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# Corneal Lumps and Bumps

## Introduction

Patients present to the ophthalmologist with various corneal pathologies, and it is imperative to differentiate the benign from the malignant at the slit lamp to provide them proper guidance and treatment. These conditions tend to play a more significant role in the pre-operative cataract evaluation as they typically affect post-operative visual rehabilitation. In this review, we aim to examine the differentiating factors of the many lumps and bumps that affect the cornea and the available ways for surgeons to treat them in Canada.

## Pterygium

**Pterygium** is one of the most common degenerations of the bulbar conjunctiva that invades the cornea causing astigmatism and ocular surface inflammation.[1-3] Its prevalence is higher in certain populations with excessive long-term exposure to ultraviolet light such as outdoor workers, but its exact pathogenesis and underlying causes are not completely understood.[1]

### Clinical Features

While most pterygia are asymptomatic and only cause cosmetic concern, some may lead to refractive changes when impinging on the visual axis and cause significant visual disturbances. Others may cause surface inflammation and irritation decreasing quality of life (QOL).[1-3] Pterygium is generally associated with an increased prevalence of dry eye.[2]

### Diagnosis

**Slit lamp examination:** Triangular or wing-shaped fibrovascular connective tissue overgrowth of the bulbar conjunctiva and invading the cornea. It can be associated with subepithelial corneal scarring but usually does not involve any thinning of the limbus and cornea.[1-3]

**Corneal topography:** The degree of flattening of the curvature along the axis of the lesion is directly dependent on the size of the pterygium and is related to the induced refractive astigmatism.[4,5] Pterygia invading the limbus for more than 1.5mm–2mm in length tend to cause refractive disturbance.[5]

### Management

Management is usually divided into **1)** Medical management of any associated ocular inflammation and associated refractive error; **2)** Surgical management of growing ocular surface lesion.[2,3,6] Within the conservative approach in patients who have a stable pterygium, UV protection plays a major role, as well as modifying dry eyes risk factors with heavy lubrication and associated anti-inflammatory topical medications as needed.[2,3] Mitigating these factors not only helps improve QOL for those patients but also prevents growth of the lesion overtime.

Surgical Management, on the other hand, is reserved for patients who exhibit any one of the following features:

- Growth over time of the pterygium toward the visual axis
- Decrease in vision secondary to induced astigmatism
- Cosmetically bothersome lesion
- Pre-operatively for any refractive surface or intraocular surgery especially cataract surgery
- Ocular discomfort and conjunctival inflammation[3,6-8]

Multiple surgical techniques have been employed to manage pterygium excision. The current consensus is to avoid any technique that leaves the sclera bare as the recurrence rate induced by post-operative inflammation is quite elevated.[3,7] Advancing conjunctival tissue over bare sclera is preferred and can be accomplished using multiple techniques that vary depending on the lesion's size, tissue availability and surgeon preferences.[6–9]

Conjunctival autografting tends to be the gold standard procedure with better cosmetic results and lower recurrence rates.[3,7] Amniotic membrane grafting is also a valid approach for larger scleral bed defects and can help preserve the natural superior conjunctiva.[3,6,7] Clinical studies have studied the use of fibrin glues versus suturing techniques to approximate conjunctival

tissues. Fibrin sealants show decreased postoperative inflammation compared to sutures with less associated risks of recurrence.[3,7] **Table 1** summarizes the recurrence rates associated with each technique.

| Pterygium excision techniques | Recurrence rate |
|---|---|
| Bare Sclera Technique | 38%–88% |
| Primary Closure | 40%–70% |
| Conjunctival Autograft | 5%–20% |
| Conjunctival Autograft with fibrin sealant | 0%–10% |
| Amniotic Membrane Grafting | 14%–27% |

**Table 1.** Pterygium recurrence rates depending on the surgical technique used for reconstruction of ocular surface.[3,7]

## Complications of Pterygium Surgery

Recurrence remains the most challenging component of pterygium surgery and is related to increased surface inflammation. Most recurrences occur 3–6 months after surgery. Risk factors for recurrence include demographic factors such as continuous UV exposure; dry eyes and ocular surface inflammation; older age; and darker skin pigmentation.[7,10] They also include surgical factors such as use of conjunctival sutures, retained Tenon's layer over scleral bed.

Peri-operative adjuvant management aims to decrease rates of recurrence.[3,6,9] Using post-operative anti-inflammatory management (topical corticosteroids or cyclosporine) for a -3 to 6-month period is important in decreasing rates of inflammation. Intraoperative use of anti-fibroblastic agents such as Mitomycin C (MMC) 0.02% for 1–3 minutes can help inhibit the proliferation of fibroblasts. Clinical studies have demonstrated its efficacy even in primary pterygium cases.[9,10] Other adjuvant treatments with less proven efficacy than MMC include the use of perioperative 5-Fluorouracil (5-FU) to decrease progression of disease or sub-conjunctival injections of monoclonal antibodies against vascular endothelial growth factors (anti-VEGF).[6,7]

## Ocular Surface Squamous Neoplasia (OSSN)

**Ocular Surface Squamous Neoplasia (OSSN)** is on the differential of many conjunctival and corneal lesions occurring on the surface. Although OSSN is rare, it is a slowly progressive disease ranging from pre-malignant to malignant epithelial cells and leads to ocular surface damage. The incidence of OSSN is reported as 0.1–35 cases/1,000,000 people.[11] OSSN can start as a corneal and conjunctival intraepithelial neoplasia (CIN) and lead to squamous cell carcinoma (SCC) when it invades the basement membrane.[12]

### Clinical features

Risk factors associated with OSSN progression include UV light exposure, history of human papilloma virus (HPV); human immunodeficiency virus (HIV) infection; smoking us; and history of OSSN or skin cancers.[12,13]

Alarming features raising suspicion for malignancy transformation are the lesion's appearance (gelatinous, leukoplakic, papilliform, presence of pigmentation), its location (tarsal, forniceal or caruncular lesions being more suspicious) and its multifocality.[13,14]

### Diagnosis

**Slit lamp examination:** The above clinical features are associated with higher risks of conjunctival intraepithelial neoplasia (CIN) and malignancy transformation especially when they occur unilaterally. The presence of feeder vessels around the lesions is also another factor to keep in mind. Positive staining with Rose Bengal stain on exam is a clinical tool that helps differentiate these lesions. Leukoplakic adherent white-gray corneal lesions can also be characteristic of squamous cell disease.[14]

**Anterior Segment Optical Coherence Tomography (AS-OCT):** This imaging technique shows characteristic hyperreflectivity and thickened epithelium with an abrupt transition from normal to abnormal tissue (**Figure 1**) which help to differentiate it from other conjunctival lesions such as pterygium.[15]

### Management

In current practice, the gold standard for diagnosis of OSSN is histopathologic specimen by incisional or excisional biopsy. AS-OCT has the potential to provide a non-invasive evaluation of the conjunctiva and cornea with high axial

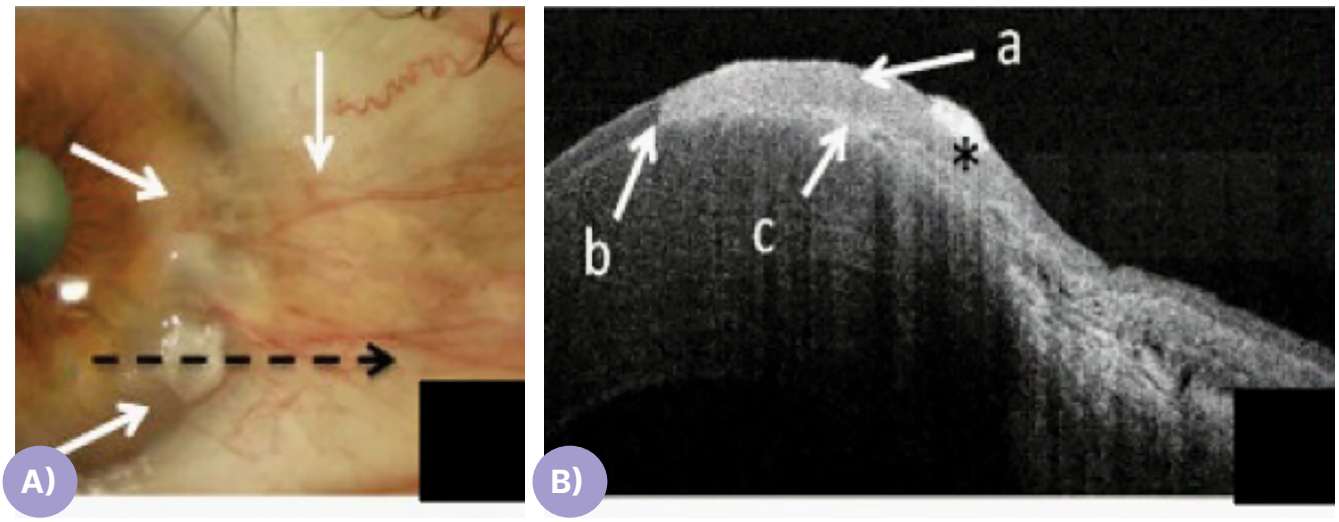


**Figure 1. A)** slit-lamp photo demonstrating gelatinous, leukoplakic, and papillary OSSN, respectively (white arrows). The black dotted arrows represent the direction and location of the AS-OCT taken.
**B)** AS-OCT shows a thickened hyperreflective epithelium (arrow a). Note the abrupt transition between abnormal and normal epithelium (arrow b). A plane of cleavage between the lesion and the underlying tissue is also noted (arrow c); *adapted from Kieval et al.*[15]

| | Concentration | Dosing | Endpoint |
|---|---|---|---|
| **Interferon alpha-2-b (IFN)** | 1 MIU/mL | 1 drop every 6 hours | 4–6 months or until clinical resolution of lesions |
| **Mitomycin C (MMC)** | 0.4 mg/mL | 1 drop 4 times daily for 1 week and drug holiday for 1 week | Until clinical resolution of lesions, or failure to respond within 2 months |
| **5-Fluorouracil (5FU)** | 1% | 1 drop 4 times daily for 1 week and drug holiday for 3 weeks | Until clinical resolution of lesions, or failure to respond within 2 months |

**Table 2.** Various topical pharmacotherapies available for primary treatment of OSSN or adjuvant therapy in patients with margin positive disease.
**Abbreviations: MIU/mL:** Million International Unit per microlitre, **Mg/mL:** milligrams per microlitre.[11,16]

tissue resolution and allows examination of the morphological and histological features of tissues.

If diagnosis is established clinically, treatment can include topical pharmacotherapy alone or surgical excision. In a recent meta-analysis, there was no difference in tumor recurrence rates between proceeding with primary pharmacotherapy and surgery.[11] **Table 2** outlines the topical treatments available with their adopted dosing.[11,16] While Interferon alpha-2-b (IFN) is the most tolerated treatment in terms of side effects profile, its worldwide shortage is causing a significant shift in treatment protocols toward 5-fluorouracil (5FU) management. In a recent review, 5FU was shown to be a good substitute for IFN treatment.[14] Mitoymycin C (MMC) is usually reserved as management of last resort due to its high ocular surface toxicity and side effects.[11]

OSSN is routinely removed surgically using a no-touch technique removing 4 mm to 5 mm margins, with alcohol epitheliectomy of the cornea. Cryotherapy and topical chemotherapy applied to the conjunctival margins is important to clean out the area before conjunctival reconstruction.[17]

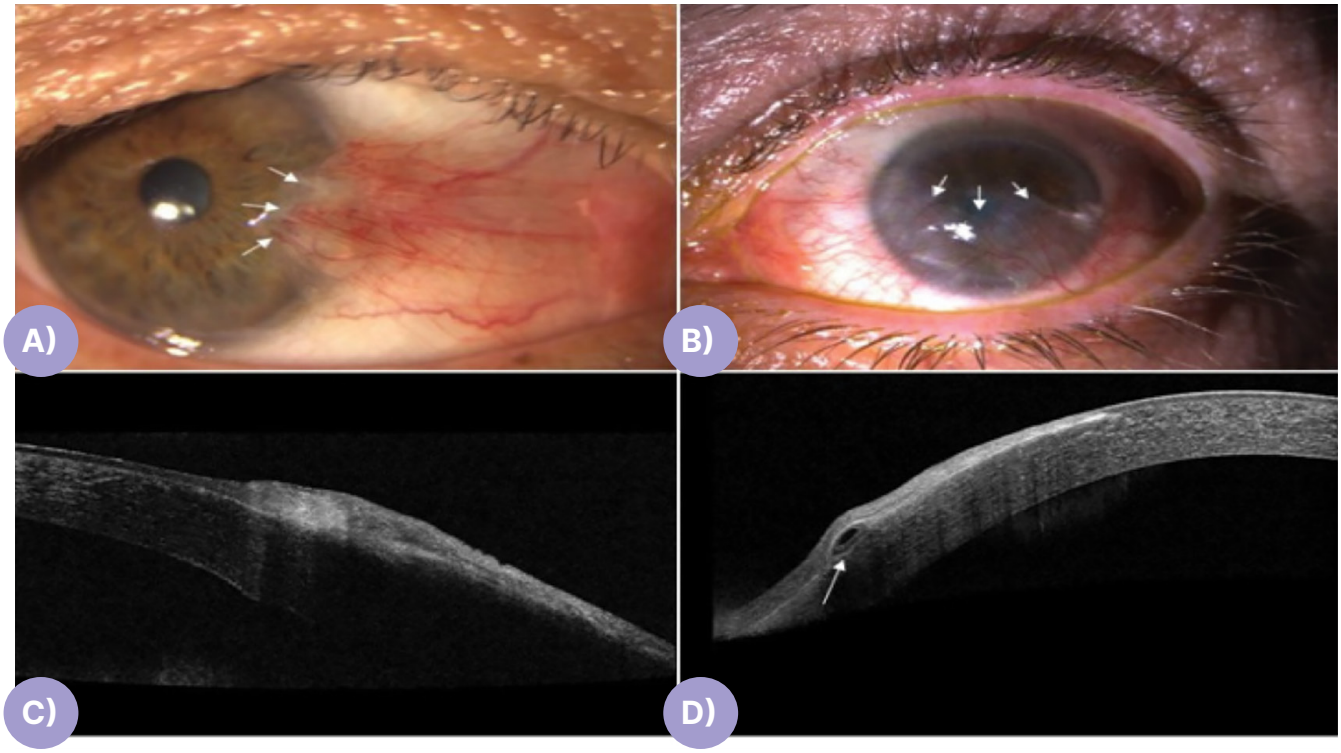


**Figure 2.** Clinical features of pterygium and pseudo-pterygium. **A)** Pterygium in slit-lamp (arrow); **B)** pseudo-pterygium in slit-lamp (arrow); **C)** AS-OCT of pterygium with no epithelial cleavage plane. **D)** AS-OCT of pseudo-pterygium with well- demarcated normal epithelial cleavage plane and membrane overgrowing cornea (arrow); *adapted from Urbinati et al.*[18]

## Pseudo-Pterygium

**Pseudo-pterygium** is a secondary pathology related to damage that occurs to the limbal epithelium. It is characterized by conjunctival adhesion to the peripheral cornea in areas of limbal stem cell deficiency and can occur in any quadrant.[18,19]

### Etiology

Etiologies leading to pseudo-pterygium formation include:

- Eye trauma
- Corneal degenerations such as marginal Terrien's degeneration
- Corneal burns (thermal, chemical or gas)
- Iatrogenic limbus pathology due to ocular surgery
- Chronic inflammation due to infections, ocular cicatricial pemphigoid or rosacea[18]

### Diagnosis

**Slit lamp examination:** Reveals a fibrovascular growth of the conjunctiva over areas of limbal cell deficiencies. The lesions typically are associated with concurrent corneal thinning, and ocular surface inflammation and scarring. They can occur anywhere around the cornea.[18,19]

**AS-OCT:** Lesions show an overgrowing membrane over an intact corneal epithelium in pseudo-pterygium. A clean cleavage plane is a characteristic feature differentiating it from a pterygium that can invade a thickened corneal epithelium (**Figure 2**).[18,19]

### Management

Management includes primarily treating the underlying condition causing the limbal stem cell deficiency before any surgical intervention is advised. Medical management includes ocular surface optimization and chronic topical immunomodulatory agents. Surgery is reserved for patients who have visual disturbance related to the ocular scarring and can include lysis of the adhesions, excision of the scarred conjunctival

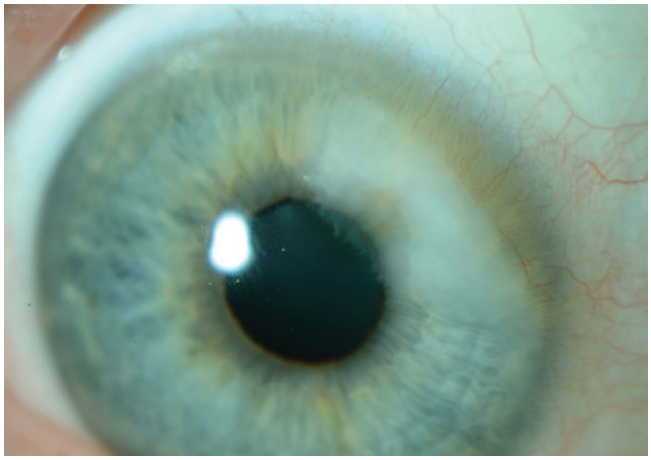

**Figure 3.** Slit lamp photography of elevated grayish opacification in the perilimbal area with associated increased vascularization characteristic of PHSCD; *adapted from Jarventausta et al.*[24]

tissue, and coverage of the defect through a free conjunctival graft or amniotic membrane.[18]

## Nodular and Subepithelial Degeneration

**Salzmann's nodular degeneration (SND)** is a rare, non-inflammatory condition that affects the corneal epithelium. It is characterized by mid-peripheral nodularity anterior to Bowman's layer of the cornea.[20-22] Typically, these nodules are bilateral and are more prevalent in female patients (72%) and in older age groups.[20-22] Histologically, SND is a dense hyalinization occurring between the epithelium and Bowman's layer and occurs with thinning of the overlying epithelium and late disruption of Bowman's layer with duplication of membranes.[21,22] Most patients are asymptomatic, although some may present with significant ocular surface irritation and foreign body sensation.

A variant of this condition is called peripheral hypertrophic subepithelial corneal degeneration (PHSCD). These patients have bilateral, symmetrical, perilimbal, hypertrophic, subepithelial corneal opacification that is always associated with limbal neovessels (**Figure 3**).[23,24]

### Etiology

The exact cause SND and PHSCD is not well understood, but risk factors associated with ocular surface inflammatory conditions such as dry eye, chronic blepharitis, previous interstitial keratitis, meibomian gland dysfunction have been established. Long term contact lens wear, trauma and previous ocular surgeries have also been associated with SND.[21,22,25]

### Diagnosis of Nodular Degenerations

**Slit lamp examination:** Nodules appear as bluish-white subepithelial elevations that may occasionally stain with fluorescein. They typically range from 2mm–4mm in size. The nodules may appear in any part of the cornea, and their location depends on the underlying risk factor. Some cases have been reported with circumferential peripheral corneal involvement.[20-22]

**Corneal Topography:** Peripherally located nodules can cause flattening of the central cornea and a hyperopic change. Irregular astigmatism can also be seen with multifocal nodularity.

**AS-OCT:** This imaging technique shows bright, hyperreflective, subepithelial deposits above the Bowman layer. The epithelium overlying those lesions is thinned out, and the demarcation of the Bowman's layer can be lost in more severe disease (**Figure 4**).[20-22]

### Management

Medical management is applicable in most cases with aggressive ocular surface treatments including lubrication and meibomian gland dysfunction therapy. Long-term topical immunomodulation with cyclosporine and/or lifitegrast might be indicated to decrease the risks of disease progression and symptoms.[20-22] In more severe cases with associated vision loss surgery is an option. Restoring the proper anatomy of the cornea has been shown to improve corneal curvature and hence visual outcomes.[26] Procedures can vary from manual superficial keratectomy (SK) to excimer laser assisted phototherapeutic keratectomy (PTK). With SK, the epithelium overlying the lesion is denuded using alcohol 20% or flat blades; the lesion is peeled off using forceps.[22,27] In PTK surgery, excimer laser is applied on top of SK to deal with corneal haze (25–75 micrometers can be ablated with or without masking within the central 6 mm of the cornea).[26] PTK has been shown to improve lines of vision and decrease recurrence rates of these lesions (22% recurrence rate with SK versus 3.8% with PTK). Adjuvant MMC 0.02% applied intra-operatively has been shown to reduce recurrence of SND.[22,26,28]

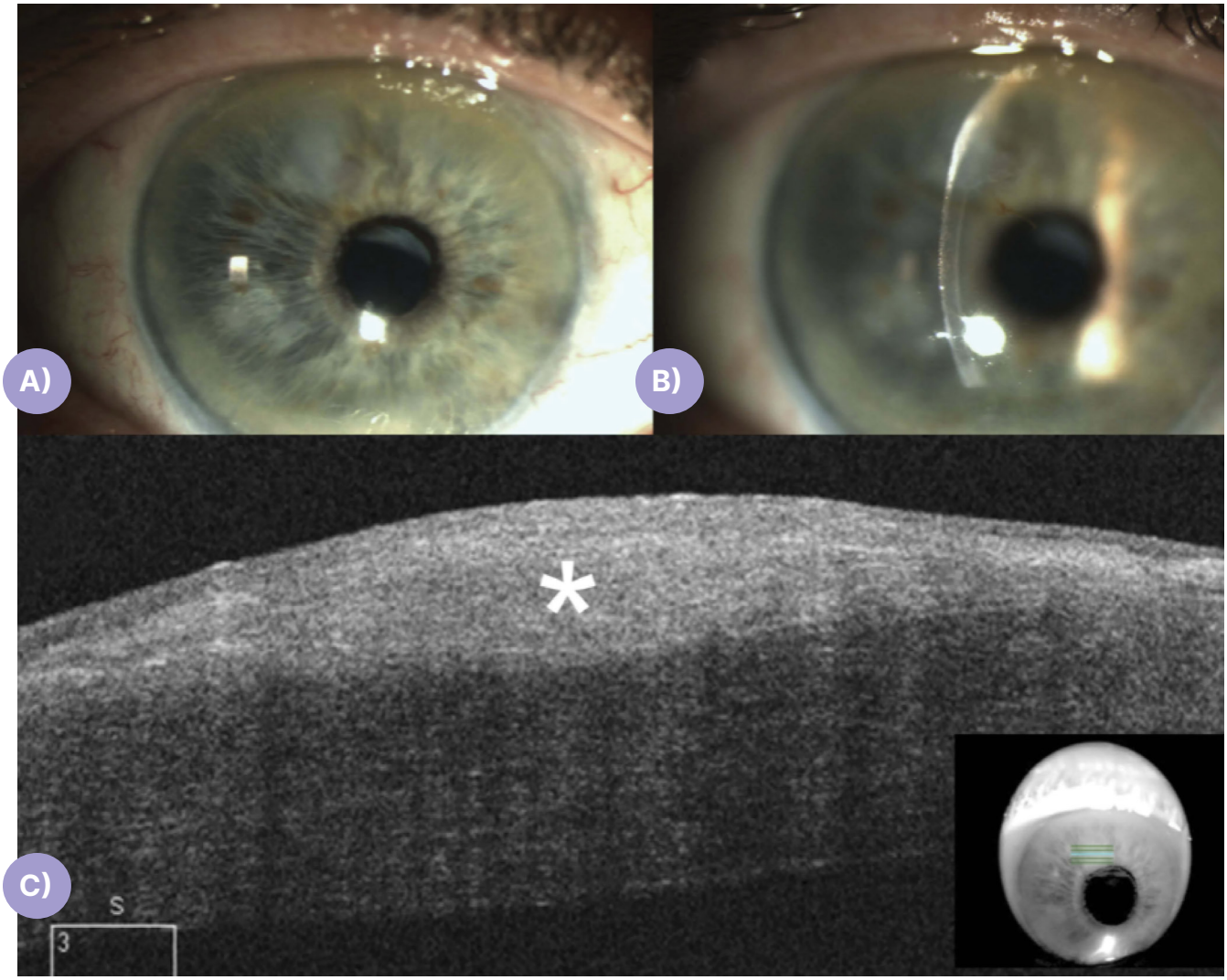


**Figure 4. A)** Slit lamp photography of SND at 11 o'clock in mid-peripheral cornea demonstrating elevated grayish opacity. **B)** Slit beam image showing hyperreflective subepithelial lesion. **C)** AS-OCT demonstrating subepithelial lesion (Asterisks) with thinning of overlying epithelium and poorly demarcated Bowman's layer; *image adapted from Paranjpe et al.*[22]

## Visual Rehabilitation with Corneal Lumps and Bumps

As most of these lesions not only affect corneal curvature but also cause significant corneal haze and opacities, they are usually associated with disruption in visual acuity and visual potential. The more centrally involved the lesion is, the greater the effect on the vision. For lesions causing astigmatism changes such as SND and pterygia/pseudo-pterygia, visual rehabilitation includes excision of lesions followed by spectacle or contact lens correction of astigmatism.[5,7,29] Typically, corneal curvature stabilizes 3–6 months after surgery allowing for changes in refractive error to stabilize. In patients with associated visually significant cataract, it is advised to delay surgical assessment of keratometry and biometry for 3–6 months after surface procedures have been performed for optimal outcomes.[4,5,29] For corneal scarring related to these lesions, visual potential might be improved with using rigid or scleral contact lenses. In rare cases where a patient's visual acuity is not improved with conservative measures, therapeutic lamellar keratoplasty might play a role in improving outcomes.[22]

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