Pterygium – An Update on Current Concepts and Treatment Modalities

BY SAI BING LEE, MD, AND ALLAN SLOMOVIC, MD

A pterygium is a relatively common eye disorder that predominates in warm, dry areas north and south of the equator. Although excision with conjunctival grafting is currently the gold standard of treatment, new treatments have been described, some of which have the potential to cause ocular surface complications. This issue of Ophthalmology Rounds describes the risk factors, pathogenesis, symptoms, and therapeutic options for a pterygium, including a description of the surgical technique for excision with conjunctival autografting.

Definition and morphology

A primary pterygium is defined as a wing-shaped fibrovascular growth from the bulbar conjunctiva onto the cornea (Figure 1). A recurrent pterygium is generally a more aggressive lesion that may rapidly occur several weeks to months after excision of a primary pterygium (Figure 2). A pseudopterygium should be distinguished from a true pterygium; it represents a conjunctival fibrovascular scar or pannus occurring secondary to mechanical or chemical trauma, or peripheral corneal degenerations such as Terrien’s marginal degeneration (Figure 3). Although similar in histology, a pingeucula is distinguishable from a pterygium by virtue of its conjunctival location away from the limbus and the fact that fibrovascular tissues underlying pingeuculae are not radially oriented towards the corneal apex.

Epidemiology of a pterygium

There is a worldwide distribution of pterygia, but they are more common in warm and dry climates. The common factor appears to be latitude, since pterygia occur primarily within the peri-equatorial “pterygium belt,” within latitudes 37° north and south of the equator. Several studies have shown that the prevalence of pterygia increases with age. The most common age of onset appears to be in the 20s and 30s.

Risk factors

The most important risk factors are environmental in nature, namely, solar and ultraviolet (UV) radiation, and chronic irritation from air-borne particulate matter.

Ultraviolet radiation

The major environmental risk factor for the development of a pterygium is exposure to UV light. UV light absorbed by the cornea and conjunctiva promotes cellular damage and subsequent proliferation. The amount of UV light absorbed is dependent on latitude (ie, within the pterygium belt), reflective terrain, and time spent outdoors. The use of protective eyewear and sunvisors may mitigate some of these risk factors.

Genetic factors

Several case reports have described clusters of family members with a pterygium, and a hospital-based case control study showed family history to be significant, suggesting a possible autosomal dominant pattern.

Other risk factors

Chronic irritation or inflammation occurring at the limbus or at the peripheral cornea has been cited as a risk factor by proponents of the “chronic keratitis” theory. This chronic

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inflammation is implicated as an important cause of limbal stem cell deficiency, and is discussed later.12 Wong has also suggested the presence of a “pterygium angiogenesis factor” and, consequently, the use of antiangiogenetic pharmacotherapy has been reported to be a therapeutic option.13 Dust, low humidity, and microtrauma from particulate matter, dry eyes, and the human papilloma virus have also been implicated.14-17

Pathogenesis of a pterygium

The exact pathophysiological mechanisms underlying the development of pterygia, their progression, and recurrence are still a matter of debate.18

Degeneration versus a proliferative disorder

Classically described as “elastotic degeneration” on light microscopy, pterygia are comprised of abnormal subepithelial tissue containing altered collagen fibers that are demonstrable with elastic stains. These are thought to be purely degenerative processes caused by sun exposure.19 Clinically, there are also behavioural features of pterygium that suggest a proliferative growth disorder.20 A primary pterygium is locally invasive, growing towards the corneal apex.

The link between UV radiation and cancer is well known, and UV light is able to induce mutations in solar keratosis and skin carcinomas.21 Pterygia have a high propensity for recurring aggressively after surgical excision, and treatment modalities therefore mimic anticancer treatments.

Limbal stem cell deficiency

The classic signs or clinical hallmarks of limbal deficiency include conjunctival ingrowth, vascularization, chronic inflammation, destruction of basement membrane, and fibrous ingrowth.12 These signs are also the hallmarks of a pterygium and, therefore, many researchers today have suggested that a pterygium is a manifestation of localized, interpalpebral, limbal, stem cell dysfunction or deficiency, perhaps as a consequence of UV light-related stem cell destruction.12

These new and emerging studies on molecular and cellular mechanisms occurring in pterygium will be important, as new insights into the pathophysiological mechanisms of pterygium and pterygium recurrence may alter our approach and offer new strategies in the medical and surgical management of pterygium.

Symptoms of a pterygium

Early pterygia may be asymptomatic or may cause occasional symptoms of dry eyes, such as burning, itching, or tearing, since the lesion causes irregular wetting of the ocular surface. As the lesion grows, recurrent inflammation, irritation, or the appearance of the lesion may trouble patients. Visual disturbance may occur due to induced astigmatism or secondary to direct obstruction when the lesion covers the visual axis.

Therapeutic options for pterygium

Symptomatic treatment with ocular lubricants to treat dry eyes is usually sufficient in the early stages of the disease. Surgical treatment is indicated when the lesion is large, threatens or affects the visual axis, or causes significant astigmatism, irritation, redness, tearing, or pain. Dissatisfaction with the cosmetic appearance of the lesion is a relative indication for removal.

Current pterygium surgery varies from the simplest procedure of bare sclera excision to more complex surgical techniques such as lamellar keratoplasty and amniotic membrane transplantation. Recurrence of the pterygium after surgical excision is the single most common cause of failure of the operation. Reported recurrence rates vary widely from 0% to 89%.22-30

Surgery

Pterygium surgery can be divided into 4 main groups, in order of increasing complexity:

• bare sclera excision
• excision with conjunctival closure/transposition
• excision with antimitotic adjunctive therapies
• ocular surface transplantation techniques

Bare sclera excision

The technique of excising the head and body of the pterygium back to the nasal canthal region and laying the scleral bed bare to re-epithelize was first described in 1948 by D’Ombrain.22,30 Although many early studies reported success with this procedure, the main drawback is that bare sclera excision is associated with a high rate of recurrence (24% to 89%) and, for this reason, it is not recommended for the management of primary or recurrent pterygia.24-25
Topical 0.02% MMC has been used after pterygium surgery twice daily for 5 days. The side effects of topical MMC may be associated with significant and potentially sight-threatening complications, including iritis, limbal avascularity, corneal melting (Figures 4 and 5), scleral melting or calcific plaque formation, corneal decompensation, scleral or corneal perforations, secondary glaucoma, and cataract.35-38

In an attempt to reduce the toxicity and complications associated with MMC eyedrop use, several studies now advocate a single intraoperative application of MMC (as used in glaucoma filtration surgery).27,28,38,39 Recurrence rates reported with intraoperative MMC application range from 3% to 43% and are generally comparable to MMC eyedrops. Complications have also been reported with the use of intraoperative MMC, including early punctate epithelial keratitis, chemosis, delayed conjunctival wound healing, and conjunctival granulomas. One case of corneal melting after intraoperative MMC application has also been reported.40-41 We currently use intraoperative MMC for recurrent pterygia only; the application is 0.02 mg/mL MMC on a saturated Weck cell sponge for 2 minutes. This is then copiously irrigated off using 2 vials of balanced salt solution (20 mL each). The bare scleral site is then closed with a conjunctival autograft.

Ocular surface transplantation techniques

As pterygia are now considered to represent a localized form of ocular surface disease, ocular surface procedures for pterygium surgery have been developed.42 The following ocular surface transplantation procedures are currently performed for pterygium surgery:

- conjunctival autograft transplantation
- conjunctival limbal autograft
- amniotic membrane transplantation

**Excision with conjunctival closure/transposition**

Several procedures describing conjunctival wound closure of the pterygium bed have been reported. Wound closure may be a simple approximation of undermined conjunctival margins. Alternatively, a conjunctival transposition using a rotational pedicle flap from above or below can be used to close the pterygium bed. However, recurrence rates do not appear to be significantly lower than for bare sclera excision. Two recent studies using simple closure or a superior rotational flap, both show high recurrence rates of 37% and 29%, respectively.26-27

**Excision with adjunctive medical therapy**

A number of adjunctive therapies have been described to decrease the risk of recurrence after surgical removal of the pterygium. Each has its benefits, but none is without drawbacks.

**Beta irradiation:** Ionizing radiation inhibits the mitosis of rapidly dividing cells and, therefore, actively proliferating tissues are most susceptible. Beta irradiation with Strontium-90 has been used at doses from 1000-7000 cGy. Although beta irradiation has been used for over half a century, reported studies on both efficacy and safety are generally lacking in numbers and follow-up time, and few prospective randomized trials exist.31-32 However, most studies show that recurrence rates are low, in the realm of 10%.

The adverse events relating to beta-irradiation surgery are believed to be dose-related and include serious complications (eg, sectorial cataract formation, irid atrophy, scleral necrosis and melting, and calcific scleral plaque formation).33-34 Milder complications include conjunctivitis, conjunctival cicatrisation, keratitis, photophobia, and ptosis. In view of the potential serious complications and the existence of effective alternate therapeutic strategies, the adjunctive use of beta-irradiation is not recommended.

**Mitomycin C (MMC):** MMC is an antibiotic-anti-cancer agent that inhibits DNA, RNA, and protein synthesis and has a long-term effect on cell proliferation. MMC has been used as an adjunct to glaucoma and pterygium surgery, where it induces prolonged localized inhibition of Tenon's fibroblasts. This reduces trabeculectomy bleb scarring and pterygium recurrence.

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Conjunctival autografting

Conjunctival autograft transplantation is the procedure of choice for the management of primary pterygia and is used in conjunction with 0.02 mg/mL intraoperative MMC for 2 minutes for recurrent pterygia. It is a relatively safe and effective operation, and serves as the “gold standard” against which all other pterygium operations are benchmarked. This procedure often provides the patient with an excellent cosmetic result (Figure 6).

The procedure involves obtaining a free conjunctival autograft (usually from the superior-temporal bulbar conjunctiva in a nasal pterygium) and suturing the graft over the bare scleral bed after pterygium excision. This procedure is described in detail later. Although this procedure is very successful, it is technically demanding. Consequently, significant variations in success rates have been reported, ranging from as low as 2% to as high as 39%. Along with conjunctival autograft transplantation, modifications of this technique have now been described, including the conjunctival rotational autograft and the annular conjunctival autograft.

Conjunctival limbal autograft

Since a focal limbal stem cell deficiency has been suggested as an etiological cause for pterygia, limbal autografting (otherwise known as conjunctival limbal autograft transplantation [CLAU]), has been proposed as a treatment modality. This procedure is similar to conjunctival autograft transplantation except that the limbal edge of the donor graft is extended to include limbal epithelium, either by superficial keratectomy or by superficial lamellar dissection. This side of the graft is then placed at the limbal edge of the recipient scleral bed in order to match and reconstruct the limbus with stem cell-containing epithelium. Despite the theoretical advantage of limbal autografting, there appears to be no significant reduction in reported recurrence rates as compared to conventional conjunctival autograft transplantation.

Amniotic membrane transplantation

There are reports that preserved human amniotic membrane may be used as an alternative basement membrane substrate in ocular surface transplantation procedures (eg, limbal allograft transplantation pterygium surgery). The use of amniotic membrane transplantation (AMT) has been shown to reduce pterygium recurrence. Amniotic membrane is effective in reducing scarring and fibrosis in ocular surface surgery. Most recently, it has also been shown to suppress TGF-β signaling in conjunctival and pterygium fibroblasts. Although less efficient than conjunctival autografting in preventing recurrence (14.8% versus 4.8% in a comparative study), the procedure often results in an excellent cosmetic result. It has certain advantages over conventional autografting in that the superior conjunctiva is not utilized and the procedure is relatively simple to perform. The main drawbacks are the cost and accessibility of AMT.

Other treatments for pterygium

In addition to the above procedures, other therapeutic modalities for pterygium removal deserve mention. These include lamellar keratoplasty, excimer laser phototherapeutic keratectomy, and a new pharmacological treatment for pterygium utilizing an angiostatic steroid compound. Lamellar keratoplasty has been promoted on the basis that allograft corneal lamellar tissue presents a barrier-limiting pterygium progression. Excimer laser phototherapeutic keratectomy (PTK) has been used to “smooth” both the scleral bed and corneal surface after pterygium excision, in an attempt to reduce scarring and surface irregularities that can increase the risk of recurrence.

Surgical technique: pterygium excision with conjunctival autografting

The procedure can be performed using topical plus regional anesthesia in a minor operating room. Sublingual Ativan™ (1 mg) combined with topical tetracaine 0.5% is given to the patient in the holding area. Additional tetracaine is administered intraoperatively as necessary. Intralosomal 2% lidocaine with epinephrine, injected into the pterygium bed and donor site for the conjunctival autograft, is very effective in alleviating patient pain during the operation.

If eye movements present a problem, an 8-0 silk traction suture may be placed through the superior cornea in order to position the eye in the necessary direction during the operation and reduce involuntary eye movements. Next, the conjunctival portion of the pterygium is marked preoperatively with a surgical marker.
A 69 or 57 Beaver blade is used to perform a lamellar dissection of the head of the pterygium, aiming for complete avascular removal of all pterygium tissue to the level of Bowman’s membrane (Figure 7). Once within this plane, the surgery is remarkably avascular until the limbal vasculature is reached. Blunt Wescott scissors are used to undermine the conjunctival portion of the pterygium (Figure 8). Sharp dissection is then used to remove the body of the pterygium. A 69 Beaver blade or a diamond dusted burr is used to polish the limbus, making sure that any residual fibrovascular pterygium tissue is removed and the limbal area is smooth. The episcleral bleeders are cauterized as necessary. The vertical and horizontal dimensions of the bare scleral bed are measured with Castrovejo calipers.

Next, attention is directed to the harvesting of the conjunctival autograft. The eye is rotated inferonasally and the appropriate sized graft is marked on the superotemporal bulbar conjunctiva. Blunt Wescott scissors are used to obtain a thin, Tenon-free conjunctival graft (Figure 9). Care should be taken to incorporate just conjunctiva in this graft, leaving Tenon’s tissue behind. Non-toothed forceps are used to grasp the conjunctiva to prevent buttonholing or tearing of the conjunctiva. When dissecting the donor conjunctival graft, the tips of the blunt Wescott scissors should always be visualized through the conjunctiva to prevent buttonholing. With this kind of atraumatic conjunctival dissection, it is very rare to get postoperative granuloma formation in the donor site and it is also usually possible to reharvest conjunctiva from the same site at a future date should there be a recurrence of the pterygium.

The donor conjunctival graft should be large enough to incorporate the pre-placed surgical markings. Once the free conjunctival graft is dissected, it is rotated into the bare scleral bed, making sure to align the limbal side of the harvested graft with the limbus at the recipient site (this is the only side that is not marked with the surgical marking pen). The graft is then sutured into place using 3 interrupted 10-0 nylon sutures at the limbus. Wing sutures are used at both ends, anchoring donor and recipient conjunctiva to episclera. One mattress suture is used in the middle to prevent retraction of the conjunctival autograft. The ends of the nylon sutures are left long because this reduces irritation and they are removed under the slit lamp 10 days postoperatively. The remainder of the graft is secured in place with either 10-0 or 9-0 vicryl sutures, using either multiple interrupted or a running suture (Figure 10).
Conclusion

A pterygium is a relatively common disorder. Amongst the various risk factors, UV exposure is the most common. Although symptoms in early disease may be mild, they can be visually disabling in the later stages. There are many methods for treating this disorder; however, some have the potential to cause severe ocular surface complications. Excision with conjunctival grafting is currently the gold standard, with appropriate and meticulous attention to proper technique to achieve a good result and subsequent low rates of recurrence. Conjunctival autografting with the use of intraoperative 0.02 mg/mL MMC for 2 minutes followed by copious irrigation is safe and effective in treating recurrent pterygia.

Allan R. Sloane MA, MD, FRCS(C) is Clinical Director of the Cornea/External Disease Service at the Toronto Western Hospital, University Health Network, Chairman of the Canadian Cornea/ External Disease and Refractive Society, and an Associate Professor of Ophthalmology at the University of Toronto.

Sao Bing Lee, MD, was a Cornea Fellow in the Department of Ophthalmology and Vision Sciences.

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