International Journal of Medical Science and Clinical Research
www.journalofmedical.com
Online-ISSN: 2664-7761, Print ISSN: 2664-7753
Received: 15-07-2023, Accepted: 01-08-2023, Published: 16-08-2023
Volume 5, Issue 2, 2023, Page No. 1-3

Pterygium: Current concepts in its management and clinical perspectives to minimize its recurrence rate

Monika Jasrotia[1], Abhinav Mansotra[2]
[1] Senior Resident, Department of Opthalmology, GMC Kathua, Jammu and Kashmir, India
[2] Junior Resident, Department of Ophthalmology, GMC Kathua, Jammu and Kashmir, India

Abstract
Pterygium is one of the common ocular surface disorder. It is a fibrovascular subepithelial degenerative bulbar conjunctival tissue over the limbus into cornea. It is typically seen in people living in hot climates and with more exposure to ultraviolet radiation. Medical therapy is mostly ineffective in these cases and surgical treatment is advised. Simple excision which is also known as bare sclera technique is available but it is associated with high recurrence rates. Other modalities includes pterygium excision combined with conjunctival autograft, adjunctive treatments with mitomycinC or beta radiation.

Keywords: Pterygium, autograft, bare sclera, mitomycin

Introduction

Pterygium is derived from ancient greek word pterygion which means wing. It is a slow growing benign in nature and triangular wing shaped subconjunctival fibrovascular proliferation. It usually invades bowman membrane and stroma of cornea. Risk factors involved are hot temperature, UV radiation and dry eye. It is common in people living in tropical and subtropical areas. It affects the visual acuity when approaches the pupillary axis. It is most common on nasal side. There are two types of pterygium progressive and atrophic (stationary) pterygium. Progressive pterygium is thick, fleshy and vascular whereas atrophic pterygium is thin and less vascular. Pterygium should be differentiated from pseudopterygia. Pseudopterygia is a adhesion of conjunctiva to peripheral cornea and it is seen in cases of chemical injuries.

Foreign body sensation, redness, dryness, lacrimation, astigmatism or visual loss if approaching visual axis is seen in pterygium. Medical treatment includes advising patients to wear sunglasses to reduce ultraviolet radiation exposure. There is high recurrence rate varying from 2-40 % associated with surgical excision of pterygium. Surgical options includes bare sclera with intraoperative mitomycin C, bare sclera with B irradiation, conjunctival autograft, limbal conjunctival autograft (LCAG), amniotic membrane transplantation, sutureless small incision pterygium surgery with fibrin tissue glue, use of antimetabolites i.e 5-FU, mitomycin- C (MMP), deep anterior lamellar keratoplasty and medical management with avastin.

Pathophysiology

Prevalence in tropical areas is around 22 % more than latitudes above 40 degrees where prevalence is less than 2 % [1]. Previous studies have shown that risk factors associated with pterygium are UV radiation [2], viral agent [3] and environmental factors such as dust, wind [4] and immunological and inflammatory factors [5]. Recent studies suggested other risk factors involved which includes the transcription factors cAMP response element binding protein [6], aquapori -1 and aquaporin-3 [7] and phospholipase-D [8]. Even with all the recent researches, UV exposure remains important risk factor for pterygium.

UV radiation

UV B and UV A both are involved in causing pterygium. Nasal zone of conjunctiva is more involved due to increase in 20 times more irradiation of nasal limbus. UV light damage limbal limbal stem cells (LSC) and alters the function of stromal fibroblasts. Initially there is damage of LSC and pterygium cells are formed and progression is seen by disrupted limbal barrier and upregulation of inflammatory cytokines and growth factors.

Initially, p53 mutations due to UV induced LSC damage was considered to be the main pathway for development of pterygium. But later on it was found inconclusive. UV radiation cause activation of pterygium fibroblasts by damaging them through DNA alterations. UV altered LSC activates them through TGFb. There are higher levels of growth factors, MMP and inflammatory cytokines in pterygium.

Viral factors

Number of studies reported the role of human papilloma virus and herpes simplex virus in the pathogenesis of pterygium. HPV 16 and 18 are most frequent genotypes associated with pterygium. E 6 and E 7 factors produced by viruses alters the normal function of p53.

Genetic factors

Several familial genes are reported to be involved in inheritance of pterygium. MMP -1 gene is involved in familial pterygium. Polymorphism of proangiogenic genes is also involved in pathogenesis. For example polymorphism of VEGF are associated with increases vascularity of pterygium. MicroRNA are also involved in the pathogenesis of pterygium.

Surgical treatments

Early excision of pterygium can save the central cornea and visual axis from permanent corneal opacity. Pterygium can also cause astigmatism and thus can be indicated for early

surgical excision. Major concern in cases of surgical excision of pterygium remains its recurrence rate. Young patients are associated with increase rate of recurrence. Ha believed that in young patients increase recurrence is seen due to rapid reepitheliazation, aggressive angiogenesis and increase collagen synthesis [9]. In a retrospective study conducted in 205 eyes, size of pterygia is the preoperative factor directly related to recurrence rate following autografting [10].

Aidenloo and colleague conducted and observational study on 310 patients and reported that young age, recurrent pterygium and large pterygium are associated with increase risk of recurrence following limbal conjunctival autograft (LCAG) [11]. The important factors responsible for successful pterygium surgery includes removal of subconjunctival fibrovascular tissue, removal of proliferative epithelial tissue and adequate covering of surgical site [12]. Adjunctive therapies used in pterygium surgery are mitomycin C (MMC) and 5-fluorouracil which targets pterygium fibroblasts.

Bare sclera technique was the first surgical technique for pterygium in which subconjunctival pterygium tissue is removed along with tenon and sclera is left exposed. It is associated with highest rate of pterygium recurrence.

Modifications includes conjunc ival and limbal autograft, amniotic membra e transplantation (AMT), mitomycin- C, 5 Fluorouracil, b radiation and cyclosporine A can be used as adjuvants to surgical methods. Bare sclera technique is associated with 25 times increase risk of recurrence as compared to conjunctival autograft technique [13]. 5 fluorouracil and b radiation with strontium -90 and triethylene thiophosphoramide is used for reducing recurrence rates [14, 15], but mostly has been abandoned due to availability of safer options.

Mitomycin C 0.02% and 0.04% has been reported to decrease recurrence and several trials has been conducted. MMC application (0.02%- 0.04%) for 3-5 min decrease recurrence as compared to bare sclera technique [16, 17]. In a study trial, 0.02% MMC was used twice a day for 5 days following the surgery [18]. In other trials, 0.04% MMC was given 4 times a day for 2 weeks postoperatively [19].

The recurrence rate of pterygium following combined bare sclera and MMC ranges from 3 – 38%. Several studies were conducted for evaluation of subconjuctival injection of MMC as adjuvant therapy for pterygium surgery. In a trial, 50 eyes with recurrent pterygium were divided into 2 groups - preoperative mmc injection group and postoperative topical mmc group. 0.1 ml of 0.15 mg/ml of MMC injected a day before pterygium excision in group 1. It was concluded that preoperative subconjuctival injection of low dose MMC was an effective strategy for management of recurrent pterygium [20].

Several trials has been conducted to study efficacy of topical or subconjunctival antivegf combined with pterygium removal techniques. Shenanigans studied effect of Bevacizumab after excision of Primary pterygium. He and his colleagues concluded that combination therapy was not well tolerated and it cannot decrease recurrence of pterygium [21].

In a study, topical bevacizumab (5 vs 10 mg/ml) was used after pterygium surgery in 90 patients. Pterygium recurred in 13.3 % I 50 mg/ml group and there was no recurrence seen in 10 mg/ml group.It was concluded that 10 mg/ml concentration is better than 5 mg/ml in preventing recurrence [22].

Topical CsA postoperative is another adjuvant treatmentused to decrease recurrence rates [23]. Hwang and Choi conducted a study while using CsA after pterygium surgery. It was seen that 20.6 % of eyes showed recurrence and it was lower as compared to control group [24].

In 1985, Kenyon and colleagues described conjunctival autografting asan adjuvant treatment after pterygium excision surgery to reduce recurrence rate [25]. Conjunctival autografting is done to cover the sclera bed with free graft taken from patient' s own adjacent conjunctiva aftersurgical excision of pterygium. It is associated with postoperative discomfort, irritation and displacement of graft sometimes.

Many trials reported great results with conjunctival autograft over bare sclera in the decreasing recurrence I pterygium [25]. Pterygium recurrence rate after conjunctival autograft ranges from 1-40 % [26]. Recurrence rate following combined MMC and autograft varies from 6.7 % to 22.5 % [27].

Fibrin glue can be used instead of graft suture in pterygium surgery [28]. Low recurrence rates and less operative time can be seen with fibrin glue but it is associated with risk of infections, dehiscence and graft retraction. Kumar and Singh conducted a study on 60 casesof pterygium and compared 3 methods - suturing, fibrin glue and autologous blood. It was reported that fibrin glue is most efficient method [29].

Amniotic membrane transplan ation c n be used for surgical reconstructio after pterygium excision. Amniotic membrane protects sclera nerve ends and reduces pain. It also acts as a barrier for abnormal growth of conjunctival stem cells I limbus and cause normal proliferation of LSC.

A study was conducted which includes analysis of 20 studies in 2016 concluded that AMT is associated with increased risk of recurrence 6 months after surgery compared to conjunctival autografting.

Conclusion

Pterygium is a ocular surface disease and till date, ultraviolet rays remains the most important causative factor. Other factors like viral and hereditary factors are still inconclusive. Pterygium is a diffuse ocular surface disease and comitant conditions such as dry eye shoul be treated. It can cause astigmatism and aberrations of cornea. The cells mostly responsible for pterygium development are altered limbal stem cells and stromal changes are also involved. Altered stem cells are mostly located in the apex of the pterygium so complete removal of pterygium is very important. Most common surgical treatment advised for pterygium patients are conjunctival limbal autograft and use of MMC as an adjuvant. The use of CsA and Bevacizumab is still inconclusive and is still not preferred.

References

1. FD Mackenzie LW Hirst D Battistutta A Green Risk analysis in development of pterygium ophthalmology 199299710566110. 1016 / S01616420(92)31850-0.
2. Moran DJ and Hollows FC. Pterygium and ultraviolet radiation: a positive correlation. *Br J Ophthalmol*,1984:68:343-346.
3. Gallagher MJ, Giannoudis A, Herrington CS, *et al*. Human papilloma virus in pterygium. *Br J Ophthalmol*,2001:85:782-784.

4. Coroneo MT. Pterygium as an early indicator of Ultraviolet insolation: a hypothesis. *Br J Ophthalmol*,1993:77:734-739.
5. Hill JC, Maske R. Pathogenesis of Pterygium. *Eye*,1989:3:218-226.
6. Nubile M, Curcio C, Laznzini M, *et al.* Expression of CREB in primary pterygium and correlation with Cyclin D1, ki-67, MMP7, p53, p63, surviving and vimentin. *Ophthalmic Res*,2013:50:99-107.
7. Tong L, Li J, Chew J, *et al*. Phospholipase D in human ocular surface and in pterygium. Cornea,2008:27:693-698.
8. Ortak H, Callie S, Ocakli S, *et al*. Increased expression of aquaporin-1 and aquaporin-3 in pterygium. Cornea,2013:32:1375-1379.
9. UHa SW, Park JH, Shin IH, et al. Clinical analysis of risk factors contributing to recurrence of pterygium after excision and graft surgery. *Introduction J Ophthalmol*,2015:8:522- 527.
10. Yin D, Lee OL. Risk factors for pterygium recurrence after primary excision. *Invest Ophthalmol Vis Sci*,2011:52:3367.
11. Aidenloo NS, Motarjemizadeh Q, Heidarpanah M. Risk factors for pterygium recurrence after limbal-conjunctival autografting: a retrospective, single- centre investigation. *Jpn J Ophthalmol*,2018:62:349-356.
12. Kim KW, Kim JC. Curren appro ches and future directions in the management of pterygium. *Int J Ophthalmol*,2018:11:709-711.
13. Sanchen-Thorin JC, Rocha G, Yelin JB. Meta-analysis on the recurrence rates after bare sclera resection with and without mitomycin C use and conjunctival autograft placement in surgery for primary pterygium. *Br J Ophthalmol*,1998:82:661-665.
14. Hovanesin JA, Starr CE, Vroman DT, *et al*. Surgical techniques and adjuvants for the management of Primary and recurrent pterygia. *J Cataract Refract Surg*,2017:43:405-419.
15. Nogy D, Kayembe L. [A comparative study of thio-tepa and mitomycin C in the treatment of pterygium. Preliminary results]. *J Fr Ophthalmol*,1998:21:96-102.
16. Cano- Parra J, Diaz- Llopis M, Maldonado MJ, et al. Prospective trial of intraoperative mitomycin C in the treatment of Primary pterygium. *Br J Ophthalmol*,1995:79:439-441.
17. Yanyali AC, Talu H, Alp BN, et al. Intraoperative mitomycin C in the treatment of pterygium. *Cornea,2000:*19:471-473.
18. Calista S, Orhan M, Irkec M. Intraoperative and postoperative use of mitomycin- C in the treatment of primary pterygium. *Ophthalmic Surg Lasers*,1996:27:600-604.
19. Mahar PS, Nwokora GE. Role of mitomycin C in pterygium surgery. *Br J Ophthalmol*,1993:77:433-435.
20. Zaky KS, Khalifa YM. Efficacy of preoperative injection versus intraoperative application of mitomycin recurrent pterygium surgery. *Indian J OphtHalmol*,2012:60:273-276.
21. Shenasi A, Mousavi F, Shoa-Ahari S, et al. Subconjuctival bevacizumab immediately after excision of primary pterygium: the first clinical trial. *Cornea*,2011:30:1219-1222.
22. Motarjemizadeh Q, Aidenloo NS, Sepehri S. A comparative study of different concentrations of topical bevacizumab on the recurrence rate of excised primary pterygium: a short term follow up study. *Int Ophthalmol,2016:*36:63-71.
23. Yalcin Tok O, Burch Nurozler A, Ergun G, et al. Topical cyclosporine A in the prevention of pterygium recurrence. *Ophthalmologist*,2008:222:391-396.
24. Hwang S, Choi S. A comparative study of topical mitomycin C, cyclosporine and Bevacizumab after primary pterygium surgery. *Korean J Ophthalmol*,2015:29:375-381.
25. Kilic A, Gurley B. The efficency of limbal conjunctival autografting in pterygium surgery. *Eur J Ophthalmol*,2006:16:365-370.
26. Ozer A, Yildirim N, Erol N, et al. Long term results of bare sclera, limbal-conjuctival autograft and amniotic membrane graft techniques in primary pterygium excisions. *Ophthalmologica*,2009:223:269-273.
27. Thakur SK, Khaini KR, Panda A. Role of low dose mitomycin C in pterygium surgery. *Nepal J Ophthalmol*,2012:4:203-205.
28. Cohen RA, McDonald MB, Fixation of conjunctival autografts with an organic tissue adhesive.*Arch Ophthalmol*,1993:111:1167-1168.
29. Choudhary S, Dutta J, Mukhop dhyay S, et al. Comparison of autologous in situ blood coagulum versus sutures for conjunctival autografting after pterygium excision. *Int Ophthalmol*,2014:34:41-48.