

## Interstitial Keratitis

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### Clinical Case:

A 41-year-old man presented to the emergency room with a one-month history of right eye redness, light sensitivity and dull pain. He attributed his symptoms to exposure to "hot vapors" from a dishwashing machine at work. There was no previous history of episodes of eye discomfort, ocular trauma or injury with chemical substances.

Past Ocular History: not contributory

Past Medical History: not contributory

Allergies: none

Review of Systems: not contributory

Social History:

-Born and lived in El Salvador until 2 years earlier, when he immigrated to the U.S.

-No history of smoking, alcohol, or drug abuse

Examination:

External: No evidence of facial burns or trauma

Vision: OD:20/40 ph 20/25                      OS:20/50 ph 20/20

Pupils: Normal ÇAPD                      Tensions: 15 OU

Slit Lamp Examination: See Figure 1

Figure 1: Photo slit lamp Nasal Cornea: Active Interstitial keratitis

Figure 2: Photo slit lamp Temporal Cornea: Stromal scar with ghost vessels.

Laboratory Work-up: Negative

Chest X-Ray:

Figure 3: Old pulmonary scar

Skin Test: + PPD

Diagnosis: Interstitial Keratitis

### Interstitial Keratitis

Interstitial keratitis (IK) is a non-ulcerative inflammatory reaction in the corneal stroma, characterized by a non-suppurative cellular infiltrate and often vascularization of the stroma, without primarily involving the epithelium or endothelium. It is an immune-mediated process thought to be caused by a cellular and humoral response against antigens in the corneal stroma, residual infectious antigens or both. The presence of mainly T cells in pathological specimens from corneas with IK suggest a role of this population of cells in this disease.

The inflammatory lesions of IK can present clinically as active or inactive. In active IK, there is an on-going immune-mediated inflammation characterized by stromal infiltration, edema and in some cases the presence of an immune-ring reaction. Inactive IK is defined by the evidence of previous episode of stromal inflammation, which has remained quiet for a period of at least one year. The typical corneal findings include mid or deep stromal scarring and sometimes reduplication of Descemet's membrane. Deep neovascularization of the stroma can also be seen in IK, resulting in the formation of ghost blood vessels in the absence of blood flow in chronic cases.

IK can also be described by its pattern of clinical presentation: unilateral vs bilateral, diffuse or sectorial and central vs paracentral. Careful attention to the description and characterization of the IK presentation can be extremely helpful in establishing a differential diagnosis (refer to differential diagnosis section).

The presence of IK in a patient should alert the ophthalmologist to perform a comprehensive clinical history, review of systems and physical examination. Many etiologies of IK occur in conjunction with systemic diseases. IK can be the initial presentation of a systemic infectious or non-infectious disease, which has not either been diagnosed or treated at the time of the patient initial evaluation. Moreover, some of the causes of IK can be life

threatening and a prompt diagnosis and correct treatment is critical. The differential diagnosis of IK will be discussed using the following classification: Bacterial Infections, Viral Infections, Parasitic Infections, Systemic Diseases and Non-systemic diseases.

Differential Diagnosis and Comments:

I) Bacterial Infections:

1) Congenital Syphilis:

-IK Pattern: Bilateral, diffuse stromal disease with deep vasculature.

-87% of syphilitic IK worldwide is congenital

-It can be transmitted from mother with primary, secondary or early latent *Treponema pallidum* infection

-Occurs between ages 5 and 20. Peak ages 9-11.

-Other ocular findings: atrophy iris stroma, posterior synechia and salt-and-pepper fundus.

-Systemic Manifestations: Hutchinson's Triad: IK, Deafness and Anomalous Teeth

-Saddle nose, frontal bossing, overgrowth maxilla (Figure 3)

Figure 3 (Photo Saddle nose, frontal bossing and Teeth)

2) Acquired Syphilis

-IK Pattern: Unilateral, sectorial stromal disease with mild vasculature.

-Occurs 10 years after infection

-Usually milder than the congenital form

-Less vascularization and greater response to PCN

3) Mycobacterial: Tuberculosis

-IK Pattern: Unilateral, sectorial stromal disease with anterior or mid-stroma vasculature.

-It represents 2 % of worldwide cases of IK.

-Associated with sectorial sclerokeratitis

-Resolution is slow and incomplete, leaving a dense sectorial scar without thinning

-IK is a rare finding even in patients with active pulmonary disease: 1/1073 (Glover) 0/1000 (Goldenberg) 10/1052 (Donahue)

-Even though IK is due to host response, systemic work up is necessary.

-Treatment (if systemic disease active): isoniazid, rifampin, ethambutol, streptomycin: multi-drug therapy.

3) Mycobacterial: Leprosy

-Pattern IK: Bilateral, superotemporal stromal disease, avascular.

-IK occurs in 3% to 6% of affected individuals.

-IK is present late in the disease

-Corneal disease is aggravated by anesthesia and exposure due to CNVII palsy and lid deformity.

-Diagnosis is made by clinical characteristic of leprosy.

-Treatment: multi-drug (dapsone, rifampin)

4) Lyme Disease

-Pattern IK: Bilateral, poorly defined/focal stromal disease, avascular.

-Infection by the spirochete *Borrelia burgdorferi*

- IK is a late manifestation of disease with preceding systemic symptoms: skin, joint, heart and CNS
- History of travel or living in endemic areas.
- Diagnosis: serology with ELISA and Western blot
- Antibiotic systemic treatment for untreated disease
- IK responds to topical steroids with slow tapering.

## II) Viral Diseases

### 1) Herpes Simplex Virus (HSV):

- IK Pattern: Unilateral, diffuse or sectorial, vascularized and associated with iritis.
- Leading cause of IK in the United States.
- Decreased corneal sensation, iris atrophy and recurrent disease.
- Treatment with topical or systemic antiviral agents and minimum dose of topical steroid is required to reduce inflammation and edema.

### 2) Herpes Zoster Virus (HZV):

- IK may develop 2 to 3 weeks after onset of acute infectious epithelial keratitis.
- Anterior stromal keratitis with deep vessels and lipid deposition.
- Diminished corneal sensation, sectorial iris atrophy and history of cutaneous lesions
- Treatment: Similar to HSV

### 3) Epstein-Barr Virus (Mononucleosis)

- IK Pattern: Bilateral with nummular keratitis, avascular.

- Treatment: topical steroid t

### 4) Mumps

- IK pattern: Unilateral, with focal mild stromal disease, avascular.

- Onset 5 days after parotiditis and subsides spontaneously within 3 to 4 weeks

### 5) Human T-Lymphotropic virus Type I (HTLV-I)

- IK Pattern: Bilateral anterior stromal, peripheral IK
- New cause of IK
- Chronic with poor response to topical steroids

## III) Parasitic Infections:

### 1) Leishmaniasis

- IK Pattern: Bilateral, focal or diffuse stromal diseases with superficial vasculature.
- Disease caused by the protozoa *Leishmania* sp.
- Transmitted by mosquito vector and sandfly
- Found in Asia, Africa, South America and Mediterranean region
- Systemic manifestations: nasal cartilage and oropharynx destruction due to nasal mucosa inoculation.

### 2) Onchocerciasis - River Blindness<sup>2</sup>

- IK Pattern: Bilateral, with interpalpebral stromal disease, sclerosing.

- Caused by the nematode *Onchocerca volvulus*

- Transmitted by the Blackfly vector.
- Found in Tropical Africa, Central and South America, and Southern Mexico.
- IK results from inflammatory response to dead microfilariae in the cornea.
- The entire cornea is involved resulting in sclerosing keratitis.
- Treatment: Ivermectin

### 3) Trypanosomiasis

- IK Pattern: Bilateral, diffuse stromal disease with severe opacity of all corneal layers, vascularization and potential perforation.
  - Two variants: African (sleeping sickness) and American (Chaga's disease).
  - IK is seen in the African: Found in Tropical West and Central Africa, along Congo River.
  - Systemic manifestations: fever, lymphadenopathy, delayed pain sensation, splenomegaly and anemia
- IV) Systemic Diseases:

#### 1) Cogan's syndrome

- IK Pattern: Bilateral, with variable stromal disease and variable vasculature.
- Idiopathic inflammatory condition that affects young individual, with average age of 30 years.
- Autoimmune etiology against antigen present in the cornea and ear.
- Clinical characteristics: Vertigo, tinnitus, hearing loss and IK
- IK is bilateral, of sudden-onset, gradual resolution with recurrences
- Ocular and vestibuloauditory symptoms develop within 1 month of each other
- Vestibuloauditory may precede or postdate ocular symptoms.
- 10% of patients develop systemic vasculitis of large vessels, weeks to years later: aortic insufficiency, coronary stenosis or brain infarcts.
- Treatment: Systemic high dose steroids for 3-4 months, and immunosuppressive therapy if no improvement is observed.

#### 2) Other Systemic Diseases

- 2 a) Sarcoidosis
- b) Lymphoma (Hodgkin's disease)
- c) Kaposi's sarcoma
- d) Mycosis fungoides (T-Cell Lymphoma)

#### IV) Non-Systemic Disorders:

- 1) Contact Lens
  - 2) Toxicity due to gold
- Treatment
- 3) Toxicity due to arsenic
  - 4) Intraocular sclerosing inflammatory pseudotumor

#### Interstitial Keratitis in the United States:

A study performed by Schwartz et al looked at the causes of IK in the US over a period of 10 years in their cornea service. Their data showed that HSV is the most common cause of IK in the United States. (Table 1)

Table1 : Etiologies of Interstitial Keratitis in the United States in the last 10 years

Causes	Total Cases
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HSV	34 (35.1%)
Idiopathic	31 (32%)
Syphilis	18 (18.6%)
Contact Lens	4 (4.1%)
HZV	3 (3.1%)
Tuberculosis	3 (3.1%)
Measles	1 (1%)
Collagen Vascular Disease	1 (1%)
Lyme	1 (1%)
EBV	1 (1%)

Concluding Points:

• The etiology of IK is associated with systemic diseases and can be the initial presentation.

• The differential diagnosis for IK is extensive and should be familiar to the ophthalmologist.

• HSV needs to be strongly suspected in the US

• A basic systemic work-up guided by history, review of systems, social history and physical examination is essential.

• Systemic treatment of the disease is necessary in many instances

Suggested Readings:

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