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Post-Streptococcal Uveitis: A Narrative Literature Review

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A B S T R A C T

Streptococcus spp. are gram-positive bacteria and common human pathogens and commensals, causing diseases of various organs in children and adults. They are etiological factors of scarlet fever, pharyngitis, tonsillitis, pneumonia, endocarditis, erysipelas, impetigo, meningitis, necrotising fasciitis, and sepsis, among others. The post-streptococcal syndrome is a presumed autoimmune condition that has been associated with rheumatism, reactive arthritis, glomerulonephritis, and erythema nodosum. This literature review aimed to describe post-streptococcal uveitis in clinical practice. The onset of the immune-mediated complications has varied from 7 to 35 days post-infection. The ocular complications present mainly in the form of blepharoconjunctivitis. There are anecdotal case reports of episcleritis. Keratitis is another possible complication. Preseptal or orbital cellulitis has also been described. Uveitis has been a much rarer finding, and it is hypothesized that the pathogenesis is immune-mediated rather than due to intraocular bacterial infection. Post-streptococcal uveitis has been described in cases of both group A and group B infections. The onset of uveitis has been from 1 week to 36 months after the infection. Post-streptococcal presents mostly as nongranulomatous, bilateral anterior uveitis with a good prognosis and affects mostly young people. Nevertheless, all anatomic types of intraocular inflammation have been observed. The common denominators between the varying clinical pictures appear to be the history of streptococcal infection, most frequently pharyngitis, an elevated anti-streptolysin O titer, and in the more recent studies-the raised anti-deoxyribonuclease antibodies. Furthermore, there has been a generally good therapeutic response to corticosteroids. Few cases have required immunomodulation with methotrexate, mycophenolate, and adalimumab.

1. Introduction

Streptococcus spp. are gram-positive bacteria and common human pathogens and commensals, causing diseases of various organs in children and adults.[1,2] Streptococci can be classified by their hemolytic properties into alpha- (group A), beta-hemolytic (group B), which cause complete hemolysis, and gamma, which are not hemolytic 1. Group A (*Streptococcus pneumoniae, Streptococcus viridans)* and B are the most important for human diseases.[1,2] Streptococci are etiological factors of scarlet fever (Figure 1), pharyngitis (Figure 2), tonsillitis, pneumonia, endocarditis, erysipelas, impetigo, meningitis, necrotising fasciitis and sepsis, among others.[1-5] The post-streptococcal syndrome is a presumed autoimmune condition that has been associated with rheumatism, a peculiar form of reactive arthritis, including sacroilitis, glomerulonephritis, and erythema nodosum.[2-6] The onset of immune-mediated complications has been described from 7 to 35 days post-infection.[6]

The ocular complications of streptococcal infections present mainly in the form of blepharoconjunctivitis, which may be the only manifestation of the disease or a sequela of adjacent sinusitis or rhinitis. There are anecdotal case reports

of episcleritis.[7] Keratitis is another possible complication. Preseptal or orbital cellulitis has also been described. Uveitis has been a much rarer finding, and it is hypothesized that the pathogenesis is immune-mediated rather than due to intraocular bacterial infection (Figure 3).[6] Molecular mimicry has been reported between group A streptococcal antigens and the retinal S antigen.[6,8] Moreover, cross-reactive antibodies and T-cells have been thought to partake.[6,9] Post-streptococcal uveitis has been described in cases of both group A and B infections. The onset of uveitis has varied from 1 week to 36 months.[6] This literature review aimed to describe post-streptococcal uveitis in clinical practice.

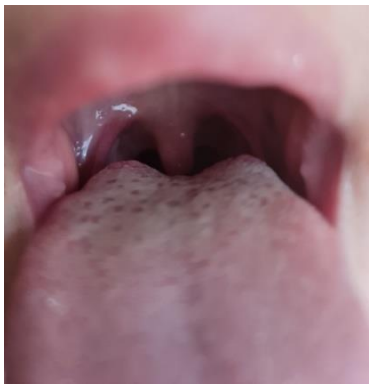

Figure 1. A child with streptococcal pharyngotonsillitis.

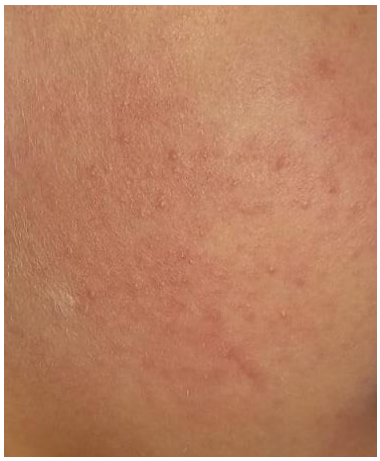

Figure 2. A child with scarlet fever.

Figure 3. A child with nongranulomatous post-infectious uveitis.

Post-streptococcal uveitis

Post-streptococcal uveitis has been described infrequently in the literature.[10-13] The first case of an associated bilateral nongranulomatous uveitis two weeks after pharyngitis was published by Cokingtin et al. in 1991.[13] Nongranulomatous uveitis is the rule, although rare cases of granulomatosis intraocular inflammation have been documented as well. Gallagher et al. have reviewed 11 patients with this condition, the majority from the existing literature at the time.[14] Most of them had a high anti-streptolysin O (ASO), which also depended on age and season. Their ages varied from 5 to 56 years. Anterior uveitis was described in 8 cases, intermediate in two patients, and panuveitis in a patient. The treatment included corticosteroids, antibiotics, and tonsillectomy in four patients.

In a case series by Rehman et al., the uveitis was bilateral and nongranulomatous in all of the affected 10 cases.[15] ASO had been elevated. Most patients were younger than 40 years. The authors have also described posterior segment involvement in the form of vitritis, focal retinitis, multifocal choroiditis, and optic disc swelling. A study by Viel et al. has documented four cases of post-streptococcal uveitis.[16] The intraocular inflammation had occurred from 2 to 10 weeks after episodes of sore throat or pyrexia. All of them had a high ASO. In all patients, the uveitis was bilateral, and in one, it had become recurrent. Two patients had anterior segment inflammation, one was intermediate uveitis, and another was posterior uveitis, with macular and optic disc edema with multifocal white dot lesions. All patients had been treated with corticosteroids without antibiotics.

Atypical cases have also been described. De Smet documented a case of papillophlebitis and uveitis following streptococcal infection.[17] Bilateral panuveitis with diffuse multifocal retinitis was observed by Ebert et al. in an immunocompromised patient.[18] Panuveitis has also been observed by Medina et al. following pharyngotonsillitis.[19] Bilateral retinal vasculitis has been noted by Reddy et al. in a 17-year-old African American female.[20] Unilateral vitritis and macular edema were also present. Kishikova et al. reported on a case of a 30-year-old pregnant woman with multifocal choroiditis and raised ASO, who improved significantly with corticosteroid therapy.[21] A 29-year-old woman with acute idiopathic maculopathy elevated ASO and anti-deoxyrubonuclease antibodies was also thought to have post-streptococcal association by Shute et al.[22]

With regard to the pediatric age group, Fretzayas et al., have treated a child with anterior uveitis 2 weeks post group A *streptococcus* infection.[23] Abderrahim et al. have published a report on a 9-year-old girl with bilateral granulomatosis anterior uveitis and reactive arthritis.[24] ASO was high. She achieved remission with corticosteroid (CS) therapy. Another granulomatous case in a 13-year-old black female was reported by Besada et al.[25] She had bilateral hypertensive anterior uveitis after streptococcal pharyngitis. ASO was also elevated. Han et al. observed a 14-year-old child with bilateral non-granulomatous anterior uveitis, retinal vasculitis (periphlebitis), and disc edema.[26] Nine months previously, she had had a sore throat and proteinuria. ASO during the uveitis was elevated. After treatment with topical and oral CS, the patient went into remission. Feldon et al., and Ahmad et al., have also treated children with post-streptococcal uveitis and glomerulonephritis.[27,28] A larger cohort of pediatric patients with post-streptococcal uveitis was investigated by Curragh et al.[6] Many had high ASO, and some patients had elevated anti-deoxyribonuclease. The uveitis was bilateral in 5 and unilateral in 6 of the children. Anterior uveitis was observed in 55% of patients, and intermediate uveitis in 45% of patients. Posterior segment involvement was noted in 4 patients. The process was chronic in 73% of patients. Also, 73% of patients presented in the winter and spring months. There were cases of ocular hypertension, vitreous hemorrhage, cystoid macular edema, papillitis, and cataract. Therapy included CS and immunosuppressive medications like methotrexate, mycophenolate, and adalimumab, which improved the control of inflammation and the prognosis. An unusual case was reported by Filloy et

al.[29] An 8-year-old child had presented with bilateral anterior uveitis, vitritis, macular edema, and frosted-branch angiitis. The child had significantly increased ASO and improved CS.

2. Conclusion

Post-streptococcal uveitis is a rare form of intraocular inflammation. It presents mostly as nongranulomatous, bilateral anterior uveitis with a good prognosis, occurring in a wide interval of time following the bacterial infection in most young people. Nevertheless, all anatomic types of intraocular inflammation have been observed. The common denominators between the varying clinical pictures appear to be the history of streptococcal infection, most frequently pharyngitis, an elevated anti-streptolysin-O titer, and in the more recent studies-the, raised anti-deoxyribonuclease antibodies. Furthermore, there has been a generally good therapeutic response to corticosteroids. Few cases have required immunomodulation with methotrexate, mycophenolate, and adalimumab.

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