World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:18, No:11, 2024

Necrotising Anterior Scleritis and Scleroderma: A Rare Association

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***Abstract*—**Necrotising scleritis is a severe form of scleritis and poses a significant threat to vision. It can manifest in various systemic autoimmune disorders, systemic vasculitis, or as a consequence of microbial infections. The objective of this study is to present a case of necrotizing scleritis associated with scleroderma, which was further complicated by a secondary *Staphylococcus epidermidis* infection. This is a retrospective analysis, which examines the medical records of a patient who was hospitalised in the Eye Unit at University Hospital Southampton. A 78-year-old woman presented at the eye casualty department of our unit with a two-week history of progressively worsening pain in her left eye. She received a diagnosis of necrotising scleritis and was admitted to the hospital for further treatment. It was decided to commence a three-day course of intravenous methylprednisolone followed by a tapering regimen of oral steroids. Additionally, a conjunctival swab was taken, and two days later, it revealed the presence of *S. epidermidis*, indicating a potential secondary infection. Given this finding, she was also prescribed topical (Ofloxacin 0.3% - four times daily) and oral (Ciprofloxacin 750 mg – twice daily) antibiotics. The inflammation and symptoms gradually improved, leading to the patient being scheduled for a scleral graft and applying an amniotic membrane to cover the area of scleral thinning. Rheumatoid arthritis and granulomatosis with polyangiitis are the most commonly identifiable systemic diseases associated with necrotising scleritis. Although association with scleroderma is extremely rare, early identification and treatment are necessary to prevent scleritis-related complications.

***Keywords*—**Scleritis, necrotizing scleritis, scleroderma, autoimmune disease.

I. Introduction

SCLERITIS is a serious inflammatory condition characterised by infiltrating inflammatory cells in the scleral layer, leading to significant swelling and acute congestion of blood vessels [1]. Consequently, the underlying choroid can be exposed, and the surrounding scleral tissue thins.

Scleritis can be classified into anterior and posterior forms, with the former being more prevalent. The anterior form can be further subdivided into four types: diffuse anterior, nodular anterior, necrotising anterior with inflammation, and necrotising anterior without inflammation, also known as scleromalacia perforans [1]. Among these, necrotising scleritis (NS) represents the most severe and destructive type of anterior scleritis [1]. If left untreated, the condition typically progresses rapidly within 2 to 4 weeks, leading to complications such as keratitis, uveitis, glaucoma, cataract, macular oedema, and perforation, resulting in vision loss. It is often linked with systemic vasculitis, especially in patients with long-standing rheumatoid arthritis. In rare instances, it may also be associated with granulomatosis with polyangiitis (GPA) and relapsing polychondritis.

This study aims to document scleroderma-associated NS complicated by a secondary Staphylococcus epidermidis infection.

II. Case Description

A 78-year-old woman presented to the eye casualty at Southampton with a two-week history of progressively worsening pain in her left eye.

Her medical history included scleroderma (morphoea), previously treated with ciclosporin; Barrett's esophagitis; and chronic obstructive pulmonary disease (COPD). Her ophthalmic history involved well-controlled glaucoma managed with dorzolamide/timolol and tafluprost in both eyes, with bilateral pseudophakia following uncomplicated cataract surgeries. She had also experienced previous episodes of episcleritis and scleritis in her left eye. Her Antineutrophil Cytoplasmic Antibody (ANCA) tests have always been negative.

At the time of presentation, her best-corrected visual acuity (BCVA) was 6/4 in the right eye and 6/9 in the left. Intraocular pressure (IOP) was 12 mmHg on the right and 14 mmHg on the left. Upon examination, the left eye displayed a lesion suggesting necrotizing scleritis with signs of impending perforation [Fig. 1]. The patient reported severe pain in the left eye, accompanied by significant emotional distress. Due to the severity of the condition, hospital admission was deemed necessary for accurate diagnosis and comprehensive management.

Following discussions with rheumatologists, an extensive range of blood tests were conducted, including a lupus screen, rheumatoid factor, polymyositis/scleroderma antibodies (PM-SCL75 antibodies), Anti-RNA polymerase III antibodies (RNAP3 antibodies), ANCA, antinuclear antibody (ANA), complement C3, complement C4, *immunoglobulins, QuantiFeron, Borrelia burgdorferi, Treponema* pallidum, c-reactive protein (CRP), erythrocyte sedimentation rate (ESR), full blood count (FBC), as well as renal and liver function tests. The results showed positive PM-SCL75 antibodies and

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borderline RNAP3 antibodies. A conjunctival swab was taken, and after 48 hours of incubation, Staphylococcus epidermidis was identified, suggesting a potential secondary infection. Moreover, upon admission, a conjunctival biopsy of the scleral lesion was performed. Histopathological analysis revealed dystrophic calcification within collagenous tissue, with unclear aetiology [Fig. 2]. Regarding systemic imaging, head and orbital magnetic resonance imaging (MRI) were obtained, and both tests were normal.

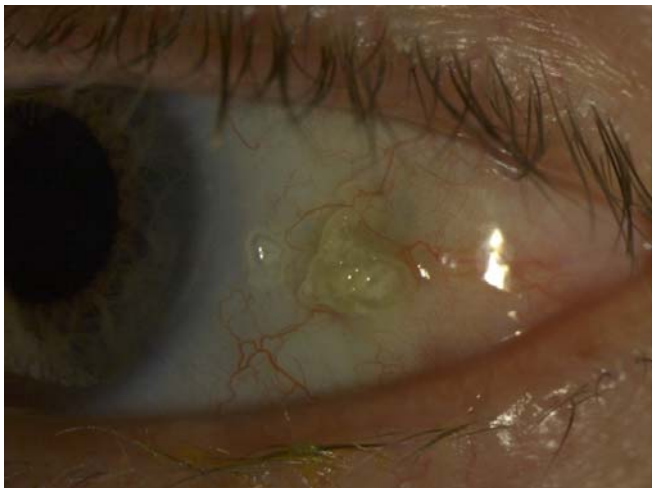

Fig. 1 (a) Scleral appearance of the left eye six months before NS onset shows prior inflammation without active pathology

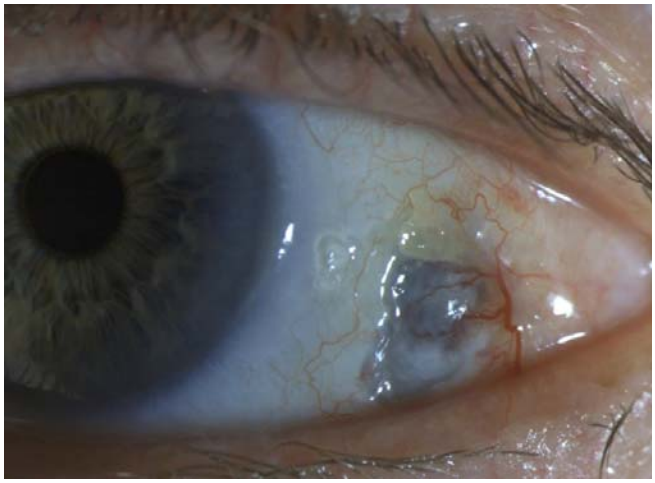

Fig. 1 (b) Necrotizing scleritis with signs of active inflammation and impeding scleral perforation (left eye)

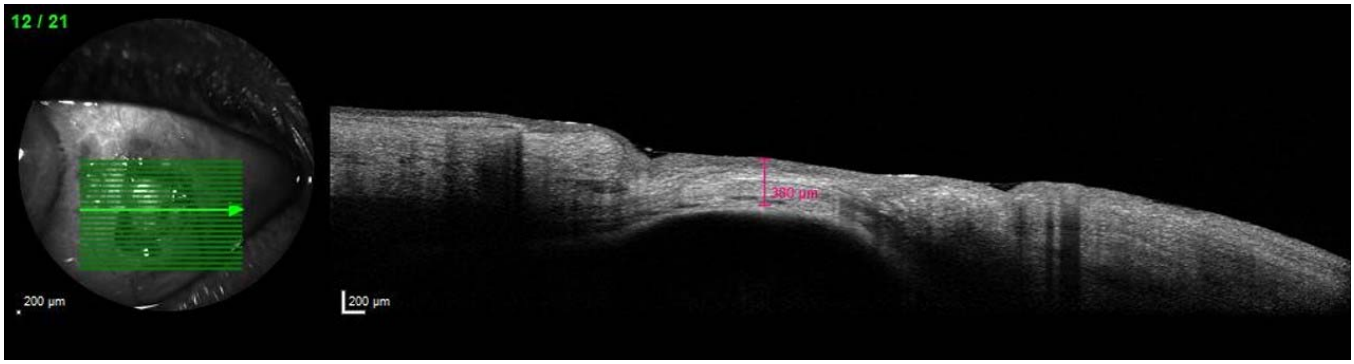

Fig. 1 (c) Anterior segment Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany) shows the scleral thinning area (left eye)

The patient was initiated on a 3-day course of intravenous methylprednisolone at 500 mg per day, followed by a tapering regimen of oral prednisolone, starting at 30 mg daily. In response to the positive conjunctival swabs, indicating a

potential secondary infection, she was also prescribed oral ciprofloxacin 750 mg twice daily and topical ofloxacin 0.3%, to be applied four times daily for two weeks.

After initiating steroids and antibiotics, the patient's symptoms began to improve. She continued her regular antiglaucoma medications throughout this period. Before her discharge, she was scheduled for a left amniotic membrane and scleral graft.

Upon discharge, she was prescribed a tapering course of systemic prednisolone and topical prednisolone 0.5% [preservative-free (PF)]. She continued the systemic prednisolone until she was reviewed in the clinic. The patient remained in the hospital for five days.

The patient was reviewed in the clinic two weeks post-discharge. BCVA was 6/5 in the right eye and 6/6 in the left eye. The pain related to the scleritis had significantly improved, and there was no evidence of active inflammatory activity. Furthermore, the scleral thinning stabilised after the resolution of inflammation [Fig. 3]. She was advised to continue with her antiglaucoma eye drops. She was kept on a maintenance dose of topical (prednisolone 0.5% PF) and oral steroids (prednisolone 5 mg) while waiting for her surgical treatment.

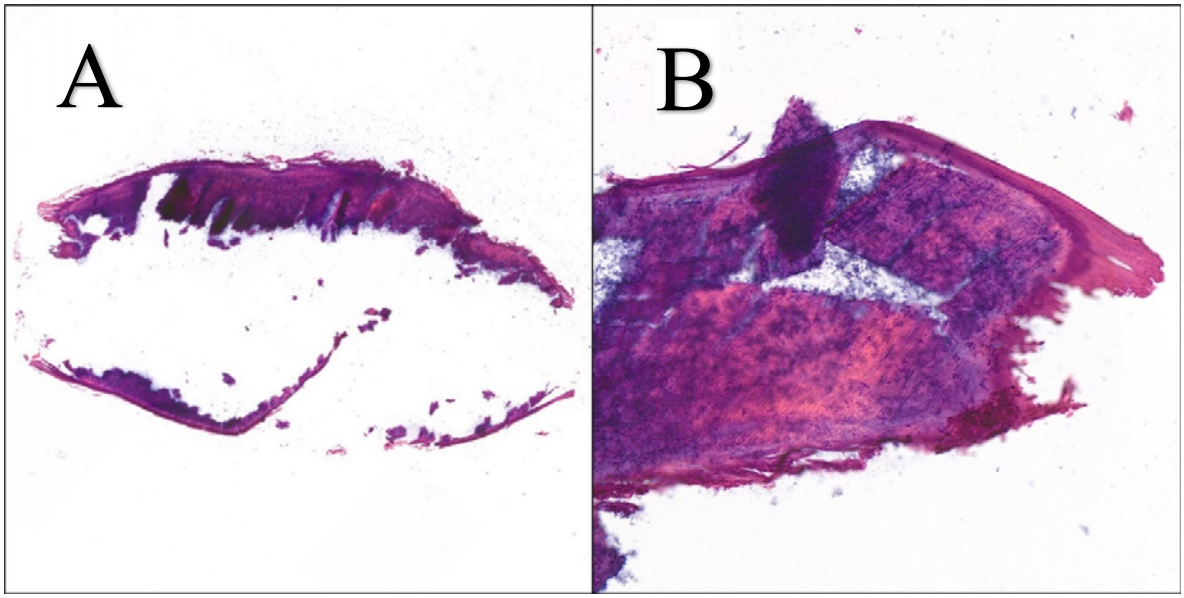

Fig. 2 Biopsy specimen showing dystrophic calcification within the dense collagenous stroma (A: H&E, 5x; B: H&E, 25x)

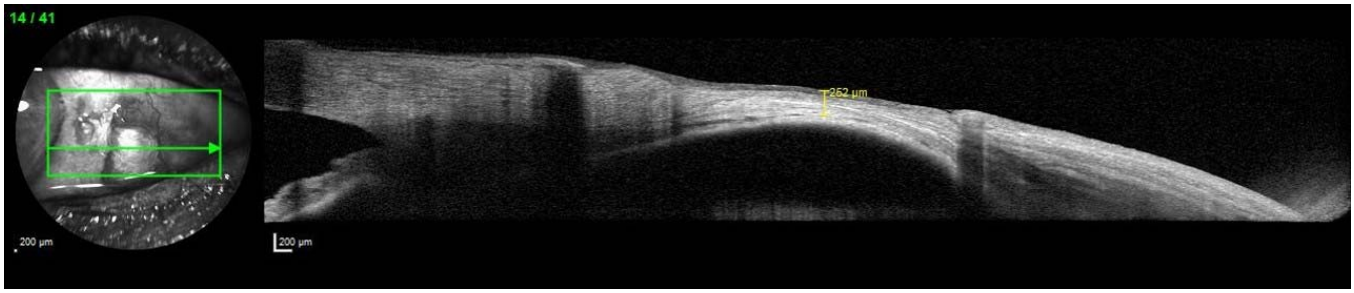

Fig. 3 Anterior segment Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany): Two weeks post-discharge, the scleral thinning appears to have stabilised following the resolution of inflammation

III. Discussion

Our case report highlights the rare association between scleroderma and NS. In the case presented, urgent intervention was crucial due to the evidence of imminent perforation. The primary aim of this treatment was to promptly address the inflammation to prevent severe complications such as vision loss. A high dose of methylprednisolone was administered, followed by oral prednisolone to reduce inflammation, and alleviate symptoms effectively. Antibiotics were prescribed to combat the secondary Staphylococcus epidermidis infection. Furthermore, the patient underwent an immediate amniotic membrane graft to the thinned sclera to reduce the risk of perforation.

The association between scleritis and scleroderma was first reported by Nizam et al. [2], who described a patient with ANA-positive scleroderma who presented with a painful right eye and associated ulceration. She was diagnosed with NS and treated with 40 mg of systemic prednisolone, along with both topical and systemic ciclosporin. However, when the steroids were tapered, she experienced relapsing symptoms, leading to the initiation of azathioprine. Due to intolerance to azathioprine, her treatment was subsequently switched to mycophenolate

mofetil, which proved to be successful.

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used as the first line of treatment for uncomplicated idiopathic diffuse or nodular scleritis, particularly when there is minimal or no inflammation [3]. Steroids are generally effective in managing scleral inflammation [3]. A study investigated the efficacy of topical steroids as a monotherapy for non-necrotizing anterior scleritis, finding that 1% of prednisolone acetate successfully resolved symptoms in only 47% of patients [4]. In more severe cases, such as NS or when NSAIDs are ineffective, oral steroids are widely used [5]. Methylprednisolone is the preferred corticosteroid for intravenous administration and has been proven effective as a monotherapy in more than half of the patients [6].

Immunomodulator therapy (IMT) is used in one in four patients with scleritis and, even more commonly, in NS to achieve and maintain disease remission [3]. Depending on the underlying systemic disease and patient-drug compatibility factors, such as blood pressure and liver function, some of the commonly used IMT drugs are cyclophosphamide, methotrexate, azathioprine, and mycophenolate mofetil [3]. Alkylating agents such as cyclophosphamide have shown high efficacy in disease control [3]. Methotrexate has proven to be successful in controlling the disease and decreasing or ceasing steroid use [7]. The use of azathioprine, in combination with steroids, is well documented [3], yet a case report has also documented the successful use of azathioprine as monotherapy [8]. Kolomeyer et al. have recognised reduction and stability in inflammation in up to 100% of the patients on mycophenolate mofetil throughout 6 to 24 months of treatment [9].

Biologic response modifiers are increasingly used in patients with NS on a background of systemic diseases who have poor response to corticosteroids and/or corticosteroid-sparing immunosuppressive drugs. A literature review of the biologic therapy in scleritis carried out by de Fidelix et al. [10] concluded that 96% of the patients on infliximab noticed ocular benefits, whilst 64% reduced or stopped the use of steroids [10]. This paper identified two patients who used adalimumab and one on certolizumab pegol with favourable outcomes [10]. Using rituximab in patients with scleritis on a background of GPA showed efficacy in all cases, with an associated reduction in immunosuppressive agents [10]. On the contrary, etanercept was associated with adverse outcomes, such as worsening symptoms of uveitis, Crohn's disease and psoriasis. The use of etanercept in systemic conditions, such as rheumatoid arthritis, was linked with the development of scleritis [10].

Relapse of scleritis following the cessation of corticosteroids is well documented [2]. Prolonged use of corticosteroids such as methylprednisolone and prednisolone can lead to systemic side effects, including immunosuppression [11]. Oral ciprofloxacin, a fluoroquinolone antibiotic, carries risks such as gastrointestinal disturbances and tendon rupture, particularly in older patients [12]. Topical ofloxacin, another fluoroquinolone, can cause localised side effects such as burning, stinging, or eye irritation and the potential development of antibiotic resistance with prolonged use.

The patient was given gastroprotection and bone protection to manage the above risks, and the GP was kept well informed. Thorough safety-net information and education regarding red-flag symptoms were communicated to the patient. Fortunately, our patient did not experience any side effects from the corticosteroids or antibiotics.

Anterior uveitis is a frequent complication in patients with scleritis, affecting up to 42% of individuals [13]. This inflammation of the uvea exacerbates overall outcomes. Approximately 1 in 5 patients with scleritis complicated by uveitis develop peripheral ulcerative keratitis, and 19% can develop glaucoma [13]. Almost half of the patients with uveitis secondary to scleritis can experience decreased vision [13].

Literature suggests that as high as 50% of the patients with scleritis have a background systemic disease [14]. Seropositive rheumatoid arthritis is the most common autoimmune condition associated with scleritis, followed by systemic vasculitides, for instance, Wegener's granulomatosis [14]. Relapsing polychondritis is seen in up to 6% of the cases, and Systemic Lupus Erythematosus in up to 4% [14]. Less commonly, seronegative spondyloarthropathies, irritable bowel syndrome and polyarteritis nodosa have been recognised in patients with scleritis [14]. Other causes of scleritis can be infection, commonly secondary to *Pseudomonas aeruginosa*, malignancy in ocular adnexal lymphoproliferative lesions, and trauma, including iatrogenic [14]. This highlights the need to treat patients with scleritis in a multidisciplinary approach involving rheumatologists. Early and prompt referring to the rheumatologists assists with the diagnostic workup and decreases the likelihood of new diagnoses of autoimmune conditions being missed.

IV. Conclusion

NS, the most severe and sight-threatening form of scleritis, can manifest in systemic autoimmune disorders, systemic vasculitis, and microbial infection. Among identifiable systemic diseases associated with NS, rheumatoid arthritis and GPA are the most observed, yet this paper highlights the rarity between scleritis and scleroderma. Infectious NS is primarily caused by *Pseudomonas* species, with surgical procedures being the predominant risk factor. Compared to other types of scleritis, NS exhibits higher rates of complications and is more susceptible to secondary glaucoma and cataract development. Differentiating between infectious and non-infectious NS can be challenging but is crucial for effective management. Non-infectious NS necessitates aggressive treatment involving a combination of immunosuppressive therapies. Infectious scleritis often proves refractory and challenging to control, requiring prolonged antimicrobial therapy, surgical debridement, drainage, and patch grafting due to deep-seated infection and the sclera's lack of blood supply.

Conflict of Interest

None to declare.

Acknowledgments

None to mention.

PATIENT ANONYMITY

Patient anonymity has been rigorously maintained throughout this study, with all identifiable data carefully concealed. No information could lead to the identification of the individual involved.

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