HERPES SIMPLEX KERATITIS

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EPIDIMIOLOGY

Herpes simplex virus

- DNA virus
- Two types- HSV-1 and HSV-2
- Morphologically similar
- similar morphologically to other herpesviruses including varicella-zoster, Epstein-Barr, and cytomegalovirus
- Different in viral antigen

EPIDIMIOLOGY

- HSV-1 usually involves the oropharynx
- HSV-2 usually involves the genital area
- Ocular disease is caused by type HSV-1
- neonates - 75% is caused by HSV-2

EPIDIMIOLOGY

- Humans are the only natural reservoir of HSV.
- major portals of entry are the mucous membranes and external skin
- primary infection manifests clinically in only 1 -6% of people infected with the virus.
- male:female ratio (1.67:1).

EPIDIMIOLOGY

- After peripheral entry into the host and primary infection HSV travels in a retrograde fashion to trigeminal ganglion.
- Here it resides during the lifespan of the host
- Cornea itself can be a reservoir of virus.

EPIDIMIOLOGY

Reactivation Factors:-

- Sunlight, trauma (including surgery), heat, abnormal body temperature, menstruation, other infectious diseases, emotional stress, Prostaglandin analog.

- After reactivation virus spreads down the nerves to the eye to cause recurrent disease

CLASSIFICATION

- Congenital and neonatal ocular herpes
- Primary ocular herpes
- Recurrent ocular herpes

Congenital and neonatal ocular herpes

- acquired through genital herpes in the mother and during parturition
- 80% of cases - HSV-2
- periocular skin lesions, conjunctivitis, epithelial keratitis, stromal keratitis, and cataracts.
- progress to disseminated disease and/or central nervous system involvement

Primary ocular herpes

- By the age of 5 years- 60% of the population infected with HSV
- Only 6%- develop clinical manifestations

Primary ocular herpes

- typically affect the perioral region
- follicular conjunctivitis
- keratoconjunctivitis
- preauricular adenopathy
- and periocular and eyelid skin vesicles

Recurrent ocular herpes

- Blepharitis-
- Canjunctivitis
- Keratitis

Recurrent ocular herpes

Blepharitis-

- Vesicular lesion
- Ulceration
- Heals without scar

Recurrent ocular herpes

Conjunctivitis -

- Recurrent Follicular
- Dendritic ulcer

Recurrent ocular herpes

Keratitis-

- typically unilateral
- Bilateral - 3% of patients (40% history of atopy)

Classification of HSV keratitis

- Infectious epithelial keratitis
- Stromal keratitis
- Endothelitis
- Neurotrophic keratopathy

Infectious epithelial keratitis

- Cornea vesicles
- Dendritic ulcer
- Geographic ulcer
- Marginal ulcer

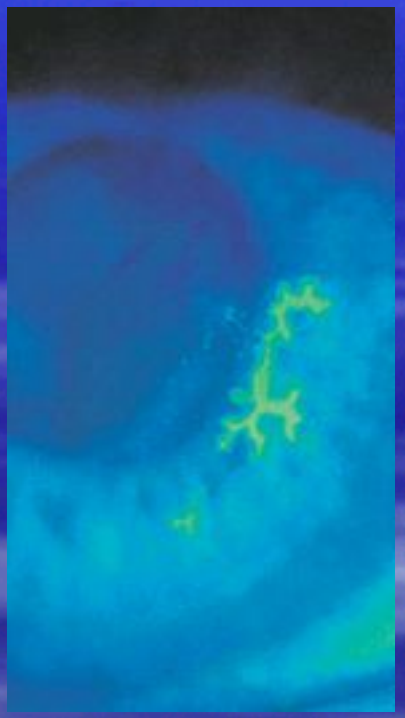
Infectious epithelial keratitis

Corneal vesicles

§ small vesicles in the epithelium

Infectious epithelial keratitis

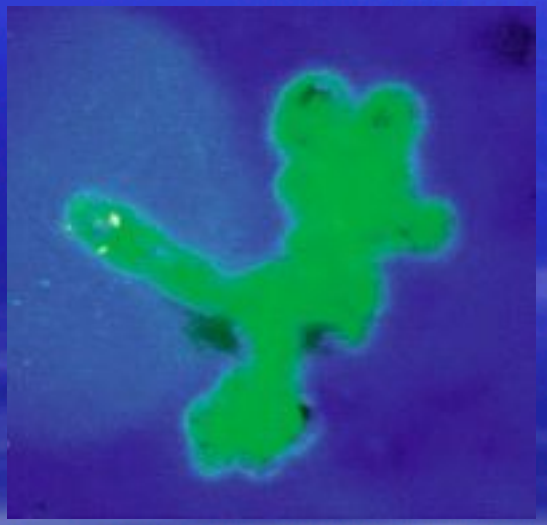
- Within 24 hours, the vesicles coalesce to form the typical **dendritic ulcer:-**



- most common presentation of HSV keratitis
- branching, linear lesion
- terminal bulbs
- swollen epithelial borders that contain live virus.
- Rose Bengal stain taken up by the swollen epithelial cells at the ulcer's border

Infectious epithelial keratitis

Geographical ulcer



§ An enlarged dendritic ulcer

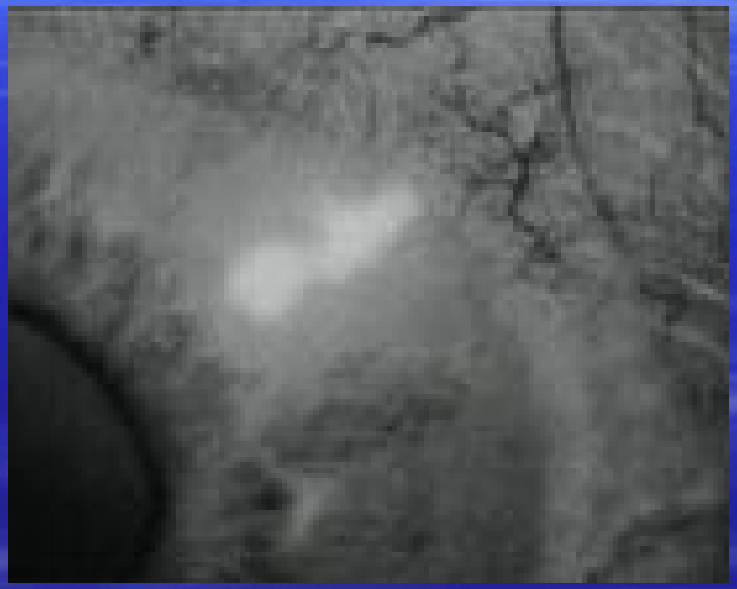
§ previous use of topical corticosteroids

§ Scalloped margin

§ differentiate from
healing abrasions and neurotrophic keratopathy - smooth margin

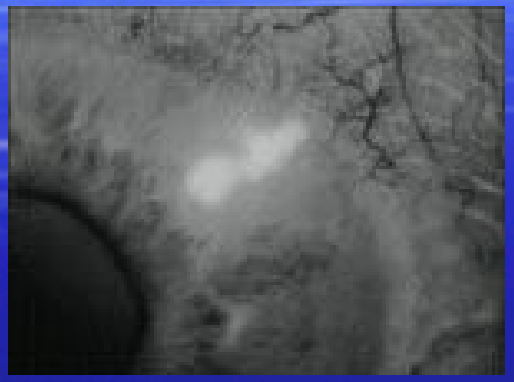
Infectious epithelial keratitis

Marginal Ulcer



- proximity to the limbus
- accompanying blood vessels
- infiltrated with white blood cells
- anterior stromal infiltrate
- more symptomatic than central dendritic ulcers

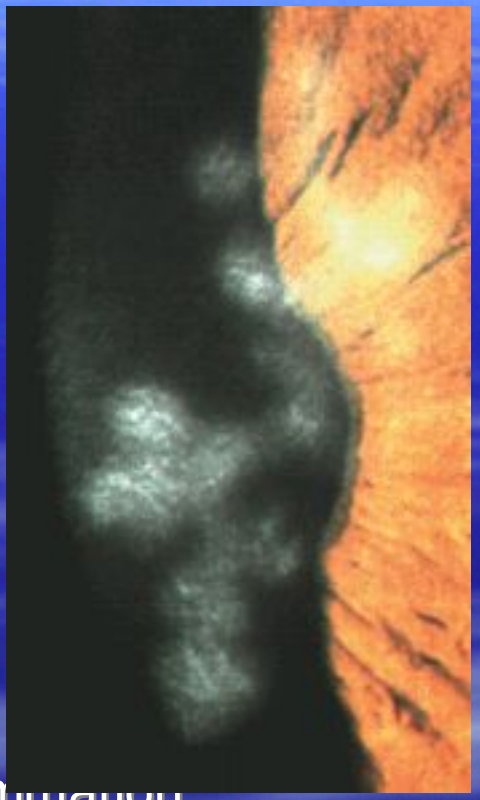
Infectious epithelial keratitis



	HSV marginal ulcer	Staphylococcal marginal infiltrate
Etiology	Active HSV	Immunologic response to staphylococcal antigen
Epithelial defect	Always	Absent (if present, late)
Neovascularization	Often	Rare
Progression	Centrally	Circumferentially
Blepharitis	Unrelated	Usually
Location	Any meridian	Typically 2, 4, 8, 10 o'clock meridians

Infectious epithelial keratitis

Sequelae of infectious epithelial keratitis-



- complete resolution of the infectious lesion
- dendritic epitheliopathy
- stromal scarring
- 25% of patients develop subsequent stromal inflammation

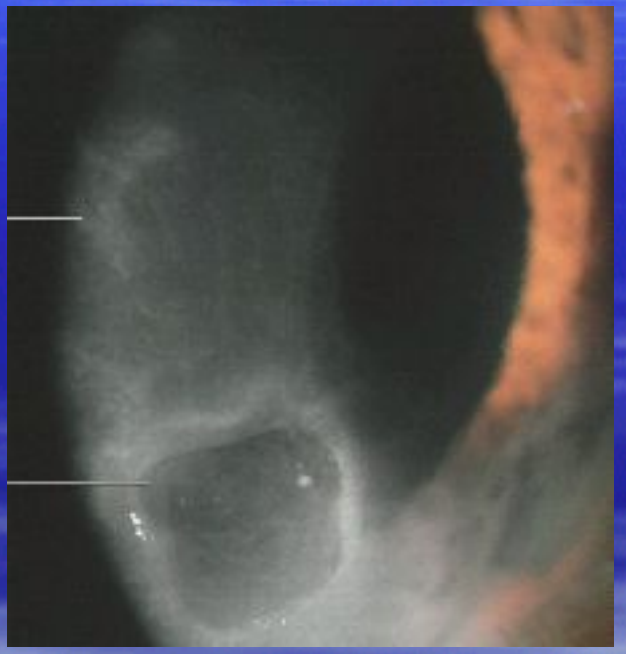
Neurotrophic keratopathy

- impaired corneal sensation
- decreased tear secretion
- chronic use of topical medications

  especially antivirals.

Neurotrophic keratopathy

- irregularity of the corneal surface and lack of the normal corneal luster
- Punctate epithelial erosions
- persistent epithelial defect
- stromal ulceration



- oval in shape with smooth borders. The neurotrophic ulcer has a thickened border formed by heaped-up epithelium

Neurotrophic keratopathy

Complications

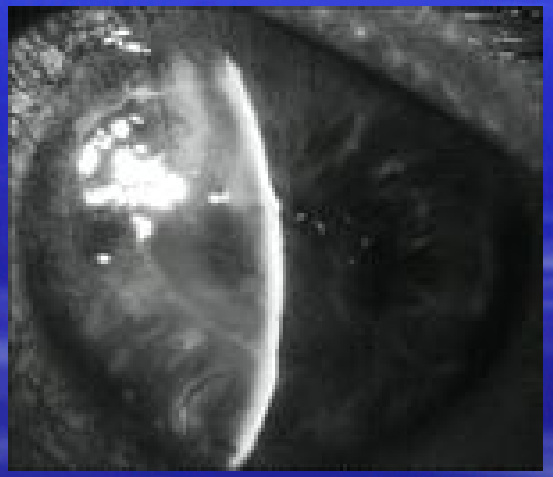
- stromal scarring
- neovascularization
- necrosis, perforation
- secondary bacterial infection.

Stromal keratitis

- Necrotizing stromal keratitis
- Immune stromal (interstitial) keratitis

Necrotizing stromal keratitis

- Direct viral invasion of the corneal stroma
- The combination of replicating virus and severe host inflammatory response
- Necrosis, ulceration, and dense infiltration of the stroma with an overlying epithelial defect



- Treatment with high-dose anti-inflammatory and antiviral medications
- Thinning and perforation within a short period of time

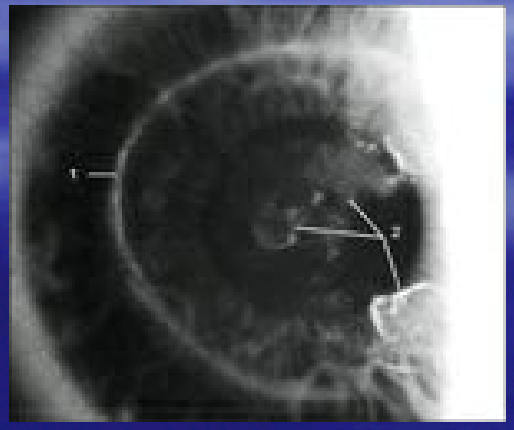
Immune stromal (interstitial) keratitis

- incidences - 21% within 2 years and 26% to 48% within 7 years of infectious epithelial keratitis.
- due to retained viral antigen within the stroma.
- This antigen triggers an antigen-antibody-complement (AAC) cascade that results in intrastromal inflammation

Immune stromal (interstitial) keratitis

Clinical features

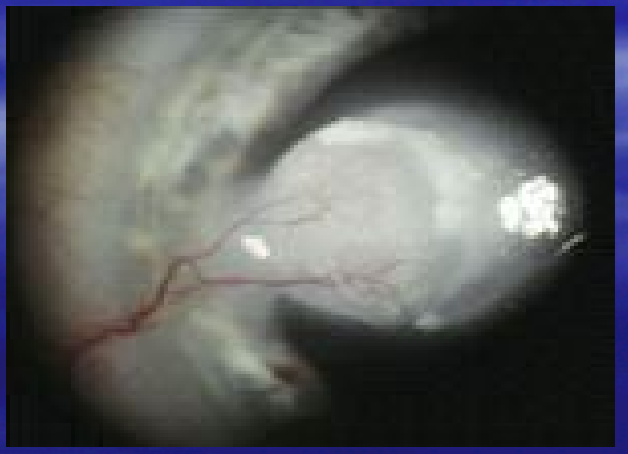
- ciliary conjestion
- Stromal infiltration
- punctate stromal opacities- focal, multifocal, or diffuse.
- Stromal edema.
- Immune Wessely ring- AAC precipitate in ring form.
- anterior chamber inflammation
- significant discomfort
- Decreased vision



Immune stromal (interstitial) keratitis

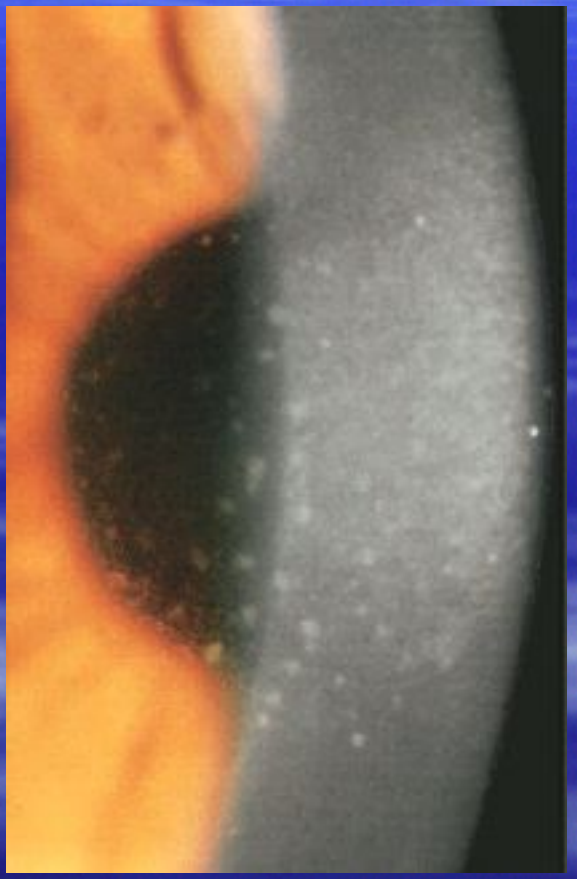
Sequelae –

- Deep neovascularization
- Lipid deposition
- Ghost vessels
- Stromal scarring, Thinning
- Severe loss of vision.



Endotheliitis

- Localised keratic precipitates
- overlying stromal and epithelial edema without stromal infiltrate
- iritis
- Immunologic reaction to HSV-1 antigen in corneal endothelial cells



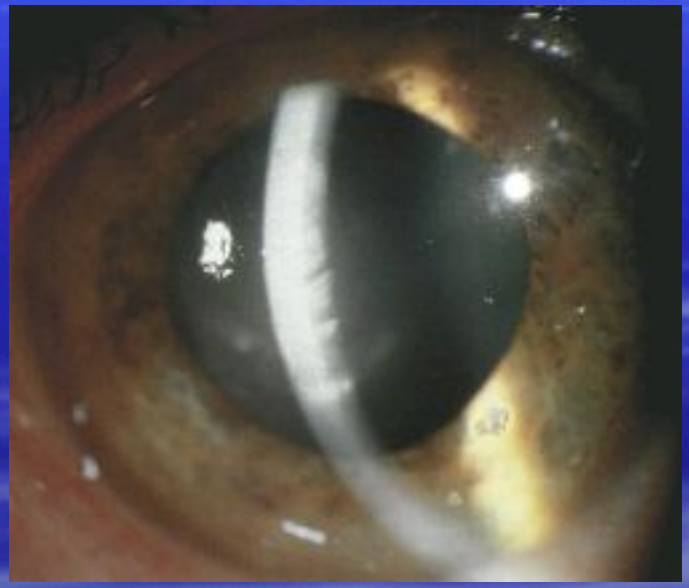
Endotheliitis

Types:-

- Disciform
- Diffuse
- Linear

Endotheliitis

Disciform endotheliitis –



- most common presentation of endotheliitis
- Disc-shaped distribution of KP in central or paracentral cornea
- Disc-shaped area of edema corresponding to distribution of KP
- Photophobia, mild to moderate ocular discomfort, Limbal injection, visual acuity normal to severely reduced

Endotheliitis

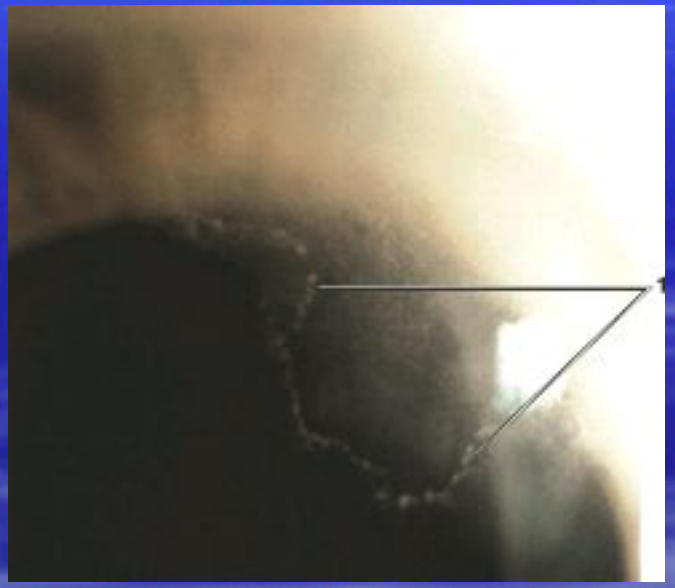
Diffuse endotheliitis –

- A rare presentation
- Scattered KP spread over the entire endothelium
- Stromal edema involving the entire cornea

Endotheliitis

Linear endotheliitis –

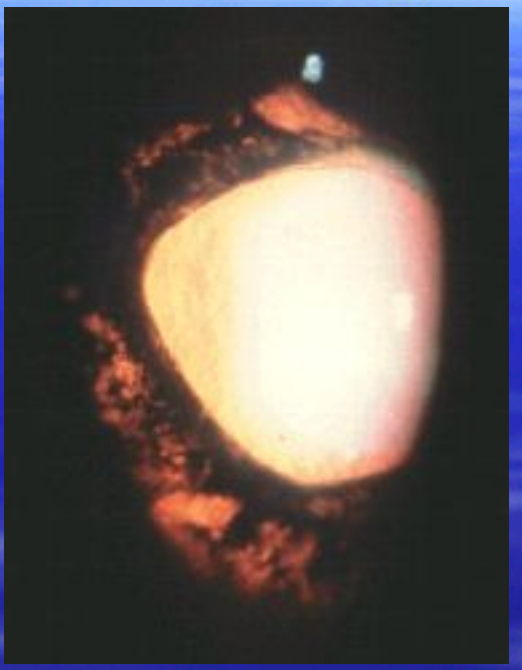
- Line of KP progressing from the limbus
- May be sectoral or circumferential
- Edema present peripheral to the line of KP, extending to the limbus
- Corneal decompensation common



Iridocyclitis

- concomitant or subsequent
- fine KP
- Segmental iris atrophy
- Iris masses, hemorrhages, hyphema.
- elevation of intraocular pressure
  -trabeculitis

  -inflammatory cells blocking aqueous outflow



Diagnosis

- Clinical findings
- Cell culture
- Immunologic tests
- Polymerase chain reaction (PCR)

Antivirals

	Rout of administration	Therapeutic Doses	Prophylactic doses
	Oral,IV, Topical	Topical 5times x 7-10 days. 400 mg PO 5 times/day for 7-10 days	400mg PO bid
Valacyclovir	Oral	500 tid x 7-10 days	500 mg PO/day
Gancyclovir	Topical, IV	5 times/day until cornea heals then 3 times/day for 7 days	-

Management

Infectious epithelial keratitis-

- Physical debridement of the ulcer
- Topical antivirals
- Topical cycloplegics
- Broad-spectrum antibiotic- large geographic ulcers
- No steroids unless associated with stromal inflammation

Management

Neurotrophic keratopathy-

- discontinuation of all unnecessary topical medications, especially topical antivirals
- Frequent use of nonpreserved artificial tears
- broad-spectrum antibiotic
- gentle debridement of abnormal epithelium at the ulcer edge.
- persistent ulceration secondary to chronic low-grade inflammation-mild topical corticosteroid.
- therapeutic soft contact lens
- temporary tarsorrhaphy

Management

Immunologic disease

Stromal keratitis

- Topical corticosteroids
- Oral corticosteroid (severe)

- topical antiviral (Acyclovir 3% ointment)
- Oral antiviral for prophylaxis (Acyclovir 400 mg BD)

Management

Immunologic disease

Endothelitis

- Disciform- Topical corticosteroid
- Diffuse- Topical corticosteroid and oral antiviral
- Linear- Topical and oral corticosteroid
  Oral antiviral

Management

Necrotising stromal keratitis-

- high-dose anti-inflammatory (oral and Topical)
- antiviral medications (oral and topical)

Management

Iridocyclitis/trabeculitis

- Topical corticosteroids

In Severe cases-

- oral acyclovir 400 mg five times a day
- Oral corticosteroids

Topical corticosteroids

- marginal keratitis
- immune stromal keratitis
- moderate disciform & diffuse endothelitis
- Moderate iridocyclitis & trabeculitis

Oral corticosteroids

- severe stromal keratitis
- severe disciform & diffuse endothelitis
- all cases of leniar endothelitis
- severe iridocyclitis & trabeculitis

Topical antivirals

- HSV blepharitis
- HSV conjunctivitis
- infectious epithelial keratitis
- prophylaxis for corticosteroids treatment of stromal keratitis

Management

Oral antivirals

- Primary HSV infection
- severe diffuse endotheliitis
- Linear endotheliitis
- severe iridocyclitis/trabeculitis
- Immunocompromised patients
- Pediatric patients refractory to topical medications
- Prophylaxis against recurrent infectious epithelial keratitis and stromal keratitis
- Prophylaxis for post-PK patients with history of HSV keratitis

Herpetic Eye Disease Study

A set of multicenter, randomized, placebo-controlled trials under the name Herpetic Eye Disease Study (HEDS) sponsored by the National Eye Institute was designed.

- Oral antiviral prophylaxis reduces recurrences of epithelial and of stromal keratitis.
- Use of topical corticosteroids is of benefit in stromal keratitis.
- Use of oral acyclovir may be of help in iridocyclitis
- Prophylactic oral acyclovir helps prevent recurrences of herpetic keratitis, particularly stromal with a history of recurrence


Thank you