An unusual progression of corneal and conjunctival intraepithelial neoplasia and insights into primary treatment with topical Interferon alpha 2b : A case report

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Abstract: A case study documenting an atypical presentation of corneal and conjunctival intraepithelial neoplasia (CIN) and an alternative therapy that involves the use of Interferon alpha 2b eye drops as a PRIMARY treatment for this condition.

Background: Although conjunctival and corneal intraepithelial neoplasia (CIN) is the most common ocular surface malignancy, it’s occurrence in the United States is relatively rare. Classic clinical findings involve a fine dysplastic tissue that begins at the limbus and can spread onto the cornea in a scalloped fashion, often presenting as a foreign body sensation or asymptomatic to the patient. These lesions have the potential to become invasive squamous cell carcinoma, thus the significance of CIN diagnosis.

Methods: This case report includes an atypical presentation of CIN and a review of clinical findings leading to the final diagnosis. It also discusses the etiology, histopathology, clinical presentation, treatment, management, and upcoming research regarding CIN.

Conclusion: Because of its malignancy potential, CIN is an important differential to consider as a clinician. The condition can present in a variety of ways and this discussion is aimed to assist the clinician in prompt diagnosis. The newest diagnostic tools and promising medications for treatment are reviewed in this report. This case report will hopefully encourage eye care professionals to consider the diagnosis of CIN even in atypical cases such as our patient and to explore the options of primary treatment with Interferon to avoid surgery.

I. Case History
   a. Patient demographics
      • 62 year old white male
   b. Chief complaint
      • Pt said he has blurred distance vision in his right eye x several years.
   c. Ocular history
      • Cataracts both eyes
      • Right eye cataract surgery March 2010
   d. Medical history
      • Diabetes mellitus, diagnosed in 2007, diet controlled, last Hemoglobin A1C 6.6% on 09/02/2009
• Sleep apnea - uses CPAP machine
• Hyperlipidemia
• Hypertension
• GERD
• BPH with urinary obstruction
• Obesity

e. Medications
• Aspirin 325 mg once daily
• Omeprazole 20 mg once daily
• Clonidine 0.1 mg twice daily
• HCTZ 25 mg in the morning
• Amlodipine 10 mg twice daily
• Simvastatin 80 mg ½ tablet at bedtime
• Lisinopril 40 mg twice daily

II. Pertinent clinical/physical findings
a. 12/09
• BCVA: OD 20/50+2 variable refraction (potential acuity 20/20-), OS 20/20-2
• Slit lamp exam:
  1. Severe meibomian gland dysfunction both eyes
  2. Large pingueculi nasal and temporal both eyes
  3. Inferior corneal opacity right eye - corneal pannus vs pterygium 3:00 to 7:00 inferior extending 1.5 mm onto cornea
  4. 1+ NS both eyes
  5. See photo 1-3
• Initial treatment: Warm compresses twice daily for two weeks then once daily thereafter. Tobradex ointment twice daily for two weeks, once daily for two weeks then stop. Recheck in one month and if improved consider cataract surgery
b. 1/14/10:
• Patients states eyes water less, vision is the same
• Slit lamp unchanged, inferior corneal opacity thought to be reaction to chronic inflammation right eye
• See photo 4
• Plan: continue warm compresses once daily and Tobradex until gone
• Consult sent for cataract extraction due to BCVA 20/50+ and potential acuity 20/20- with no other signs contributing to decreased vision
c. 4/19/10:
• Had cataract surgery OD the 1st week of March 2010
• Current meds: Omnipred qid OD
• Complains that vision is right eye is still blurry
• BCVA: OD 20/60- (variable refraction), OS 20/20-1
• Slit lamp exam:
  1. Inferior corneal opacity right eye- corneal pannus vs pterygium 3:00 to 7:00 inferior extending 1.5 mm onto cornea - new pertinent findings: general haze centrally with mild SPK right eye
  2. See photo 5
• Plan:
  1. Continue warm compresses at least once daily and artificial tears four times daily both eyes.
  2. Begin Maxitrol ointment at bedtime both eye and oral Doxycycline 100 mg twice daily for 30 days then once daily for 30 days. Educated patient on possibility of stomach upset and sensitivity to sunlight.
  3. RTC 2 months or sooner with problems
d. 7/27/10:
• Continues to have blurry vision in right eye
• BCVA improves to 20/30- right eye
• Slit lamp reveals same appearance of blepharitis and cornea
• Patient admits he has not done warm compresses
• Plan:
  1. Continue current treatment with warm compresses twice daily, artificial tears four times daily, lubricating ointment at bedtime
  2. Due to persistent symptoms and minimal improvement in appearance will get second opinion from corneal specialist in office
e. Clinical 10/15/10:
• BCVA 20/30- variable with blink
• Same appearance
• Plan:
  1. Continue warm compresses twice daily, artificial tears four times daily both eyes, lubricating ointment at bedtime and begin using moisture shield at bedtime. Return to clinic in 3 months and will monitor with corneal specialist
f. Clinical 1/14/11:
• BCVA 20/100- hard to subjectively refract
• Slit lamp exam:
  1. Moderate papillary reaction upper tarsal right eye greater than left eye
  2. General haze centrally with linear line of SPK centrally with diffuse spk today, very poor wetting today with instant TBUT right eye
  3. Schirmer test with anesthetic: Right: normal, Left: normal
  4. Exophthalmometry: 24/24 base 100 similar appearance to photo id card taken 2009, normal TSH 2009
• Assessment:
1. Inferior corneal pannus vs haze with severe blepharitis right eye - floppy eye lid syndrome with papillary reaction under tarsal

• Plan:
  1. Continue warm compresses twice daily, artificial tears four times daily both eyes, lubricating ointment and moisture shield at bedtime over right eye at night.
  2. Will restart Doxycycline 100mg a day indefinitely, and Restasis twice daily right eye.
  3. Follow-up 3 months to see if improvement, if no improvement may consider scrape to biopsy to rule out pathology, and consider temporary tarsoraphy to see if helps cornea heal.

  g. Clinical 4/8/11:

  • Patient has not noticed any change in vision- OD sometimes better after blinking
  • BCVA 20/50+1
  • Slit lamp exam
    1. Moderate MGD- improved
    2. Corneal opacity 3 to 7 o’clock inferior extending 1.5 mm onto cornea-some areas of grayish haze and leukoplakic area inferior nasal, also mild limbal opacity superiorly
      a. pannus secondary to chronic inflammation vs. CIN (corneo-conjunctiva intraepithelial neoplasia)

• Assessment:
  1. Inferior corneal opacity right eye.
    a. Acuity ranging from 20/30 to 20/100 due to cornea & tear film
    b. Floppy eyelid syndrome, chronic posterior blepharitis, unstable tear film
    c. Ocular surface improved today
    d. Some characteristics concerning for CIN (corneo-conjunctiva intraepithelial neoplasia)

• Plan:
  1. Continue doxycycline 100mg daily, Restasis twice daily, artificial tears four times daily, lubricating ointment at bedtime, warm compresses 1-2 times daily, moisture shield at bedtime.
  2. Begin compounded interferon alpha 2b 1 million units per mL to be used in right eye four times daily for 1 month trial.
  3. Return to clinic in 3 months and will monitor with corneal specialist. If no improvement, consider biopsy.

  h. Clinical 5/13/11:

  • Refraction: Right eye: -0.75 +0.50 x180 20/40+ slower
  • Slit lamp exam:
1. Lids/Lashes/Conjunctiva: mild meibomian gland dysfunction - pingueculi nasal and temporal both eyes
2. Cornea: corneal opacity 3-7:00 inferior extending 1.5 mm onto cornea, with history of some grayish haze - improved and appears slightly lighter today and leukoplakic area inferior nasal-pannus secondary to chronic inflammation vs. CIN (corneo-conunctiva intraepithelial neoplasm)
   • Assessment: Inferior corneal opacity right eye very concerning for corneo-conjunctiva intraepithelial neoplasia
     1. acuity ranging from 20/30 to 20/100 due to cornea & possible tear film
     2. improved to 20/40+ today after 2-3 weeks of interferon treatment
     3. floppy lid syndrome, chronic posterior blepharitis, unstable tear film
     4. ocular surface improved today
   • Plan: Seen with and discussed options with corneal specialist today- since vision improving and haze of cornea improved, patient elects to continue with drops at this time. If no improvement, consider biopsy
     1. Continue current meds: (compounded) interferon drops four times daily in right eye , Oral doxycycline 100mg daily , Restasis twice daily, artificial tears four times daily, lubricating ointment at bedtime, warm compresses 1-2 times daily, moisture shield at bedtime.
     2. RTC in 1 month
   i. Clinical 6/17/11:
      • Refraction: OD: -1.75+0.75x180  20/40+1 myopic shift from last visit
      • Lids/Lashes/Conjunctiva: pingueculi nasal and temporal both eyes, moderate chronic meibomian gland dysfunction with telengectaic vessels on lid margin
      • Cornea: corneal opacity 3-7:00 inferior extending 1.5 mm onto cornea, greyish haze with neo with much improvement and more quiet temporally greatest, and leukoplakic area inferior nasal, pannus secondary to chronic inflammation vs. CIN
        1. New findings confirmed by corneal specialist: linear line of stain starting under pupil and wrapping up into pupil- early CIN extending onto central corneal with mild spk inferior cornea- demarcation line in center with some CIN in center of this demarcation line (lesion is beginning to clear peripherally first)
        2. See photo 6
      • Assessment: Corneo-conjunctiva intraepithelial neoplasm inferior right eye
        1. acuity ranging from 20/30 to 20/100 due to cornea & possible tear film stable at 20/40+ today after 2 months of interferon treatment
        2. floppy lid syndrome, chronic posterior blepharitis, unstable tear film
        3. inferior cornea again shows improvement especially temporally when compared to photos
4. new area of demarcation line in central part of cornea- part of neoplasia that was in central vision

- Plan: Seen with and discussed options with corneal specialist - still improving on interferon drops for 2 months. Patient will continue current meds:
  1. RTC in 1 month
  2. if no further improvement over next couple of months, consider surgical removal with 5 fluororacil drops to follow.

j. Clinical 7/15/11:
   - Refraction: Right eye: -2.50 +0.75 x180  20/40+
   - Lids/Lashes/Conjunctiva: pingueculi nasal and temporal both eyes, mild, chronic meibomian gland dysfunction with telengectaic vessels on lid margins
   - Cornea: Right eye: inferior limbal opacity from about 3-7:00 extending 1 mm onto cornea - improved from previous; greyish haze/demarcation line with irregular surface appearance, ovaly shaped & centrally located but extending nasally from just temporal to visual axis - measures about 4.5mm horizontal by about 3mm vertical - which appear to have improved from previous; Left eye clear
   - See photo 7-8
   - Assessment: Corneo-conjunctiva intraepithelial neoplasia inferior right eye - improving on treatment based on photo review
     1. Acuity ranging from 20/30 to 20/100 due to cornea & possibly some decrease attributed to tear film status, ring of superficial epithelial irregularity centrally on cornea
     2. History of refractive shift likely due to corneal changes
     3. floppy lid syndrome, chronic posterior blepharitis, unstable tear film
     4. inferior cornea has improved from 05/11 photos

   - Plan: Patient to continue with current medications and follow-up in 1 month

k. 8/19/10 follow-up:
   - Manifest Refraction: Right eye: -2.50+1.25x180  20/30-1 (was 20/40+ last visit)
   - Slit Lamp Exam:
     1. Lids/Lashes/Conjunctiva: pingueculi nasal and temporal both eyes, mild, chronic meibomian gland dysfunction with telengectaic vessels on lid margins
     2. Cornea: Right eye: inferior limbal opacity from about 3-7:00 extending 1 mm onto cornea, still present and stable, mild stain overlying previous area of demarcation line much improved, can see small area with stain, but appears very faint, still irregular surface with negative stain and some mild punctate staining, but oval area previously present not as apparent today, appears much improved and more clear- little to no staining is present with sodium fluorescein.
3. Note: Rose Bengal was instilled and photos were taken—entire area of cornea affected by the CIN picked up diffuse punctuate staining—characteristic of CIN lesions (see photos 9-11)

- Assessment: Corneo-conjunctiva intraepithelial neoplasia inferior right eye - improving on treatment based on photo review again
  1. history of refractive shift likely due to corneal changes
  2. floppy lid syndrome, chronic posterior blepharitis, unstable tear film
  3. inferior cornea has showed significant improvement in photo review since starting of interferon treatment
  4. ring of superficial epithelial irregularity centrally on cornea that has shown significant improvement compared to last exam 7/15/11

- Plan: Patient to continue with current medications (see below) and follow-up in 1 month since showing still improvement with treatment.
  1. compounded interferon drops four times daily in right eye
  2. Oral doxycycline 100mg daily
  3. Restasis twice daily
  4. artificial tears four times daily
  5. lubricating ointment at bedtime
  6. Warm compresses 1-2 times daily
  7. Moisture shield at bedtime.

III. Differential diagnosis
   a. Primary/leading
      • Corneo-conjunctival intraepithelial neoplasia right eye
   b. Others
      • Floppy eyelid syndrome ---> pannus
      • Chronic posterior blepharitis ---> pannus
      • Pterygium
      • invasive SCC of the Conjunctiva
      • atypical conjunctival papilloma
      • amelonotic melanoma
      • keratinization of the corneal epithelium
      • anterior basement membrane dystrophy
      • benign intraepithelial dyskeratosis

IV. Diagnosis and Discussion
   a. Backround/Prevalence
      • The term conjunctival intraepithelial neoplasia (CIN) was first coined in 1978 by Pizzarello and Jakobiec. CIN is generally described as an uncommon, slowly progressing disease of the conjunctiva that is a precursor to invasive squamous cell carcinoma. It is the most common conjunctival malignancy and has been reported to occur at a rate of 0.03 per 100,000 in the United States.
CIN is the third most common ocular tumor after melanoma and lymphoma. Most CINs reported occur in middle age to elderly white men, with an average onset of 56 years.\textsuperscript{1-4}

b. Risk factors/Etiology
   - Many risk factors predisposing individuals to CIN have been described, including sun exposure, HPV infection, smoking, HIV and AIDS, exposure to petroleum products, ocular surface injury, vitamin A deficiency, light complexion, and xeroderma pigmentosum. The strongest arguments have been made towards sun exposure and HIV as known causes of CIN, while others remain likely to play a role but have inconsistent findings between studies.\textsuperscript{1,4-7} Patients older than 70 years of age, those with lightly pigmented irides, and smokers are at increased risk.\textsuperscript{17}

c. Histopathology
   - CIN can be categorized according to the degree of dysplasia present in the neoplastic tissue. If 25\% of the epithelial thickness is made up of dysplastic cells, this is CIN grade I. CIN grade II shows dysplasia in 25-75\% of the epithelial thickness and CIN grade II involves more than 75\% of the epithelium. Full thickness dysplasia is termed carcinoma in situ. Once the growth invades the basement membrane, it becomes squamous cell carcinoma and has the potential for metastasis.\textsuperscript{1,4}

d. Diagnostic techniques
   - CIN can be identified via several diagnostic methods. Traditionally the lesion is excised with biopsy for histological analysis. Exfoliative cytology using a platinum spatula to scrape a sample of the tissue to examine histopathologically is one of the less invasive techniques causing only mild discomfort, although it does not allow localization of the lesion or assessment of the degree of tumor invasion. CIN is diagnosed with this method when a mixture of dysplastic and malignant cells are seen in the specimen. Impression cytology can also be performed and has been shown to identify CIN in up to 80\% of histologically diagnosed cases. This method is likely the least invasive, although the use of high frequency ultrasound and ultra high resolution optical coherence tomography for diagnosis of CIN lesions is also on the horizon.\textsuperscript{9,10}

e. Clinical presentation/unique features:
   - Patients with CIN may present with ocular irritation, foreign body sensation, redness, or reporting a growth on the ocular surface. Patients may be asymptomatic or in rare cases, present with reduced visual acuity. CIN lesions typically appear as a well demarcated, leukoplakic or gelatinous, slightly elevated mass at the corneoscleral limbus with associated feeder vessels showing a characteristic tuft or hairpin appearance.\textsuperscript{1,3-5} More than 95\% of CINs appear at the sun exposed interpalpebral limbal region.\textsuperscript{8} CIN can rarely be diffuse with ill-defined borders, similar to the patient featured in this case report. The diffuse type is the least common and can easily be misdiagnosed as a unilateral inflammatory condition. Vision loss is the least common upon presentation (this symptom also occurred in our patient) and is caused by a diffuse clouding of the cornea on slit lamp biomicroscopy.\textsuperscript{4}
   - Corneal lesions typically appear as a frosted-membranous type tissue with scalloped margins encroaching from the limbus. Both the conjunctival and
corneal portion of the CIN can take on a dull appearance with loss of luster and wetting of the lesion itself. Rose Bengal has been shown to diffusely stain CIN lesions in a punctate pattern- a very helpful aid in diagnosis.

f. Discussion:

• Our patient featured in this case report was followed for a vague clinical presentation of a diffusely cloudy cornea and longstanding visual decrease associated with associated severe blepharitis and inferior pannus for over one year before a diagnosis of CIN was achieved. Several physicians treating the patient suspected blepharitis and inflammation along with cataracts to be the culprit of our patient’s symptoms. Although CIN eventually became a differential, it was not considered initially because of such an atypical presentation. Over the course of a year of unsuccessful treatment, our patient’s cloudy cornea became more like the classic CIN lesion, with plaque-like borders and punctate rose Bengal staining. This case report will hopefully encourage eye care professionals to consider the diagnosis of CIN in atypical cases of vision loss and unilateral inflammation.

V. Treatment, management

a. Treatment options and response to treatment

The treatment of CIN has traditionally involved surgical excision of the tumor with wide margins and application of cryotherapy. However, studies have shown there to be a 53-56% recurrence rate when there is pathological evidence of residual tumor in the surgical margin and anywhere from 5-33% recurrence with clear margins. Pathological examination of the excised margins has been important due to the fact that many lesions are incompletely excised because of diffuse lateral growth and CIN can spread along the basal conjunctival layers far beyond the clinical lesion. Due to the difficulty of complete surgical excision and the resultant risk of recurrence with standard treatment, and because repeated surgery can cause conjunctival scarring or limbal stem cell deficiency, other alternatives for the treatment of CIN have recently been under investigation.

Topical agents have shown promise in the management of primary and recurrent CIN according to recent evidence. These agents include mitomycin C (MMC), 5-fluorouracil (5-FU), and interferon alpha 2-beta (IFNα2b). Along with avoiding potential complications of surgery, medical therapy has the advantage of treating microscopic disease that may be present throughout the entire ocular surface, although not visible clinically. Even in eyes with apparent unifocal disease, multiple sites of origin may be present and may lead to recurrent dysplasia at a site separate from the original lesion. Even with vast improvement of our patient's corneal condition, scattered staining with Rose Bengal revealed how diffuse this metaplasia can be and why it is difficult to remove the whole neoplastic area surgically.

Mitomycin C (MMC) is an antimetabolite isolated from Streptomyces caespitosus that has significant anti-tumor activity. MMC and 5-FU have been used to prevent recurrence of pterygium and posttrabeculectomy bleb failures and recently, to eliminate primary acquired melanosis, by inhibiting the proliferation of fibroblasts. Mitomycin and 5-FU have been used in several studies showing the successful role of MMC as both a primary and supplemental therapy in treating CIN, with success rates of up to 88-100% and with low recurrence rates from 0-22%. However, there are concerns about side effects from the use of these drops including one study that reported side effects in 76% of patients. These ranged from mild, transient changes such as toxic keratoconjunctivitis, corneal epithelial defects, eyelid skin erythema, photophobia and less frequently side effects increasing in severity including corneal haze or edema, pseudomembrane, intumescent cataract, punctal occlusion, corneal-scleral melting,
limbal stem cell deficiency, and the induction of superficial cytologic change mimicking malignancy.\textsuperscript{2,4,17-21} Although some studies report these to not be a big issue, Russell et al reported that persisting complications following MMC treatment were of more concern and occurred at a higher rate than they had anticipated and that the serious complication of limbal stem cell deficiency should be taken into careful consideration when contemplating use of topical MMC.\textsuperscript{18}

Topical interferon alpha 2-beta (IFN\textgreek{a}2b) therapy has achieved promising results in recent studies by providing effective treatment while eliminating some of the risks of side effects involved with other treatment options. Interferons are a family of naturally occurring glycoproteins, which bind cell surface receptors and trigger a cascade of intracellular activity promoting antiviral and antitumor properties through direct and indirect mechanisms.\textsuperscript{2,16-17} The recombinant form of IFN\textgreek{a}2b has been approved by for the treatment of chronic hepatitis B and C, condylomata acuminata, malignant melanoma, follicular lymphoma, Kaposi’s sarcoma, and hairy cell leukemia. Intralocional use of IFN\textgreek{a}2b has been effective for the treatment of small, primary, skin squamous and basal cell carcinomas and for the treatment of cervical intraepithelial neoplasia.\textsuperscript{11,15-17}

While intralocional IFN\textgreek{a}2b treatment has been reported to cause myalgias and flulike symptoms for two to three hours in up to one third of patients, and intramuscular and subcutaneous IFN\textgreek{a}2b injections have been reported to cause retinopathy and neuropathy, the use of topical therapy does not necessarily include these risks.\textsuperscript{16-17} In a study by Karp et. al. topical IFN\textgreek{a}2b was used four times a day on histologically proven CIN or recurrences of proven CIN, and complete resolution in all five patients was observed on average in 11.6 weeks (range 4-22 weeks). This was longer than studies with the combined intralocional and topical interferon, in which the mean time to resolution was 4.5 weeks (range 3-6 weeks), but there were no systemic side effects. One patient had an asymptomatic follicular conjunctivitis develop at the two month visit, which resolved after treatment cessation.\textsuperscript{16}

Schechter et. al evaluated seven patients with presumed CIN lesions (clinically diagnosed by corneal specialists with slit-lamp biomicroscopic criteria) and treated them with 1 million units/ml topical IFN\textgreek{a}2b drops four to six times daily. Follow-up was performed biweekly until there was a complete clinical resolution of the presumed CIN lesions, which averaged 77 days (range 28-188). Patients were continued on topical IFN\textgreek{a}2b drops for one month after clinical resolution and average post-treatment follow up was 12.4 months (range 9-16 months) and no recurrences had been seen at the point.\textsuperscript{11,17} This is a relevant study which parallels our patient, showing that topical IFN\textgreek{a}2b is not only an effective as a combination therapy or as a single agent therapy for recurrent CIN, but that it can also be effective as a single agent therapy for primary CIN. Galor et. al. discovered no statistical advantage of treating CIN with a 3 million IU/ml dose compared to the standard 1 million IU/ml dose and thus, and since there was a trend towards higher side effects in the 3 million IU/ml group, it appears that the consensus for a standard treatment for CIN should remain 1 million IU/ml four times daily with treatment continuing one month after clinical resolution of the lesion.\textsuperscript{11}

Many studies have reported minimal to no side effects with topical IFN\textgreek{a}2b treatment. In the majority of cases that did report an adverse reaction, side effects were limited to mild conjunctival hyperemia and follicular conjunctivitis, which was thought to be induced by the vehicle in the preparation, not the medication itself. In all cases, there was total resolution of conjunctival hyperemia and follicular changes within one month after cessation of the medication without additional treatment.\textsuperscript{11,17} In a study by Boehm and Huang, topical IFN\textgreek{a}2b drops were prepared with preservative-free balance salt solutions and no side effects were
noted in any patient. One case has been reported in which a patient developed epithelial microcystic edema which persisted after discontinuation of therapy. However, this occurred in a patient with poor corneal integrity and documented limbal stem cell compromise after use of topical IFNα2b, and no other studies in current literature have reported such or similar event.

Due to the fact that side effects from MMC seem to be dose dependent, another potential treatment may be a very short course of MMC followed by topical IFNα2b.

Although traditionally used as a combination treatment, there are a series of studies that have demonstrated topical IFNα2b to be an effective alternative as a single agent therapy for primary or recurrent CIN. Primary treatment with a topical agent allows one to treat the entire ocular surface and avoid potential complications of surgery, which can include scarring of the conjunctiva and cornea, limbal stem cell failure, and incomplete excision of the lesion. These topical agents offer the advantage of treating the entire ocular surface, avoiding the limitations of focal destructive procedures and eliminating the need to obtain clear surgical margins with excision. Clear surgical margins are notoriously difficult to obtain for this condition, most likely due to diffuse lateral or basal growth of the lesions. In addition, recurrent CIN can manifest in different locations on the ocular surface away from the site of the primary lesion. Topical IFNα2b treatment is extremely well tolerated and has minimal side effects in contrast to other topical treatments with MMC and 5FU, which can cause epitheliopathy, ocular surface inflammation, pain, and dry eye symptoms. Recurrences of CIN have been reported anywhere from 33 days to 11.5 years, and therefore even after observing resolution of a patient’s CIN, long-term follow-up will be necessary to detect any recurrences early on.

Discussion/Conclusion:

Because of its malignancy potential, CIN is an important differential to consider as a clinician. The condition can present in a variety of ways. Typically the patient experiences a foreign body sensation or is asymptomatic. CIN lesions generally appear well demarcated and slightly elevated at the corneoscleral limbus with associated feeder vessels showing a characteristic tuft or hairpin appearance. CINs are usually found in the interpalpebral limbal region. CINs can rarely be diffuse with ill-defined borders, similar to the patient featured in this case report. The diffuse type is the least common and can easily be misdiagnosed as a unilateral inflammatory condition. Vision loss is the least common upon presentation (this symptom also occurred in our patient) and is caused by a diffuse clouding of the cornea on slit lamp biomicroscopy. Corneal lesions typically appear as a frosted-membranous type tissue with scalloped margins encroaching from the limbus. Both the conjunctival and corneal portion of the CIN can take on a dull appearance with loss of luster and wetting of the lesion itself. Rose Bengal has been shown to diffusely stain CIN lesions in a punctate pattern- a very helpful aid in diagnosis.

Topical IFNα2b is likely to be an effective alternative as a single agent therapy for primary or recurrent CIN. Topical therapy with IFNα2b can be advantageous to surgery because it eradicate the histological, nonvisible nest of neoproliferative cells, all while treating CIN with less invasive means and virtually no serious side effects. Disadvantages of topical therapy include a longer length of treatment with close follow-up throughout and more compliance.
requirements from the patient. Length of treatment seems to be related to the size of the lesion; the larger the lesion, the longer the resolution time. Our patient presents a case in which it may be justified to rely more heavily on extended duration topical therapy. Resolution and/or eradication of the disease may not be as simple as excision or short-term topical therapy. Even though the cornea initially appeared clear after slit lamp examination and staining with sodium fluorescein drops after treatment with interferon, scattered diffuse staining with Rose Bengal remained, indicating (an improved, yet persistant) widespread sign of neoplastic cells. It is very important to monitor these lesions with Rose Bengal since CINs can be more diffuse than initially suspected. Corneal portions of CIN lesions appear to respond more rapidly than conjunctival portions in clinical studies. This is similarly our experience - even though the cornea has begun to clear up drastically since the initiation of interferon treatment, the area inferiorly at the limbus with a pannus-type appearance looks will likely take more time to resolve, as it also displays the most Rose Bengal staining. Topical therapy offers the advantage of sparing the surrounding normal tissue, which is usually excised around the lesion, and patients may prefer topical treatment such as IFNα2b rather than a surgical procedure.

Bibliography: