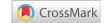


Case Report



A case study of benign nodular episcleritis and management

Abstract

Episcleritis is an inflammatory condition that affects episcleral tissue underlying the sclera and conjunctiva.^{1,2} It is a recurrent and mild self-remitting surface disease. Its etiology is unknown but may be associated with systemic diseases.^{3–5} It has been recognized for over a century as sub-conjunctivitis or subconjuctivitis phlegmatous. The condition is unilateral in two thirds of cases and bilateral in one third. Two major clinical types are noticed diffuse and nodular. The case outlined Nodular episcleritis and its clinical diagnosis and management. The condition was mild and didn't progress to a more severe disorder. An episcleral nodule adjacent to the cornea is very rare.

Keywords: vascular endothelial growth factor, exudative retinal detachment, fundus fluorescein angiography, superior limbic keratoconjunctivitis, systemic nonsteroidal antiinflammatory drugs

Case report

A 28-year-old Asian female presented mild discomfort, slight ache, irritation, watering, burning sensation, pain around the eyes, and sudden red eye for two weeks in the left eye. She felt that the intensity of redness increased over time. She denied any photophobia and discharge. She denied any vision change. History showed spectacle dependency for eight years of - 2.50DS. She denied any ocular trauma or surgery history. She had a history of joint pain two years ago. Her general medical history was none, and she lacks any known allergic history. Ocular examination revealed a visual acuity of 20/30 in both eyes with spectacles. Her manifest refraction was 20/20 with spherical -3.00DS in both eyes. Intraocular pressure was 12 mmHg in both eyes. Extraocular muscle movements and pupil reaction were normal. Confrontation showed normal fields. Anterior examination showed normal Lid adnexa and puncta. Left eye conjunctiva showed mild sectoral congestion, a mobile pinkish-white, soft edema with a raised mass, measuring 2.8 mm in size and 1 mm in height, and around 1mm from the temporal limbus with some yellowish deposits at the edge. *Cornea revealed early corneal Dellen due to episcleritis (Figure 1). The Plexus of the sclera could be discriminated deep to the nodule lying flat mobile on the sclera, which showed its normal contour. The anterior chamber was quiet and deep. At the same time, the right eye anterior segment was within normal limits. Both eye chamber angles were open with von Herrick 4/4 method. The rest of the Posterior segment examination showed a normal disc, and the macular reflex was normal. Anterior Ultrasound Biomicroscopy of the left eye revealed no extension of the nodule to the sclera. She denied any lymphadenopathy. Systemic workup was within normal limits.

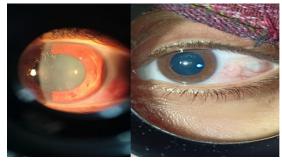


Figure I Photo courtesy Rubina shah national eye center.

Volume 13 Issue 1 - 2023

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Received: January 16, 2023 | Published: March 31, 2023

Note: A slit lamp Biomicroscopy showed inferior corneal Dellen due to inflammation with temporal sectoral congested vessels. B. Indirect Ophthalmoscopy reveals a raised focal mass temporal conjunctiva around 1mm from the limbus.

The clinical diagnosis was based on history and slit lamp examination. Eventually, the study revealed features of episcleritis. The Conjunctival epithelium was unharmed and capillary proliferation was noted. The patient subsequently responded well to a Maxidex eye drop with two follow-ups. An episcleral nodule within the episcleral was surrounded by some congestion overlying the sclera, which was moving on the underlying sclera, and the scleral edema was not involved. In contrast, with simple episcleritis, the edema and infiltration of nodular episcleritis were localized to one part of the globe. The nodules are usually solitary but may sometimes have multiple, reaching the size of a large pea.

Differential diagnosis

It is crucial to discriminate episcleritis from scleritis regarding prognosis, benign, malignant, and systemic associations. Scleritis is rare and is more often associated with connective tissue problems and vasculitis disease than episcleritis. Moreover, other ocular diseases, such as defective vision, anterior uveitis, peripheral ulcerative keratitis, and ocular hypertension, are commonly associated with scleritis. There are several differentials diagnoses that can challenge our final diagnosis.

Superior limbic keratoconjuctivis

Superior limbic keratoconjunctivitis (SLK) is known as an inflammation superior limbus with involvement of the superior bulbar conjunctiva causing adjacent epithelial keratitis and papillary hypertrophy of the upper tarsal conjunctiva. Thygeson and Kimura 1963 defined it as localized filamentary and chronic conjunctivitis.⁶ Theodore gave its name after five years as superior limbic keratoconjunctivitis (SLK), by Theodore. Tenzel and Corwin each described the accompanying disease with thyroid abnormalities and SLK.^{7,8} A same disorder has also been seen in soft contact lens (SCL) wearers, specifically with exposure to thimerosal-preserved solutions.^{9,10} Superior limbic keratoconjunctivitis comprises the natural history of the chronic clinical course with gradual improvement. Examining the upper bulbar conjunctivae or flipping the upper

Adv OphthalmolVis Syst. 2023;13(1):44-48.



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eyelids is essential. It has been reported to be with thyroid disease; hence initial investigations into thyroid function, including thyroidstimulating hormone (TSH), free thyroxin (T4), thyroid-stimulating immunoglobulin, or TSH binding inhibitory immunoglobulin, may be appropriately tested. The treatment protocol includes pressure patching, placement of a bandage contact lens, mast cell stabilizers, and silver nitrate solution application.^{11,12} The preparation of vitamin A,¹³ topical cyclosporine,¹⁴ autologous serum-derived drops,^{15,16} and botulinum injection to the overlying muscle of Riolan¹⁷ have been used with moderate success. Surgical resection of bulbar conjunctiva is often required because the temporary treatment might not mitigate symptoms. Steroidal therapy may lessen inflammation and can be used long-term for improvement. However, when steroid drops fail, Supratarsal Triamcinolone has been considered adequate.¹⁸ Moreover, surgical procedures might heal the conjunctiva when initial measures fail by restoring the interaction between the bulbar and palpebral conjunctiva. Several surgical therapies are at time considered, such as superior conjunctival resection, Blepharoplasty, and correction of proptosis in Graves' disease.19,20

Viral conjunctivitis (pink eyes)

Viral conjunctivitis is caused by adenovirus, which is a selflimiting condition. Other associations of viruses are herpes simplex virus (HSV), varicella-zoster virus (VZV), picornavirus (enterovirus 70, Coxsackie A24), poxvirus (molluscum contagious), and human immunodeficiency virus (HIV). It usually regresses for 10-12 days from onset. Certain precautions must be taken at the patient's side to avoid touching their eyes, shaking hands, and sharing towels, napkins, pillowcases, and other fomites, among other activities. Its transmission may aggravate through accidental inoculation of viral particles from the patient's hands or by direct eye contact with infected upper respiratory droplets, fomites, or contaminated swimming pools. The infection usually resolves spontaneously within 2-4 weeks. Treatment of adenoviral conjunctivitis is supportive. No evidence shows the efficacy of anti-viral. Medication is other than ganciclovir. A clinical trial III has shown that the combination topical agent that contains betadine and low-dose dexamethasone is currently used as a broad-spectrum agent for treating adenovirus, HSV, VZV, and infectious diseases. Treatment includes using cold compresses and ocular lubricants, such as artificial tears, for a soothing effect.

Topical antihistamines and vasoconstrictors may be used for severe itching but generally are not usually used because they are minimally helpful and may cause local drug toxicity and hypersensitivity reactions; intolerant patients can be switched to topical astringent or antibiotic to prevent bacterial superinfection. Topical steroids can be used for pseudo membranes or prone to subepithelial infiltrates to impair vision, although they can recur after stopping steroids. Extreme care must be taken while using corticosteroids, as they can aggravate an underlying HSV infection and may prolong viral infection therapy. For nodular scleritis, local causes of nodule by foreign body and granuloma or chemical injuries must be considered.

Scleritis

Scleritis is a dangerous condition that includes the severe deterioration of vision with leading ocular complications, such as Keratitis, anterior uveitis, glaucoma, and secondary cataract. Clinically, it is categorized into anterior and posterior scleritis. Anterior scleritis is subdivided into diffuse, nodular, or necrotizing scleritis.²¹ The most common scleritis is diffuse with or without the association of RA Rheumatoid arthritis. And nodular scleritis is known for firm sectoral inflammation, which can be tender. Necrotizing scleritis is the most destructive type. It can have the anterior and posterior manifestations of pain and red eye.

Conjunctivalulcer

Conjunctival ulcer causes tenderness, pain, erosion away from the limbus, typically stains with fluorescein, and temporal congestion. Mahendradas P et al.²² presented the same evidence of condition responding effectively with quinolones and co-trimoxazole.²² Furthermore, ulceration can be due to tuberculosis and herpetic conjunctival ulcer.^{23,24} The association between non-infective Crohn's and Behcet's disease is also documented.^{25,26} Rare manifestations of ulcers have also been stated after surgery of cataract extraction, which showed effectiveness with corticosteroid therapy.²⁷

Conjunctival lymphoma

Conjunctival lymphoma is an ocular surface tumor of bulbar conjunctiva that looks like a multinodular lesion and follicular conjunctivitis. Conjunctival lymphoma affects predominantly females in the fifth to seventh decades with a pink salmon patch of the bulbar conjunctiva. The typical symptoms include minimal to the leading causes. The clinical presentation includes irritation, redness of the conjunctiva, and increased tears production with palpable mass causing diplopia and ptosis. There are several differential diagnoses of conjunctival lymphomas, such as benign ocular surface tumors [squamous papilloma, pyogenic granuloma, and lymphangiectasis, lymphoid, malignant tumors [squamous cell carcinoma and amelanotic melanoma], the presence of a foreign body, scleritis, episcleritis, and chronic follicular conjunctivitis.

Pinguecula

A benign nodule, noncancerous growth on conjunctiva that can be multimodal. It is yellowish and triangular in shape, close to the limbus. It is caused by sun exposure, dust, and wind. Pinguecula makes your eye feel foreign body sensations and dryness. It's a benign condition requiring no therapy unless it causes discomfort. In some case Pinguecula can be swollen and inflamed known as pingueculitis. In such case topical steroid is given to relief the symptoms of pain.

Phlyctenulosis

Phlyctenulosis was considered to be associated with hypersensitivity to tubercular protein and was seen in the younger age group. It was noted in a poor, malnourished child with a positive tuberculin skin test.²⁸ The nodule is seen with marked elevation and focal leash of vessels near the limbus.²⁹ The case closely resembled, but the vision was not markedly reduced, and the nodule was nonulcerating. Their sequelae cause Blepharitis, conjunctivitis, and punctate epithelial keratopathy. Its prevalence is higher in females and children. It is caused by secondary to hypersensitive and allergic reactions of the cornea and conjunctiva due to exposure to light or a sensation of an infectious antigen.^{30,31} It is associated with a skin condition with a type 4 hypersensitivity reaction.^{30–32}

Ocular surface squamous neoplasia:

(OSSN) formation is typically near the limbus due to solar elastosis, the same as actinic keratosis of skin condition. In fair skin pigmentation, exposure to ultraviolet light (UV) is a higher risk factor for OSSN. The gene suppression p53 has been associated due to UV-associated mutations, and specific hereditary condition, such as xerodermatic pigmentosa, is a genetic deficiency of DNA re and pair is the greater prevalence of OSSN. The subtypes 16 and 18 of HPV and HIV human immunodeficiency virus are associated and are typically expected in the sub-Saharan African regions. Secondary factors can be older age and smoking. It causes surface keratinization, which is not pathognomic and may be expected on any elevated lesion with unstable tear layers. However, it arouses suspicion.³³ Another

Citation: Shah R.A case study of benign nodular episcleritis and management. Adv Ophthalmol Vis Syst. 2023;13(1):44–48. DOI: 10.15406/aovs.2023.13.00438

differential condition can be inflamed early Pterygium and limbal dermoid.

Treatment and management

The course of episcleritis generally clears on its own without proper treatment, and assurance is the prime step in management. However, some patients may experience symptomatic pain and discomfort or may be uncomfortable with the appearance of pink nodules. Specific measures, such as cool compress, artificial tears, topical vasoconstrictors, or medical therapy, must be initiated.

Work up

A thorough history and general review of systems may be required to tackle its management. Specific laboratory examinations are used to determine its association with other health conditions. Moreover, patients with nodular episcleritis and symptomatic recurrent or persistent diffuse scleritis may need a limited workup due to the pathophysiological association with autoimmune disease and collagen vascular diseases. A patient with a history of low back pain and stiffness must be examined for ankylosing spondylitis. The required serum uric acid was done to exclude gout, complete blood count, rheumatoid factor for Rheumatoid arthritis, an anti-nuclear antibody for connective tissue disorder, and erythrocyte sedimentation rate is required for liver disease. If syphilis or toxoplasmosis is suspected, a venereal Disease Research Laboratory (VDRL) test, fluorescent treponemal antibody absorption (FTA-ABS), a test is done, and a chest x-ray for Lyme disease and spondylitis.

Local therapy

Local therapy started for nodular episcleritis was to relieve the symptoms with more indolent local corticosteroid drops and antiinflammatory agents. Topical Maxidex eye drop was given four times a day. Further diffuse episcleritis doesn't require any treatment. A topical artificial tear (Tear naturale) was advised four times daily for corneal Dellen. However, artificial tears and topical steroids may be used for severe and extended cases.³⁴ Other eye drops such as Topical ophthalmic 0.5% prednisolone, 0.1% dexamethasone, Loteprednol etabonate 0.5%, or 0.1% betamethasone daily may also be used. Studies showed that in a small study group, patient about three quarter responded well to topical therapy.³⁵

Systemic therapy

The patient had benign nodular episcleritis without any known systemic association. General therapy systemically includes systemic anti-inflammatory agents are required when topical therapy is unresponsive. Systemic Nonsteroidal (NSAIDs) drug Froben tablet (Flurbiprofen) 100 mg bid was given for a week initially and reduced to 75mg daily with follow-up examination. The inflammation may be suppressed by Systemic Nonsteroidal anti-inflammatory drugs (NSAIDs). Other treatments of NSAIDs such as indomethacin (100 mg daily initially and decreased to 75 mg daily) and naproxen (220 mg up to 6 times per day). More severe episcleritis is mainly treated with Naproxen 500 mg. After one month, patients who are unresponsive to both therapies, local and systemic NSAIDs, can be started with corticosteroids for one month with tapering dosage.³⁶ About 20% of patients with nodular episcleritis require oral corticosteroid treatment.37 Antibiotic therapy is used for patients affected with secondary infection.

1st follow-up (1-week): On the follow-up evaluation date, the conjunctival nodule's size and color were reduced to 1.5mm, and faded focal congestion of episcleral vessels. Visual functions with visual acuity were normal. Fundi were unremarkable. The patient

was advised to taper topical steroid TID every week for three weeks. Intraocular pressure noted was 16mmHg OD and 15mmHg OS.

2nd follow up (3 weeks): The scleritis nodule was resolved on the examination date, and the patient was asymptomatic. Corneal Dellen was resolved ultimately with artificial tears therapy. Visual acuity was 20/20 with -2.50 OU for distance. The patient had healthy eyes, so only spectacle therapy with artificial tears was advised. The patient was educated about the pattern of the disease and the chances of recurrence.

Discussion

Episcleritis is known as a benign disease that rarely affects vision. The affected patients with episcleritis usually define discomfort rather than severe pain. The primary differential factors of episcleritis from scleritis is severe pain. In this case, there was no rheumatoid arthritis association. Hence responded well with the treatment followed. Alternatively, scleritis is commonly associated with Rheumatoid arthritis in one-third of patients (33.3 percent) but is least common in patients presenting with episcleritis about (5.7percent). The incidence of episcleritis estimated is approximately two patients per thousand associated with RA rheumatoid arthritis (0.017 percent). It is visionthreatening and is associated with deleterious systemic conditions; therefore, if diagnosed early can be lifesaving. It is classified into anterior and posterior types. Further anterior scleritis can be nodular, diffuse, necrotizing, and non-necrotizing, such as (scleromalacia perforans). Necrotizing scleritis is ominously associated with ulcerative keratitis and autoimmune diseases. Posterior scleritis affects the back of the globe, markedly sclera and choroid, with retrobulbar edema.38 Early diagnosis may benefit the early treatment of the general condition, extending and refining the quality of life for such patients. (Duke-Elder and Leigh, 1965) given in the literature suggested that rheumatoid arthritis is the most typical single associated disease. There is a specific systemic disease named connective tissue diseases systemic lupus erythematous, polyarthritis nodosa, relapsing polychondritis, Wegener's granulomatosis associated with scleritis, and suggesting the collagen tissues involvement.

Poor disease prognosis can be diagnosed as scleritis from systemic vasculitis diseases. Sainz de la Maza et al.³⁹ proved it depends on specific vasculitis disease related to the prognosis of association with scleritis. Systemic lupus erythematosus and spondylosis arthropathies are conditions where scleritis is benign and regresses itself. However, in granulomatosis with polyangitis may lead to a visual problem with permanent blindness. Scleritis of intermediate severity is not uncommonly seen in association with conditions such as rheumatoid arthritis and relapsing polychondritis.

The treatment of scleritis depends on halting the progression of the disease and also by relieving the pain. Oral NSAIDs are the first option in nodular scleritis, and in case of failure to respond to therapy, corticosteroids should be added as a secondary therapy. when patients with severe involvement necrotizing scleritis or diffuse and nodular scleritis don't respond to NSAID's and alternatively, corticosteroids or immunosuppressive medication can be advised.40 ANCA- positive vasculitis associated scleritis is suggested to be improved by Cyclophosphamide.⁴¹ In adult patients, a minor dosage of cyclosporine A has been recommended for those who show intolerance. To cyclophosphamide because of the increased risk of sterility.⁴² This patient with nodular episcleritis was very responsive to NSAIDs, and corticosteroid therapy markedly improved the disease. The case was assessed for the possibility of a relationship with any systemic disease. Although the condition has a possible association with systemic disease, its reports were normal, including all the laboratory and physical examinations. My goal was to evaluate

the extent of associated systemic disease. Generally, episcleritis is commonly associated with Rheumatoid arthritis, but rheumatoid episcleritis, scleritis, and non-rheumatoid scleritis had prevalence by a mean age of the sixth decade. The pattern was prominent in females as the ratio of males. Patients with non-rheumatoid episcleritis had a peak age of fifth decades; its appearance is equal in both sexes. Another widespread systemic disease is associated with rheumatoid episcleritis and rheumatoid scleritis, specifically respiratory and cardiovascular disease. The symptomology of episcleritis and scleritis was redness and pain. It is ultimately that ocular finding is more prominent in scleritis. It is more noted in non-rheumatoid inflammation. The interpalpebral area is affected by the episcleritis inflammation process. The four quadrants of the sclera are affected relatively by inflammation of the anterior sclera. It has been shown that episcleritis and scleritis associated with RA rheumatoid arthritis are more commonly associated with complications such as keratitis, anterior uveitis, and glaucoma disease than in case without rheumatoid arthritis.

Conclusion

Episcleritis is a usually benign and less severe disease that can be nodular, sectoral, or diffuse. Although scleritis and episcleritis are associated with rheumatic disease, most cases, such as nodular episcleritis, show no known underlying connective tissue disease.^{43,44} However, the association of scleritis with associated systemic connective tissue disorders/ vasculitis diseases is found in approximately half of affected patients. Nodular episcleritis is usually a self-remitting disease of the sclera that takes an average 10-15 days to resolve. Moreover, for certain patients, the symptom of discomfort must be managed with proper treatment. The treatment regime responds well with NSAIDs and corticosteroids, which ameliorate the clinical signs.⁴⁵ In most cases, eye care physicians should be able to manage their nodular episcleritis patients with effective measures for this typically benign disease with a very low incidence of complications.^{46–48}

Acknowledgments

None.

Conflicts of interest

The author declares that there are no conflicts of interest.

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