

# Isolated Corneal Intraepithelial Neoplasia

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**Objectives:** To report two cases of isolated corneal intraepithelial neoplasia.

**Material and Method:** The present study included 2 cases presenting with isolated corneal intraepithelial neoplasia. Both patients were treated by corneal epithelial scraping.

**Results:** The authors present the clinical picture and histopathological findings of 2 patients suffering from corneal intraepithelial neoplasia that did not arise from the corneoscleral limbus. Both patients showed no recurrence after treatment for a period of time.

**Conclusion:** Isolated corneal intraepithelial neoplasia is rare. Corneal scraping may be an effective treatment.

**Keywords:** Corneal intraepithelial neoplasia, Carcinoma in situ, Squamous cell carcinoma

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Squamous lesions of the cornea and conjunctiva are uncommon but important because of their potential in causing ocular and even systemic morbidity and mortality. The clinical presentation of these lesions extends across a wide spectrum and differs based on the degree of pathologic involvement. The nomenclature of squamous neoplasm of ocular surface is somewhat more varied. In 1995, Lee et al suggested the term "ocular surface squamous neoplasia (OSSN)"<sup>(1)</sup> which includes dysplastic and carcinomatous lesions of the cornea and conjunctiva. The currently accepted term for the localized variety is conjunctival or corneal intra-epithelial neoplasia (CIN), but others prefer the terms dysplasia (mild, moderate, or severe) and carcinoma in situ. When the abnormal cellular proliferation involves only partial thickness, it is classified as mild, moderate, or severe dysplasia. When cellular atypia extends throughout the epithelial layer, it is called carcinoma in situ (CIS)<sup>(2)</sup>. In all of these, the extension of abnormal cells does not occur past the

basement membrane. Squamous cell carcinoma is described as when the dysplastic cells grow beyond the basement membrane.

Squamous neoplasms can involve the conjunctiva or the cornea individually but more commonly arise from the corneoscleral limbus and tend to grow over the cornea. Corneal intraepithelial neoplasia originating from the cornea is rare. It is a benign, slowly progressing unilateral lesion with a low malignant potential<sup>(3)</sup>. After excision of intraepithelial neoplasia, the lesion recurred in 22 of the 98 (23%) reported cases or in 2 of the 23 (8%) cases when freezing was also applied<sup>(4)</sup>.

The authors report 2 cases of carcinoma in situ that were treated with only corneal epithelial scraping.

## Case Reports

### Case 1

A 59-year-old woman was referred to the authors department in May 2004. She complained of irritation, pain, and decreased vision in her right eye for the previous 3 months. On examination, the visual acuity was 10/200 OD and 20/32 OS. Slit-lamp examination revealed a superficial, slightly elevated grayish plaque on the right central cornea without limbal involvement. Superficial corneal vascularization at the 6-o'clock position was detected. The lesion, measuring

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5.4 x 7 mm<sup>2</sup>, threatened the visual axis. It was sharply distinguishable from a normal tissue (Fig. 1).

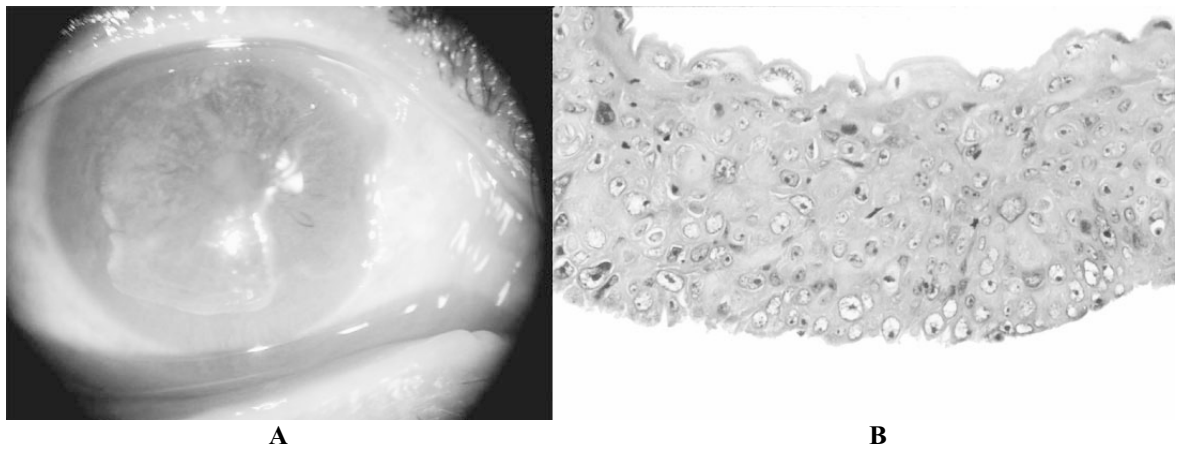
Since CIN was the provisional diagnosis, the affected epithelium was abraded and sent for histopathology. A bandage contact lens was applied, and the patient was treated with topical antibiotic for a week. The epithelium healed after 4 days. The patient was followed periodically. At the last follow up, 13 months after treatment, there was no signs and symptoms of recurrent corneal intraepithelial neoplasia. Visual acuity was 20/32 OD, and corneal epithelium was intact.

Histopathologic examination showed thickened epithelium with loss of stratification, and full thickness involvement with pleomorphic cells containing large pleomorphic nuclei with prominent nucleoli

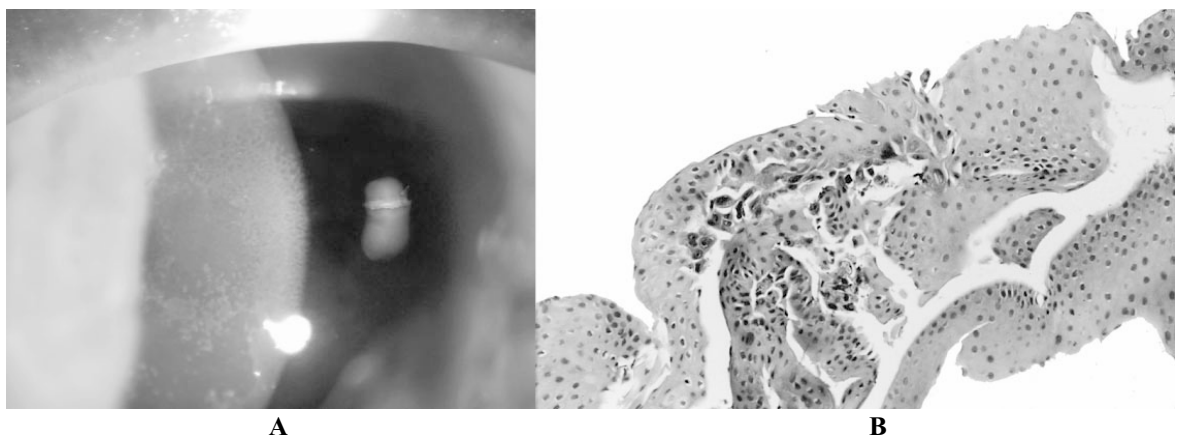
and mitotic figures. The basement membrane was intact. The pathologic report described “in situ squamous cell carcinoma”.

### Case 2

A 54-year-old woman presented to the authors' department in September 2003 with a three-month history of irritation, and decreased vision in her right eye. On examination, the visual acuity was 20/100 with pinhole 20/40 OD and 20/25 OS. Slit-lamp examination showed a superficial opacity of the right corneal epithelium. The lesion extended from the central to nasal-paracentral area without limbal involvement. No stromal infiltration was observed. The lesion had a fimbriated margin (Fig. 2).



**Fig. 1** (A) Superficial, elevated, gray white plaque without visible evidence of limbal involvement. Vascularization was noted in the inferior quadrant  
(B) Epithelium with loss of stratification, full thickness involvement with pleomorphic cells: large pleomorphic nuclei with prominent nucleoli and mitotic figures



**Fig. 2** (A) Superficial opacity of the corneal epithelium with fimbriated edge  
(B) Thickened corneal epithelium, and large pleomorphic cells with prominent nuclei. Loss of normal stratification

The affected epithelium was abraded. A bandage contact lens was applied, and the patient was treated with topical antibiotic and topical NSAID. The epithelium healed after 1 week. The patient was followed periodically. From the last follow up, 21 months after treatment, no evidence of recurrence was observed. Visual acuity was 20/25 OD. The cornea was clear with intact epithelium.

Histopathologic study showed full thickness involvement with pleomorphic cells containing large pleomorphic nuclei. The basement membrane was intact. The pathologic report described the findings as atypical squamous epithelial cells, which is highly suspicious for in situ squamous cell carcinoma.

## Discussion

The pathological changes of squamous dysplasia and carcinoma in situ of the surface epithelium are regarded as parts of a spectrum of a single disease process. Currently, the term "intraepithelial neoplasia" is used to encompass all such lesions of corneal and conjunctival epithelium regardless of severity. Squamous dysplasia and carcinoma in situ have the same neoplastic potential, that is, they are both preinvasive<sup>(3)</sup>.

Corneal intraepithelial neoplasia can originate in several ways: as an extension from an identical lesion of conjunctiva (most common type), as isolated corneal intraepithelial neoplasia starting at the limbus and extending centrally without a bulbar conjunctival component (rare), and as isolated intraepithelial neoplasia that does not involve the limbus (central)<sup>(5-7)</sup>.

Intraepithelial neoplasia of the cornea usually appears as opaque grayish plaque with well-demarcated, fimbriated edges. It may have gelatinous appearance. Although the corneal plaque is usually avascular, in rare cases, flat subepithelial vascularization may occur.

Corneal intraepithelial neoplasia has a slow progressive course with low malignant potential. None of the reported cases of isolated corneal intraepithelial neoplasia progressed to invasive squamous cell carcinoma despite the fact that microinvasive was detected in 3% of the cases<sup>(8)</sup>.

The optimal management of patients with corneal squamous neoplasia has not yet been determined. Various approaches to the treatment have been reported. Therapy depends on the histologic stage. Some authors recommend no treatment unless the lesion extends across the visual axis, with subsequent reduction of visual acuity<sup>(3)</sup>. In case of an intact Bowman's membrane and treatment is necessary, scraping of the affected epithelium with a scalpel blade

is easily carried out, and the lesion will detach easily in a sheet from the basement membrane. It is important to keep Bowman's membrane intact as it resists vertical invasion and downward growth of neoplastic cells<sup>(9)</sup>.

If Bowman's membrane is passed through, a superficial keratectomy or lamellar keratoplasty has to be performed. Keratoplasty should be aware of this because it may establish the route for intraocular invasion. Cameron and Hidayat<sup>(10)</sup> described a patient with isolated intraepithelial neoplasia of the cornea that progressed to invasive squamous cell carcinoma with involvement of Bowman's membrane and corneal stroma after lamellar and penetrating keratoplasty.

Chemotherapy with topical 5-fluorouracil<sup>(11)</sup> or mitomycin C<sup>(12)</sup>, either alone or as adjunctive therapy with surgery, has also been used in the treatment of patients with corneal intraepithelial neoplasia involving the visual axis.

Joseph F<sup>(12)</sup> described the treatment of 3 patients, who had corneal intraepithelial neoplasia with 0.02% mitomycin C four times daily for 10 to 22 days. The lesions were successfully resolved and free of re-currence for the follow-up time of 4 months, 12 months, and 16 months. The recurrent rate of intraepithelial neoplasia of the cornea and conjunctiva after simple excision has been reported to range from 25% to 40%<sup>(8)</sup>.

In the presented cases, the histopathology showed carcinoma in situ. However, both lesions extended across the visual axis. First, the authors decided to scrape the lesions for the definite diagnosis. Fortunately, it was also the therapeutic procedure according to the histologic examination. The presented patients remained asymptomatic for 13 months and 21 months in the first and second patient, respectively. However, the authors still have to follow them because several large series found that the mean interval between recurrences was about 2 years.

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### รายงานภาวะ *intraepithelial neoplasia* ที่ส่วนกลางกระจกตา

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**วัตถุประสงค์:** เพื่อรายงานผู้ป่วยที่มีภาวะ *intraepithelial neoplasia* ที่เกิดเฉพาะบริเวณส่วนกลางกระจกตา

**วัสดุและวิธีการ:** การศึกษาประกอบด้วยผู้ป่วย 2 ราย ที่มาด้วยภาวะ *intraepithelial neoplasia* ซึ่งเกิดเฉพาะภายในส่วนกลางกระจกตา โดยที่ไม่มีคามผิดปกติที่ *limbus* ผู้ป่วยทั้ง 2 ราย ได้รับการรักษาด้วยการขูดผิวกระจกตารุ่นบนออก

**ผลการศึกษา:** การศึกษานี้ได้รายงานลักษณะที่ตรวจพบทางคลินิก และผลการตรวจชิ้นเนื้อทางพยาธิของผู้ป่วย 2 ราย ที่มีปัญหาทางสายตาคงภาวะ *intraepithelial neoplasia* ที่เกิดขึ้นเฉพาะบริเวณส่วนกลางกระจกตา ผู้ป่วยทั้ง 2 รายได้รับการรักษาและติดตามอาการเป็นระยะเวลาหนึ่งและไม่พบการกลับเป็นซ้ำหลังการรักษา

**สรุป:** ภาวะ *intraepithelial neoplasia* ที่เกิดภายในส่วนกลางกระจกตาเพียงอย่างเดียวเป็นภาวะที่พบน้อย และการขูดผิวกระจกตารุ่นบนออกอาจเป็นการรักษาที่เพียงพอและได้ผลดี