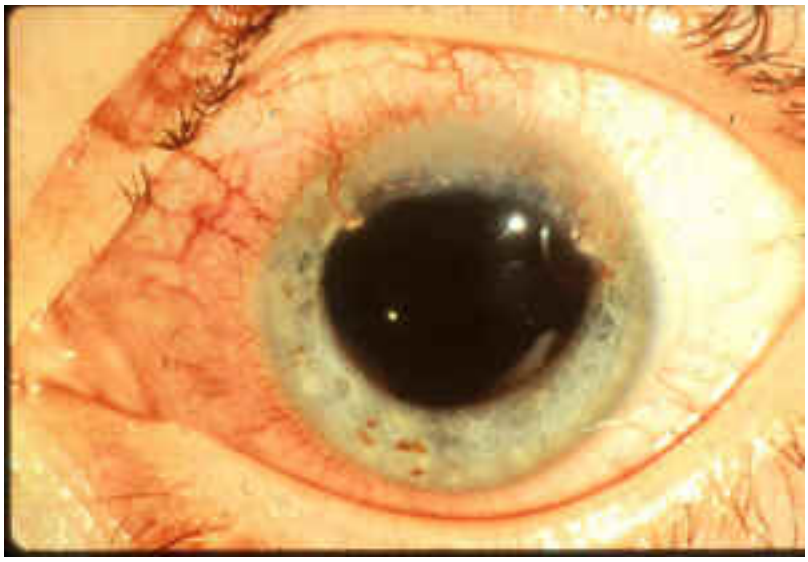


Figure 4

Rheumatoid Arthritis

Keratoconjunctivitis sicca (KCS) is the most frequent ocular manifestation, and this may cause severe non-inflammatory corneal melt and perforation but not PUK (Fig 5). Scleral involvement in RA includes anterior nonnecrotizing and necrotizing scleritis and posterior scleritis. PUK is often associated with necrotizing scleritis, a feature that differentiates it from Mooren's ulcer. The clinical appearance of the PUK is not unique to RA (Fig 6). Advanced systemic involvement is usually apparent at the time of ocular involvement. PUK may be associated with prior cataract surgery. Patients with PUK and necrotizing scleritis have a decreased life expectancy because of associated subclinical systemic vasculitis.[9-10] Treatment is initially with systemic steroids combined with methotrexate (5-25mg once weekly), reserving agents such as cyclophosphamide for therapeutic failures, drug intolerance and rapidly progressive disease.

Figure 5

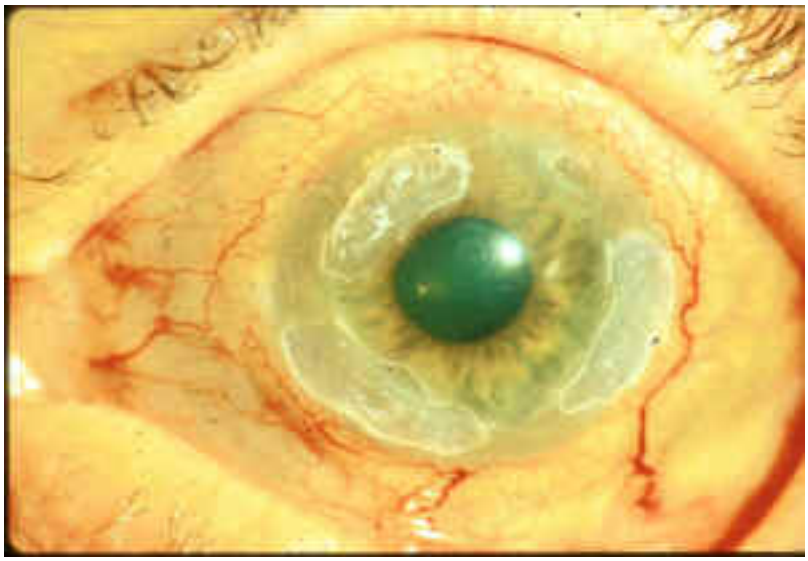
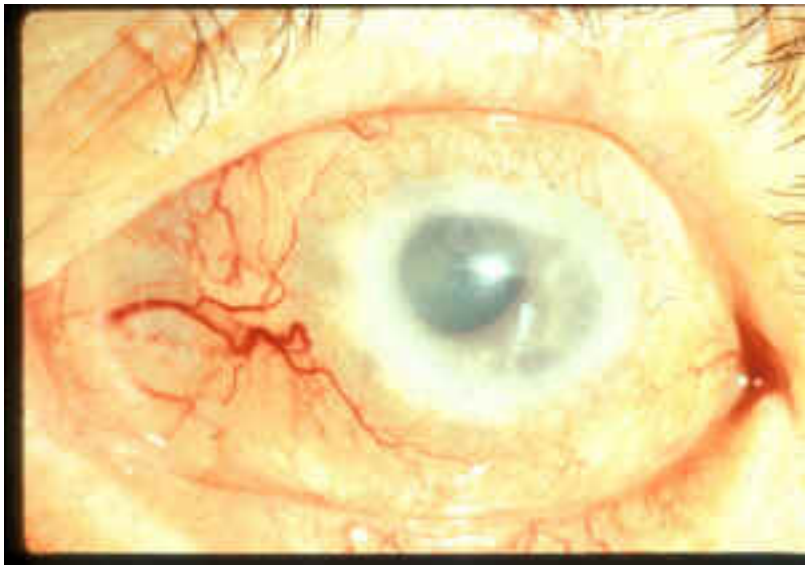
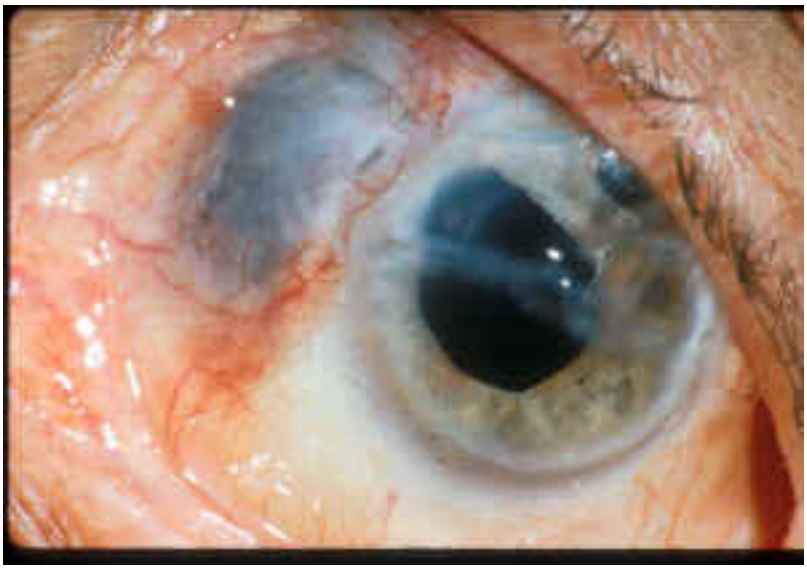


Figure 6



Wegener's granulomatosis

Orbital involvement with proptosis and scleritis are the most common ophthalmic manifestations in this multisystem necrotizing granulomatous vasculitic disease. PUK can be the initial clinical manifestation and the presenting or only sign of the disease. It is usually bilateral and classically associated with an adjacent necrotizing scleritis (Fig7). The ulcers generally progress circumferentially.

Figure 7 

Cytotoxic immunomodulatory agents, especially cyclophosphamide, is usually the treatment of choice in patients with classic Wegener's granulomatosis (renal, upper and lower respiratory tract involvement). Methotrexate may be used with limited (no renal involvement) or very limited (only ocular/orbital involvement) Wegener's granulomatosis. The 'cytoplasmic' immunofluorescence staining pattern (c-ANCA) is very specific for Wegener's granulomatosis; but some patients may show the perinuclear pattern of staining (p-ANCA). There is decreased risk of recurrence of the disease if serum ANCA level is normalized by therapy.

Polyarteritis Nodosa (PAN)

Patients with PAN have been subdivided into three major groups: classic PAN, Churg-Strauss syndrome (CSS) and microscopic PAN**.** Classic PAN is a necrotizing vasculitis affecting primarily medium sized vessels. It may be associated with Hepatitis B, C and other viral infections. Multiple organs including kidney, skin, bone marrow, CNS, lungs, the heart, GI and genital tracts may be involved. Respiratory tract involvement is absent. It is in part a diagnosis of exclusion resting on clinical signs and on histopathologic demonstration of nongranulomatosis vasculitis of medium and small arteries. In classic PAN, ANCAs are absent. An ocular involvement occurs in approximately 20% of PAN patients and includes keratitis accompanied by scleritis. CSS is defined by the combination of asthma, eosinophilia, and a systemic, necrotizing vasculitis. Microscopic polyarteritis nodosa is characterised by a small–vessel vasculitis, usually associated with necrotizing glomerulonephritis and respiratory tract lesion. In contrast to classic PAN, the majority of patients with CSS and microscopic PAN are p-ANCA positive.

PUK morphologically similar to Mooren's ulcer with the central overhanging edge may be the presenting sign of PAN. Usually associated adjacent necrotizing scleritis is present. The treatment of choice is combination of systemic corticosteroid and cyclophosphamide. Local surgical therapy may temporarily retard progession of the ulcer until immunosuppression takes effect. Treatment with topical corticosteroids may be harmful because they inhibit new collagen production.

TABLE 1

DIFFERENTIAL DIAGNOSIS OF PERIPHERAL ULCERATIVE KERATITIS

Ocular-Infectious	Bacterial	Staphylococcus, Streptococcus, Gonnococcus, Moraxella, Haemophilus
	Viral	Herpes simplex, Herpes zoster
	Acanthamoeba	
	Fungal	
Ocular-Non-Infectious	Mooren's ulcer	
	Terrien's Marginal Degeneration	
	Pellucid Marginal Degeneration	
	Keratonconjuctivis Sicca	
	Blepharitis:Staphycoccal, Rosacea	
	Neutrophic / Neuroparalytic causes	
	Nutritional deficiencies	
	Chemical injury to the eye	
	Contact Lens usage	
	Traumatic or postsurgical	
Systemic-Infectious	Tuberculosis	
	Syphillis	
	Varicella zoster	
	Gonorrhea	
	Human immunodeficiency Virus	
	Bacillary dysentery	
Systemic-Non-Infectious	Rheumatoid arthritis	Schonlein-Henoch purpura
	Giant cell arteritis	Malignancies
	Wegener's granulomatosis	Mixed cryoglobulinemia
	Systemic lupus erythematosus	Crohn's regional ileitis
	Polyarteritis nodosa	Ulcerative colitis
	Sjorgren's syndrome	Rosacea

Churg-Strauss syndrome	Psoriasis
Relapsing polychondritis	Stevens Johnson Syndrome
Progressive systemic sclerosis	Cicatricial pemphgoid
Serum sickness	Sarcoidosis
	Behcet's disease

Abbreviations: SLE, systemic lupus erythematosis; RA, rheumatoid arthritis, RP; relapsing polychondritis; PSS, progressive systemic sclerosis; PAN, polyarteritis nodosa; Sjog, Sjogren's disease; Weg, Wegener's granulomatosis; Ch-S, allergic angiitis of Churg-Strauss; G-C, giant cell arteritis; Ros, Rosacea.

Table 2

REVIEW OF SYSTEMS QUESTIONAIRE FOR PERIPHERAL ULCERATIVE KERATITIS

Manifestation	Associated **Systemic Diseases**
Skin and hair	**All vascular syndromes**
Rash/ulcers	**SLE**
Sunburn easily	**SLE, PSS**
Depigmentation	**SLE**
Loss of hair	**PSS, SLE, G-C**
Painfully cold fingers	**PSS**
Puffy hands and feet	**Sjog, Ch-S, Weg, RP**
Respiratory	**Weg, SLE**
Constant coughing	**SLE, Ch-S, Weg, PSS, RP**
Coughing blood	**Ch-S**
Shortness of breath	**Ch-S, Weg, Sjorg, RP**
Asthma attacks	**Weg, SLE, PAN, Ch-S, RP**
Pneumonia	**PAN**
Genitourinary	**All vasculitic syndromes**

	PAN, G-C, PSS, Sjog
Blood in urine	**PAN, SLE, Ch-S**
Testicular pain	**SLE**
Rheumatologic	
Painful joints	**PSS**
Muscle aches	**SLE**
	PAN
Gastrointestinal	
Abdominal pain	**SLE, G-C, RP**
	All vasculitic syndromes
Nausea, vomiting	**SLE, Weg, RP**
Regurgitation	**SLE, RP**
Jaundice	**SLE, Ch-S**
Blood in stool	**RP, Weg, G-C, Sjog**
Neurological	**RP**
Headaches	**Weg, RP**
Numbness/tingling	**Weg, SLE**
Paralysis	**Weg**
Seizures	**RP**
Psychiatric	**Weg**
Ear	**SLE, Sjog**
Deafness	**Sjog**
Swollen ear lobes	**SLE, RP**
Ear infections	
Nose/sinus	
Nasal mucosal ulcers	
Rhinitis/nosebleeds	

Swolen nasal bridge

Sinus trouble

Mouth/throat

Oral mucosal ulcers

Dryness

Persistent hoarseness

Abbreviations: SLE, systemic lupus erythematosis; RA, rheumatoid arthritis, RP; relapsing polychondritis; PSS, progressive systemic sclerosis; PAN, polyarteritis nodosa; Sjog, Sjogren's disease; Weg, Wegener's granulomatosis; Ch-S, allergic angiitis of Churg-Strauss; G-C, giant cell arteritis; Ros, Rosacea.

Table 3

GENERAL EXAMINATION OF THE HEAD AND EXTREMITIES IN PERIPHERAL ULCERATIVE KERATITIS

Clinical Finding	Associated Systemic Diseases
Sadle nose deformity	RP, Weg
Auricular pinnae deformity	RP
Nasal mucosal ulcers	Weg
Oral/lip/tongue mucosal ulcers	SLE, Sjog
Facial "butterfly" rash	SLE
Alopecia	SLE SLE, PSS, RP
Hypo/hyperpigmentation (scalp, face)	PSS
Loss of facial expression	Ros, PSS
Facial telangiectasias	Ros
Rhinophyma	All vasculitic syndromes
Facial/arms/legs rashes, ulcers	PSS
Facial/arms/legs taught skin	G-C

Temporal artery erythema/tenderness	PSS, SLE, G-C, Sjog
Raynaud's phenomenon (fingers)	All vasulitic syndromes
Ulcers in fingertips	RA, SLE, Weg, Ch-S, PAN
Subcutaneous nodules in arms and legs	All vasculitic syndromes
Arthritis in arms and legs	

Abbreviations: SLE, systemic lupus erythematosis; RA, rheumatoid arthritis, RP; relapsing polychondritis; PSS, progressive systemic sclerosis; PAN, polyarteritis nodosa; Sjog, Sjogren's disease; Weg, Wegener's granulomatosis; Ch-S, allergic angiitis of Churg-Strauss; G-C, giant cell arteritis; Ros, Rosacea.

Table 4

LABORATORY TESTS FOR SUSPECTED SYSTEMIC DISEASES IN PUK

Systemic Diseases	Laboratory Tests
Systemic lupus erythematosus	ESR, ANA (anti-dsDNA, anti-Sm) IgG, C, Cryog
Rheumatoid arthritis	ESR, RF, ANA(anti-RNP), CIC, C, Cryog, joint X-rays
Progressive systemic sclerosis	ESR, ANA (anti-centromere, anti-Scl-70), RF, IgG, CIC
Sjoren's syndrome	ESR, ANA (anti-RO, anti-La), CIC, RF, Cryo, IgG, IgA, IgM, syalography
Polyarteritis nodosa	ESR, Hep BSAg, IgG, Cryog, C, CIC, angiography
Churg-Strauss	ESR, WBC/eosinophil count, IgE, CIC, Chest X-ray
Relapsing polychondritis	CIC, C
Wegener's granulomatosis	ESR, IgA, IgE, RF, ANCA, CIC, sinus and chest x-ray, BUN, creat clearance
Giant cell arteritis	ESR, CRP, CIC, IgG ,

Abbreviations: ESR, erythrocyte sedimation rate; ANA, anti nuclear antibodies; anti-dsDNA, antibody to double -stranded DNA; anti-SM, anti-RNP, anti-RO, anti-LA, antibodie to small nuclear ribonucleoproteins-Sm, -RNP, -RO,and La; CIC, circulating immune complexes; IgG, IgA, IgM, IgE, immunoglobulins; C, complement (C3, C4, CH50); Cryog, Cryoglobulins; Rf, rheumatoid factor; Hep BSAg, hepatitis B surface antigen; WBC, white blood count; ANCA, antineutrophil cytoplasmic antibodies.

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Review Questions for Peripheral Ulcerative Keratitis

Anthony Ekong, M.D.

REVIEW QUESTIONS

1. Which of the following does not describe the peripheral cornea:

   A. It has more IgA and IgG than the central cornea.
   B. The number of Langerhans cells and the concentration of IgM and C1 is higher.
   C. More likely to be affected by auto-immune diseases and hypersensitivity reactions.
   D. Derives part of its nutrients from the limbal vascular arcades.
   E. Has a reservoir of inflammatory cells including neutrophils, plasma cells, eosinophils, lymphocytes and mast cells

2. PUK may be characterized by the following except:

A. Always associated with scleritis
B. Local microbial infections including HSV and VZV
C. Stromal inflammatory infiltrates, epithelial defects and stromal degradation or thinning
D. Collagenolytic or proteolytic enzymes released from neutrophils and/or macrophages
E. Treatment with topical steroids may be harmful and exacerbate lesions in certain cases

3. Which is not true of HSV and/or VZV keratitis :

A. Uncommon cause of stromal infiltrates and peripheral ulceration
B. Diagnosed only in the presence of a positive viral culture of the ulcer bed.
C. May be due to limbal vasculitis.
D. Can occur without history of previous infections or dermatologic findings.
E. May be diagnosed by demonstrating microbes within biopsied limbal conjunctiva vessels using immunoprobes.

4. Which of the following is not true about Terrien's marginal degeneration

A. Idiopathic, essentially non-inflammatory peripheral corneal thinning
B. Women are affected three times more likely than men .
C. Usually painless without epithelial ulceration.
D. Corneal thinning begins superiorly, progress slowly, and can perforate with minor trauma.
E. May be associated with vascularized corneal pannus and lipid deposition

5. List all that are false about Mooren's ulcer:

A. Usually caused by a diagnosable systemic disease.
B. Classically presents with scleritis.
C. Unilateral type may be effectively treated with local medical or surgical therapy.
D. Ulceration with a characteristic overhanging edge usually starts at the interpalpebral fissure and progesses circumferentially and centrally.
E. Hepatis C infections should be ruled out as associations have been reported.

6. Which of the following about PUK and Rheumatoid arthritis (RA) is incorrect:

A. Secondary Sjogren's syndrome or dry eyes may cause PUK.
B. RA is the most common cause of non-infectious PUK and may be bilateral in more than 40% of the cases.
C. Patients with mild PUK without necrotizing scleritis may respond to NSAIDs in combination with topical and/or systemic conticosteroid.
D. The occurrence of PUK or necrotizing scleritis is an indicator that the disease has changed from a synovial microvasculitis to a systemic vasculitis.
E. Post operative scleral or corneal inflammation may be the first sign of systemic vasculitis process and merits investigation.

7. The followings are true of Polyarteritis nodosa (PAN) except:

A. The respiratory tract is usually spared and a non-granulomatous vasculitis confined mainly to muscular arteries is present.
B. Choroidal vasculitis may be the most common ophthalmic manifestation.
C. PUK may be the initial presentation.

D. The presence of ANCAs can be used to diagnosed classic PAN, since PAN is typically ANCA positive.
E. PAN has been subdivided into classic PAN, allergic granulomatosis and angiitis of Churg and Strauss.

8. Wegener's granulomatosis may be associated with the following except:

A. Nasal septal perforation, collapse of the nasal arch leading to a saddle nose deformity and a focal necrotizing glomerulonephritis.
B. Chest X-rays showing waxing and waning pulmonary infiltrates, multiple modules and cavitations.
C. A limited form which spares the kidney and carries a better prognosis than does the classic WG.
D. Ocular involvement which does not differ in frequency or severity between classic and limited WG.
E. Most patients showing serum level of p-ANCA, except in the limited diseases where a c-ANCA pattern may be prominent.

9. Indicate the incorrect clinical findings or signs and associated systemic diseases

A. Saddle nose deformity: RP, Wegener's .
B. Alopecia, facial "butterfly" rash: SLE.
C. Puffy hands and feet and regurgitation: PAN.
D. Ulcers in fingertips:All vasculitic syndromes
E. Arthritis in arms and legs: All vasculitic syndromes.

10. Select all that are true:

A. Unlike in classic PAN, in Microcospic Polyangiitis and Churg-Strauss syndrome, anti-neutrophil cytoplasmic antibodies against myeloperoxide (p-ANCA) may be an important diagnostic tool .
B. Hepatitis B and C infections may be important causal factors in patients with PAN.
C. The sensitivity of the "cytoplasmic" immuno-fluorescence staining pattern (c-ANCA) test is close to 100% in patient with active generalized Wegener's granulomatosis.
D. Corneal manifestations in patients with SLE are mainly confined to the epithelium ,and KCS is the most common corneal involvement.
E. Gram and Giemsa stains of corneal scrappings in Staph. Marginal Keratitis usually show bacteria, but no neutrophilis.

ANSWERS

1. **A**
2. **A**
3. **B**
4. **B**
5. **A, B**
6. **A**
7. **D**

8. **E**
9. **C**
10. **E**