

Scleromalacia perforans in young patient: a unique case



Annisa Karima¹, Delfitri Lutfi^{1*}, Awalia², Ismi Zuhria¹

ABSTRACT

Background: *Scleromalacia perforans* is a systemic autoimmune disease such as rheumatoid arthritis, lupus, and Wegener's granulomatosis that may compromise vision and globe integrity. The great challenge to treat disease is determined by the genetic examination. This case report aims to describe a unique case of *Scleromalacia perforans* in young patient.

Case description: A 19-year-old female with a progressed protrusion of the left eye since she was 1 year old. Six years ago, she had redness, worsen protrusion, photophobia, tearing, and pain, but resolved without treatment. Her cousin had the same condition but refused to continue the examination. Visual acuity of the left eye was no light perception with 4x4 mm of corneal leukoma, and 360 degrees of anterior scleral ectasia covered with conjunctival neovascularization. USG showed posterior vitreous detachment and 28,9 mm axial length. ANA test and HLA B27 were normal, positive hypermobility joint, and Rheumatologists ruled out the possibility of autoimmune disease. Myoconjunctival enucleation was performed with a dermis fatty graft for cosmetics, and histopathological examination showed nonspecific chronic inflammation.

Conclusion: *Scleromalacia perforans* is a rare case that is strongly believed to have an association with systemic autoimmune disease. Collaboration between ophthalmologists, rheumatologists, and geneticists is essential to manage this case.

Keywords: *Scleromalacia perforans*, young patient.

Cite This Article: Karima, A., Lutfi, D., Awalia, Zuhria, I. 2023. *Scleromalacia perforans* in young patient: a unique case. *Bali Medical Journal* 12(2): 1821-1826. DOI: 10.15562/bmj.v12i2.4560

¹Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo Hospital, Surabaya, Indonesia

²Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga Dr. Soetomo Hospital Surabaya, Indonesia

*Corresponding to:

Delfitri Lutfi; Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo Hospital, Surabaya, Indonesia;
delfitri-l@fk.unair.ac.id

Received: 2023-03-28

Accepted: 2023-05-16

Published: 2023-06-12

INTRODUCTION

Scleromalacia performance is a rare eye case that has a dark blue appearance behind the thinning sclera without pain and redness.¹ The Watson and Heyreh classification divides scleritis into anterior and posterior scleritis. Anterior scleritis is divided into diffuse, nodular, necrotizing with inflammation (necrotizing), and without inflammation (scleromalacia perforans).²⁻⁴ Other literatures classify into infectious and non-infectious scleritis. Non-infectious scleritis is divided into necrotizing (scleromalacia perforans) and non-necrotizing.⁵

The prevalence of scleritis is 6 of 100,000 cases where women experience about 55-75% more than men. The mean age ranged from 45.9 to 53 years.¹ It's reported as 3.4 of 100,000 person-years with an annual prevalence ratio of 5.2 of 100,000 persons.³ Bilateral scleritis is 31-50% of cases, often starting in one eye. Scleritis is usually life-threatening and associated with systemic disease in 36-57% of cases, especially autoimmune diseases (30-40%) such as rheumatoid

arthritis, systemic lupus erythematosus (SLE), antineutrophil cytoplasmic antibodies (ANCA) associated vasculitis, inflammatory bowel disease, or relapsing polychondritis, periarteritis nodosa, Wegener's granulomatosis, Behçet disease, limited scleroderma, Crohn's disease, graft-versus-host disease, and herpes zoster infection.^{1,6}

The prevalence of non-infectious scleritis depends on several factors such as race, geographical location, and gender.³ While necrotizing scleritis is the most severe and destructive type of scleritis that causes vision loss. Mostly in women and older people. Necrotizing scleritis is also associated with many systemic diseases (50-60%) some of which are life-threatening systemic vasculitic diseases.⁶ Prevalence of scleromalacia perforans is 4% of scleritis.⁷ Thus, 11 years of research showed that among all scleritis, only 3% was scleromalacia perforans.⁸ Scleromalacia was reported to occur in adolescents, more in women with a history of rheumatoid arthritis. Childhood-onset or congenital type of scleromalacia perforans is not yet reported, therefore this

case report aims to describe *Scleromalacia perforans* case in young patient.

CASE REPORT

A 19 years old female with protrusion of the left eye that has slowly grown since she was 1 year old. She had blurred vision in her protruded eye since she was a child but she didn't go to an ophthalmologist. He had a small white lump the size of rice in his left eye that was present from birth and slowly grew.

She experienced redness of her left eye, worsening left eye protrusion, photophobia, tearing and pain since she was 13 years old, and then her symptoms subsided without treatment. There was no history of discharge in the protruded eye. His cousin has a similar disease in his right eye. Previous or systemic disease was denied. She had no skin rash, or joint pain or discomfort. Antenatal history, and developmental status were normal.

The general state examination was good. The visual acuity of the protruded eye was no light perception, whereas the visual acuity of the fellow eye was 5/5.

Intraocular pressure (IOP) of protruded eye was not evaluated, and the IOP of fellow eye 14 mmHg. The anterior segment of protruded eye was no edema of the eyelid, corneal leukoma at 3 o'clock paracentral 4x4 mm in diameter with irregular edge, limbus is visible at medial and lateral quadrant, whereas superior and inferior quadrant was more difficult to identified. Scleral ectasia at 360 degrees of anterior sclera covered with slight prominent vascular conjunctiva. Anterior chamber, pupil, iris and the lens were difficult to be evaluated, whereas the fellow eye's anterior segment was normal (clear cornea, deep chamber of anterior, round pupil, raider iris and clear lens (**Figure 1**). Fundusoscopic examination of the protruded eye was negative fundal reflect, whereas the other was normal.

The ocular motility of the right eye was good in all directions without pain, whereas the other was a -2 limitation in all directions without pain. (**Figure 2**). USG examination of the protruded eye showed an echogenic lesion with membrane and particulate form, 30% complex RCS suggesting posterior vitreous detachment, axial length 28.90 mm (**Figure 3**). Optical Coherence Tomography (OCT) and Humphrey Field Analysis (HFA) of fellow eyes were normal. The ANA test result was normal (11,3 AU/mL), and HLA B27 was negative. The rheumatologist did not suggest any autoimmune disease.

Myoconjunctival enucleation technique was performed with a dermis fatty graft for cosmetics. The result of histopathology is an infiltration of lymphocytic inflammatory cells along the uveal layer (**Figure 4**). Optic nerve without any abnormalities, no signs of malignancy.

Postoperative therapy was ceftriaxone intravenous 1 gram every 12 hours intravenous, metamizole intravenous every 8 hours, metoclopramide intravenous every 12 hours, and pressure bandage until two days after surgery. After surgery there was minimal pain, no bleeding, mild oedema and hematoma of the left eyelid, and no bleeding or pus of temporary tarsorrhaphy (**Figure 5**). Wound care with levofloxacin eye drop on the left eye, chloramphenicol eye ointment on the temporary tarsorrhaphy, and donor site wound every day. Ciprofloxacin 500 mg every 8 hours orally, paracetamol 500 mg every 8 hours orally

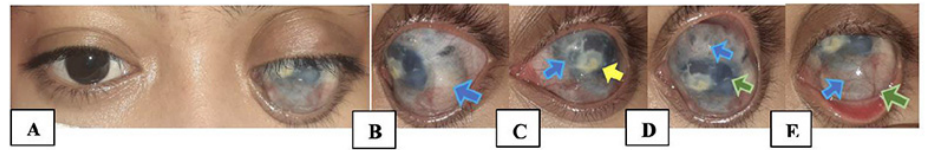


Figure 1. (A) Anterior segment examination of the patient with the normal right eye, protruded left eye; (B) The protruded eye with maximal right gaze; (C) The protruded eye with maximal left gaze; (D) The protruded eye with maximal down gaze; (E) The protruded eye with maximal up gaze. Blue arrow showed scleral ectasia, green arrow showed the cornea, and yellow arrow showed the corneal leukoma

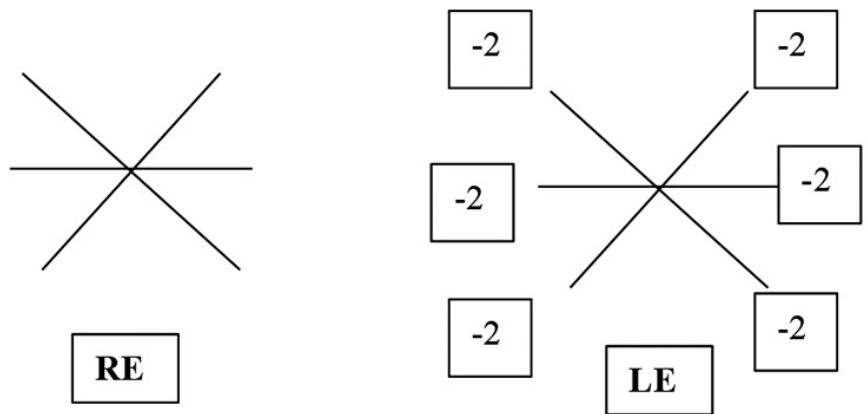


Figure 2. The ocular motility of eye (RE =right eye; LE = left eye)

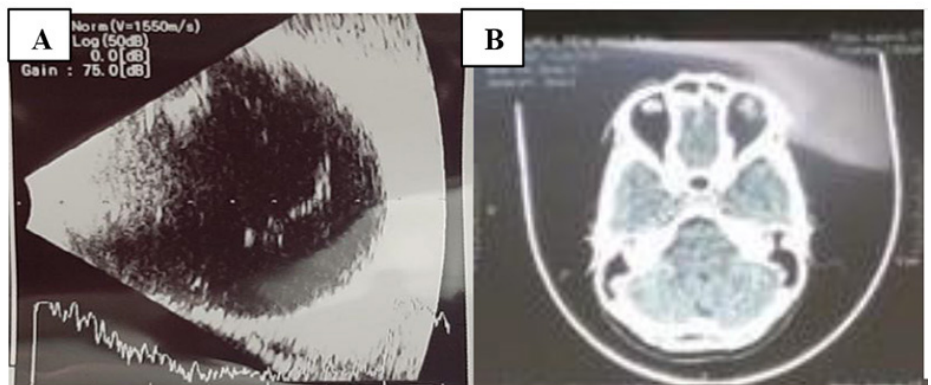


Figure 3. USG and Head CT Angiography (A) The posterior vitreous detachment was found USG of the protruded eye (AXL: 28.90 mm); (B) CT Angiography with normal vascularisation.

every 8 hours orally, paracetamol 500 mg every 8 hours orally to minimize the pain. Sixth week post-surgery showed oedema and hematoma are minimal, and the conformer was fitted with pseudoptosis.

Wound care with levofloxacin eye drop on the left eye, chloramphenicol eye ointment on the temporary tarsorrhaphy, and donor site wound every day. Ciprofloxacin 500 mg every 8 hours orally, paracetamol 500 mg every 8 hours orally

to minimize the pain. Sixth week post-surgery showed oedema and hematoma are minimal, and the conformer was fitted with pseudoptosis.

Seventeen months after surgery, conjunctiva was healthy without redness and pus, as well as deep fornix. The pseudoptosis on the left eye happened because the conformer was smaller at first and it is lessened after prosthesis implantation, but motility of prosthesis ocular was none (**Figure 6**).

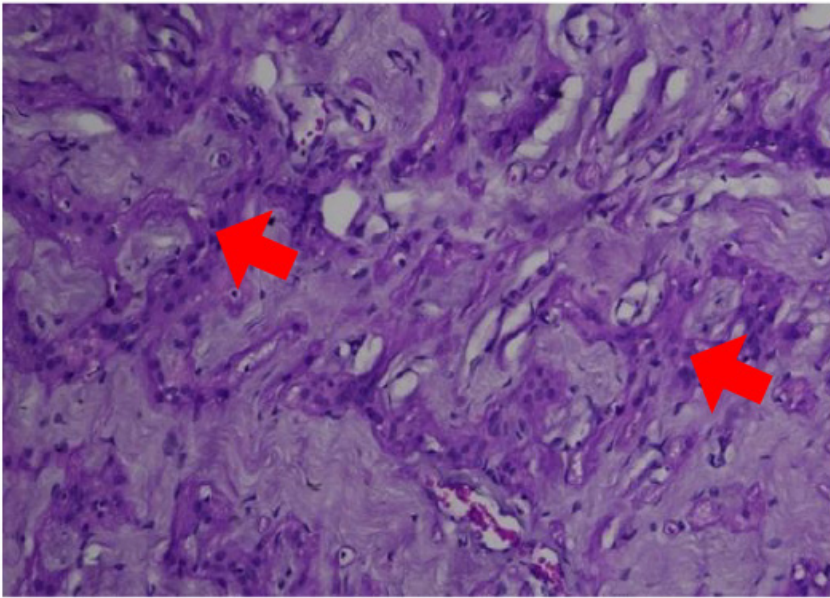


Figure 4. Histopathology examination of the protruded eye. Infiltration of lymphocytic inflammatory cells along the uveal layer (non-specific chronic inflammation of the uvea) (red arrow)

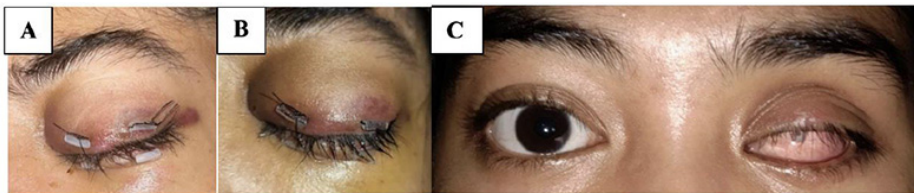


Figure 5. Anterior segment (A) 1st-day post-surgery, (B) 1st-week post-surgery, (C) 6th-week post-surgery



Figure 6. Ocular motility with ocular prosthesis at 17 months after surgery.

DISCUSSION

Patient with a unilateral protruded eye that appeared since she was child and getting bigger. There were no signs of inflammation at the time of examination/ Clinically at the time of examination could suggest it as scleromalacia perforans as its

dark blue/brown hue through a thin sclera at the anterior of eyeballs. The appearance of most case of scleromalacia that reported before were similar to our case.^{3,5}

Scleromalacia perforans or necrotizing scleritis “without inflammation” of anterior scleritis is often encountered without obvious signs of inflammation,

and is obtained by a dark blue/brown color through the thin sclera at the front of the eyeball. Scleromalacia perforans or “non-inflammatory” necrotizing scleritis in anterior scleritis is characterized by clinically minimal signs of scleral inflammation (redness, edema, pain).^{2,9} In some cases, it is difficult to know the onset of the disease with certainty because of the slow disease progression and minimal complaints. Changes in the colour of the sclera are usually noticed by the family or when the patient looks in the mirror or by the doctor who examines the patient.⁷

The abnormality development is characterized by necrosis without signs of inflammation, perforation of the uvea that is still retained by the connective tissue and conjunctiva, and usually does not perforate spontaneously. A bulging staphyloma will develop if the intraocular pressure is increased; however, spontaneous perforation is rare.⁹ The aetiology of scleromalacia perforans can be due to idiopathic, local or systemic associations.

Some authors consider scleritis associated with systemic autoimmune disease to be mediated by immune complexes, whereas scleritis unrelated to systemic disease may be due to local delayed-type hypersensitivity reactions. posterior scleritis (19%-45%). A study of 358 cases over 11 years showed that 57% of scleritis cases were associated with systemic disease, and 67% were scleromalacia perforans. The most common systemic disease associated with scleromalacia perforans was connective tissue disease or vasculitis (48%), mostly rheumatoid arthritis (RA), followed by Wegener’s granulomatosis, relapsing polychondritis, arthritis and inflammatory bowel disease, and systemic lupus erythematosus; other diseases include Reiter’s syndrome, psoriatic arthritis, polyarteritis nodosa, ankylosing spondylitis, Behcet’s disease, giant cell arteritis, and Cogan’s syndrome.¹⁰

Scleromalacia perforans usually occurs in patients with long-standing RA.⁹ As many as 50% of RA cases are genetic, and 30 % of these were abnormalities at the HLA-DR locus.¹¹ In addition to other alleles or subtypes, RA, systemic lupus erythematosus (SLE), and cytoplasmic antinuclear antibody-associated vasculitis

Table 1. Genetic syndromes reported with the blue sclera¹⁴⁻¹⁶

Syndrome	MOI	Chromosome	Gene	Protein
Ehrlers-Danlos type 1	AD	9q34.3	COL5A1	Collagen alpha-1 (IV) chain
Marfan	AD	15q21.1	FBN1	Fibrilin-1
Osteogenesis imperfecta type 1	AD	17q21.33	COL1A1	Collagen alpha-1 (I) chain
Brittle cornea type 1	AR	16q24.2	ZNF469	zinc finger protein 469
Brittle cornea type 2	AR	4q27	PRDM5	PR domain zinc finger protein 5
Incontinentia pigmentii	XLD	Xq28	IKBKG	NF-kappa-B essential modulator

AD: autosomal dominant; AR: autosomal recessive; XLD: X-linked dominant

(ANCA), were also found to be HLA-DR15 associated. A retrospective analysis of 5 patients with posterior scleritis found an association with HLA-B27.⁸ Other literature states that scleritis occurs in 0.15-6.3% of rheumatoid arthritis patients, whereas scleromalacia perforans occurs in advanced rheumatoid vasculitic patients.¹⁰ The patient in this case did not have systemic signs indicating autoimmune disease, even the suspicion of systemic vasculitis was also not confirmed by CT angiography of the normal head but calcification of the eye was found, which was also on ultrasound examination. The results of the ANA and HLA B27 tests were negative.

This patient had symptoms when he was 1 year old, so he can be considered a congenital or childhood-onset type of disease. Rheumatoid arthritis in childhood called juvenile idiopathic arthritis (JIA) may be the differential diagnosis. Based on the theory, JIA is a chronic rheumatoid disease with unknown aetiology in childhood and has several subtypes. Each subtype has characteristics such as arthritis, fever, rash, uveitis, positive ANA test and HLA-B27.^{11,12} Oligoarticular JIA has the strongest association with anterior nongranulomatous uveitis (iridocyclitis), which is often insidious and usually asymptomatic, although half of children may have some symptoms associated with uveitis (pain, flushing, headache, photophobia, and changes in vision).¹²

The patient in this case also experienced complaints of pain, redness, headache, and photophobia at 13 years old but was

not followed up with a more in-depth examination. ANA and HLA-B27 tests are normal. Scleral ectasia or blue sclera or thinning of the sclera as experienced by this patient, is also found in patients with connective tissue disorders who also have gene mutations. Most disorders that have blue sclera manifestations are Osteogenesis imperfecta, Brittle Cornea Syndrome, Ehrlers-Danlos syndrome (EDS), Marfan syndrome, blue sclera syndrome, and incontinentia pigmenti.¹³⁻¹⁶

Osteogenesis imperfecta is the most commonly inherited systemic connective tissue disease (gene mutation) with the most significant manifestation presenting in the bone (multiple fractures, thin bones).¹⁷ Brittle Cornea Syndrome is an autosomal recessive disorder (gene mutation) that is characterized by corneal thinning and blue sclera.¹⁸ Marfan syndrome is the second most common inherited connective tissue disorder. Common systemic manifestations are tall stature, scoliosis, hypermobility joints, and arachnodactyly, while ocular manifestations are high myopia, ectopia lentis, and scleral thinning.^{16,19} Blue sclera syndrome or Van der Heave is a congenital disease of connective tissues and myopia with astigmatism.^{20,21} Incontinentia pigmenti or Bloch-Sulzberger syndrome is a genodermatosis that is lethal prenatally in males, with rare exceptions. In affected females, it causes highly variable abnormalities of the skin, hair, nails, teeth, eyes (blue sclerae is less common), and central nervous system.¹⁴ Based on Brighton's criteria of EDS divided by

major and minor criteria, eye abnormality is a minor criterion.¹² A retrospective study of 21 patients with EDS in France in 2019 shows that 19 patients (90%) presented ophthalmic signs, such as ocular motility disorder, convergence insufficiency, blue sclera as much as 38%, and dry eye. Chromosome and gene mutation of those diseases showed in **Table 1.**¹⁴⁻¹⁶

General and specific examination related to Ehlers-Danlos syndrome and juvenile idiopathic arthritis was not found in this patient. The result shows hypermobility that might be a sign of Ehrlers Danlos syndrome; an increment of nonspecific transaminase was planned to examine the viral marker. Joint hypermobility is a condition when joints can move beyond the normal range of motion. The joints are very flexible. The most commonly affected joints are the elbows, wrists, fingers, and knees. In most patients, hypermobility doesn't cause any pain or medical issues. However, for some people, hypermobility causes joint pain, joint and ligament injuries, tiredness (fatigue), and bowel issues. It might be associated with another disease such as Ehlers-Danlos syndrome and Marfan syndrome.^{12,13,16} The result of abdominal USG, Gamma GT, direct and indirect bilirubin, and ALP was normal.

Some aetiology that cause scleritis are ocular infections and malignancy that may "masquerade" and present as endogenous inflammatory scleritis. Infectious scleritis is rare (4%–18% cases), and can be caused by viruses, including herpes simplex and zoster, fungi, and bacteria. It can develop contiguous to an area of infectious keratitis.²² Other data also show infectious diseases were not as much as vasculitis disease (7%), and the rest was miscellaneous diseases (4% such as rosacea, atopy, gout, and a foreign body).^{10,22}

Association with tuberculosis is also considered since Indonesia is a tuberculosis (TB) endemic area, similar to India. Presumed ocular TB was the common infectious cause of scleritis. Tsui reported scleromalacia perforans as the second most common complication (15.8%) of ocular TB.²³ Several other ocular associations have been reported, such as

ocular pyoderma pigments, neovascular glaucoma, and retinitis pigmentosa.^{22,24}

The relation of scleromalacia perforans to congenital disease was rarely reported. There is one case reported in 2013 about an anterior staphyloma secondary to scleromalacia in a patient with primary congenital glaucoma (PCG).^{25,26} There was no sign of PCG on the fellow eye, as we know PCG is usually bilateral and also had a gene mutation of CYP1B1. Moreover, another cause is surgically induced necrotizing scleritis (SINS), yet, in this case, was clearly excluded because there was no previous surgery or trauma.^{25,27} A reports of two close relatives (female) that had similar blue eyes, the older sister was solitaire without systemic disease, the younger one with chronic rheumatoid arthritis.²⁶

Histologically, scleritis is characterized by an inflammatory response of predominantly lymphocytes and plasma cells with fewer polymorphs. Necrotizing scleritis associated with rheumatoid arthritis (RA) has a zonal granulomatous inflammation with areas of tissue necrosis, meanwhile, patients with idiopathic scleritis have predominant macrophages, T and B cells, and the absence of scleral necrosis as its chronic inflammatory response fielded.²⁶ As for scleromalacia perforans or also known as necrotizing scleritis without (overt) inflammation found inflammatory cells infiltrating the sclera. The presence of a necrotizing granulomatous response leads to a gradual progression of destruction of scleral tissue. Young and Watson suggest three determinants of scleral destruction: activation of scleral fibrocytes and resorption of the pericellular matrix, infiltration of scleral stroma by inflammatory cells, and prolonged local vas occlusion.^{2,5} As for this case, the histopathology test found lymphocytes and conclude a chronic inflammation. Grocott's methenamine silver (GMS), which is the site, rules out the differential diagnosis. We might have difficulties to know the cause because the patient might have had inflammation when she was 13 years old and now as we examined the rest of the tissue remained.

Therapy that can be given is related to systemic disease, medications such

as immunosuppressants, or NSAIDs.^{1,7,4} Surgical therapy for perforated scleromalacia is performed when medical therapy is lacking. The goal is to improve the structure of the eyeball and have no effect on visual acuity. Surgical therapies that can be selected include *tectonic patch grafting* can be performed with the sclera (fresh or frozen globe or glycerine preserved scleral tissue), dermis, fascia lata, periosteum, aortic tissue, cartilage cornea, pedicle-flaps of the conjunctiva with Müller's muscle or tarsus, synthetic material, and amniotic membrane.²⁷ This case had no light perception visual acuity but the protruded was disturbing the patient's daily life. The lesion was large; including the cornea and anterior, also scleral thinning might prolapse because of small trauma. Enucleation with the myoconjunctival technique has been done.

Myoconjunctival enucleation which took the entire eyeball and the anterior part of the optic nerve indicates wide exposure of the anterior uvea and less sclera remaining has been done.²⁸ The technique tied the muscle to the conjunctival and the orbital implant. This technique was used recently as an alternative to the muscle imbrication technique, it also has better ocular motility.²⁹

For cosmetic purposes and better eye movement, orbital implants may be considered. Considerations in the selection of orbital implants are the size and material of the orbital implant to achieve the best post-enucleation cosmetic results.²⁷ Orbital implant materials such as orbital implants of porous, non-porous, or dermis fat grafts have their advantages and disadvantages. Porous orbital implants have high bio integrity so that eye movements can be better, but they have a disadvantage, such as a higher incidence of implant exposure. Non-porous orbital implants are cheaper than porous orbital implants but eye movement is not as good as porous but the lesser incidence of implant exposure.^{27,28} Surgery outcome and ocular motility were good after surgery.

CONCLUSION

Scleromalacia perforans is rare, yet it is strongly believed to be associated with systemic disease. The autoimmune

disease was ruled out based on systemic examination. The systemic, ancillary and genetic examination is needed to establish the cause or association of scleromalacia perforans on this patient. Collaboration between ophthalmologists and rheumatologists is essential to manage this kind of case.

CONFLICT OF INTEREST

The authors affirmed that there were no conflicts of interest in this study.

FUNDING

The authors were responsible for all research funding without obtaining financial support.

ETHICAL STATEMENT

Authors have secured informed consent from the patient regarding this case report.

AUTHOR CONTRIBUTION

All authors contributed equally in this research and publication of this manuscript.

REFERENCES

1. Murthy SI, Sabhapandit S, Balamurugan S, et al. Scleritis: Differentiating infectious from non-infectious entities. *Indian J Ophthalmol.* 2020;68(9):1818-1828.
2. Lane J, Nyugen E, Morrison J, Lim L, Stawell R, Hodgson L, et al. Clinical features of scleritis across the Asia-Pacific Region. *Ocul Immunol Inflamm.* 2019;27(6):920-6.
3. Ghauri MI, Riaz SU, Husain A, Jafri AR, Bashir ZTA. Scleromalacia perforans: a case report. *J Med Case Rep.* 2018;12(1):155.
4. Siska, Memed FK, Musa IR. Factors influence bullous keratopathy post cataract surgery at National Eye Center of Cicendo Eye Hospital (PMN RSMC), West Java, Indonesia. *Bali Medical Journal.* 2020;9(3):840-843.
5. Al Nawaiseh I, Nazzal RM, Nowomiejska K, Toro M, Rejda R. Scleromalacia perforans as the presenting sign for rheumatoid arthritis — a case report. *Ophthalmol J.* 2019;4(0):56-9.
6. Reddy SC, Tajunisah I, Rohana T. Bilateral scleromalacia perforans and peripheral corneal thinning in Wegener's granulomatosis. *Int J Ophthalmol.* 2011;4(4):439-442.
7. Idrus EA, Mustaram AA, Fajriansyah A, Muslima P. Bilateral keratoconus hydrops in a patient with Down Syndrome: a case report. *Bali Medical Journal.* 2023;12(1):857-860.
8. Weisenthal RW, Daly MK, Freitas D de, Feder RS, Orlin SE, Tu EY, et al. Structural and exogenous conditions associated with ocular

- surface disorders. *Am Acad Ophthalmology Sect 8 Extern Dis Cornea*. 2020;83–4.
9. Finger PT, Reddy HS, Maheshwari A. Tarsoconjunctival flap for scleromalacia related to treatments for conjunctival melanoma. *Am J Ophthalmol Case Rep*. 2023;29:101805.
 10. Dutta Majumder P, Agrawal R, McCluskey P, Biswas J. Current Approach for the Diagnosis and Management of Noninfective Scleritis. *Asia-Pacific J Ophthalmol* 2020;10(2):212–23.
 11. Barut K, Adrovic A, Şahin S, Kasapçopur Ö. Juvenile idiopathic arthritis. *Balkan Med J*. 2017;34(2):90–101.
 12. Whitlow S, Idrees Z. RD repair using 360-degree scleral graft for extensive scleral ectasia in a patient with Ehlers Danlos syndrome. *Am J Ophthalmol*. 2020;17:100554.
 13. Islam M, Chang C, Gershwin ME. Ehlers-Danlos Syndrome: Immunologic contrasts and connective tissue comparisons. *J Transl Autoimmun*. 2021;4:100077.
 14. Manoj M, Dhakad U. Leprosy mimicking rheumatoid vasculitis with scleromalacia perforans. *BMJ Case Rep*. 2020;13(7):e236796.
 15. Perez-Roustit S, Nguyen DT, Xerri O, Robert MP, De Vergnes N, Mincheva Z, et al. Ocular manifestations in Ehlers–Danlos Syndromes: clinical study of 21 patients. *J Fr Ophthalmol*. 2019;42(7):722–9.
 16. Battle R. Edgar Allan Poe: a case description of the Marfan syndrome in an obscure short story. *The American Journal Of Cardiology*. J2011;108(1):148–149.
 17. Gustianty E, Yandi N, Rifada RM, Prahasta A. Successful rate of glaucoma surgery in uveitis glaucoma. *Bali Medical Journal*. 2022;11(2): 614–618.
 18. Purolo PKM, Nättinen JE, Ojamo MUI, et al. Prevalence and 11-year incidence of common eye diseases and their relation to health-related quality of life, mental health, and visual impairment. *Qual Life Res*. 2021;30(8):2311–2327.
 19. Sutradhar I, Gayen P, Hasan M, Gupta RD, Roy T, Sarker M. Eye diseases: the neglected health condition among urban slum population of Dhaka, Bangladesh. *BMC Ophthalmol*. 2019;19(1):38.
 20. Alikadić-Husović A, Merhemić Z. Sindrom plavih sklera (Van der Heave sy) [The blue sclera syndrome (Van der Heave syndrome)]. *Med Arh*. 2000;54(5-6):325–6.
 21. Brooks JK. A review of syndromes associated with blue sclera, with inclusion of malformations of the head and neck. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2018;126(3):252–63.
 22. Sims J. Scleritis: Presentations, disease associations and management. *Postgrad Med J*. 2012;88(1046):713–8.
 23. Tsui J, Ho M, Lui G, Li T, Chen L, Iu L, et al. The clinical presentation and treatment outcomes of ocular tuberculosis: a 5-year experience in an endemic area. *Int Ophthalmol*. 2021;41(9):3199–209.
 24. Altıntaş AGK, İlhan Ç, Çıtırık M. Unusual association of inverse retinitis pigmentosa, scleromalacia, and neovascular glaucoma. *Turkish J Ophthalmol*. 2020;50(2):110–4.
 25. Wedari NLPH, Budayanti NNS, Sukrama IDM, Mayura IPB. Implementation of antinuclear antibodies in autoimmune diagnostic tests: a literature review from immunological aspects. *Journal of Clinical Microbiology and Infectious Diseases*. 2022;2(2):27–30.
 26. Yangzes S, Sharma VK, Singh SR, Ram J. Scleromalacia perforans in rheumatoid arthritis. *Qjm*. 2019;112(6):459–60.
 27. Bhardwaj A, Yadav A, Yadav M, Tanwar M. Genetic dissection of non-syndromic retinitis pigmentosa. *Indian J Ophthalmol*. 2022;70(7):2355–2385.
 28. Ali MU, Rahman MSU, Cao J, Yuan PX. Genetic characterization and disease mechanism of retinitis pigmentosa; current scenario. *3 Biotech*. 2017;7(4):251.
 29. Ruff A, Tezel A, Tezel TH. Anatomical and functional correlates of cystic macular edema in retinitis pigmentosa. *PLoS One*. 2022;17(10):e0276629.



This work is licensed under a Creative Commons Attribution