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CASE REPORT

Nodular Episcleritis in a Boy with Pulmonary Tuberculosis

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Abstract

Introduction: Episcleritis is an acute inflammation of the vascular connective tissue between the conjunctiva and the sclera's surface, which can be found unilateral and bilateral. Tuberculosis (TB) is one of the systemic infectious diseases that cause morbidity in developing countries and can affect the ocular area known as ocular tuberculosis There are still limited cases of ocular tuberculosis studies, specifically tubercular nodular episcleritis in adolescents. This case report aims to expose nodular episcleritis in pediatric tuberculosis patients in Indonesia. **Case Presentation:** A 16-year-old boy came to the Community Eye Health Hospital East Java with superior bilateral eye redness and pain with normal visual acuity. He underwent advanced anti-tubercular treatment for the last nine months. The best corrected visual acuity (BCVA) of both eyes was 6/6. Slit-lamp biomicroscopy (SLB) examination found the dilation of blood vessels located on the superior episclera accompanied by a firmly bordered, fixed, pink nodule, diameter ± 1.5 mm located at 12 o'clock in bilateral bulbar conjunctiva. Based on anamnesis and physical examination, the diagnosis of nodular episcleritis et causa pulmonary TB was established. Topical corticosteroids and artificial tears eyedrops were given in both eyes for five weeks, and continuing anti-tubercular treatment was performed. **Conclusion:** It is necessary to investigate the primary cause of episcleritis by eliminating underlying systemic diseases. Herein, we present a rare case of nodular episcleritis in an adolescent with pulmonary tuberculosis who responded very well to anti-tubercular treatment with topical corticosteroid and artificial tears eye drops.

Keywords: episcleritis; tuberculosis; nodular episcleritis; ocular tuberculosis

Introduction

Episcleritis is an acute inflammation of the vascular connective tissue between the conjunctiva and the sclera's surface. Episcleritis presents unilaterally (80%), bilaterally (20%), and self-limited. Episcleritis can develop recurrently, especially in young adults. The Minnesota study said episcleritis is common in adult women (60.1%).[1] According to different studies[1],[2], episcleritis is frequently detected in boys and children older than five. No specific risk factors are associated with episcleritis, however, between 26 and 30 percent of patients with episcleritis have systemic diseases like autoimmune (systemic lupus erythematous), collagen vascular disease (herpes zoster, herpes simplex, mumps), bacterial (mycobacterium), spirochete (Treponema, Borrelia, Chlamydia), parasitic (Acanthamoeba, Toxoplasma), and fungi (Actinomyces) that increase the possibility of recurrence.[1],[3]

Episcleritis has two different types: diffuse (70%) and nodular (30%).[4] The diffuse type requires a relatively faster healing process, approximately one week to three weeks, and symptoms are milder than nodular types. The eye redness without a decrease in visual acuity is the most typical episcleritis symptom. In severe cases[3], palpebral edema and conjunctival chemosis may occur. Another symptom that can arise is eye discomfort, dominantly in nodular-type episcleritis, caused by the friction between the episclera nodule and palpebra. Physical examination using a slit-lamp biomicroscopy (SLB) found episcleral injection as a dilation of superficial episclera blood vessels with pinkish nodules and firmly bordered were obtained in cases of the nodular type of episcleritis.[5]

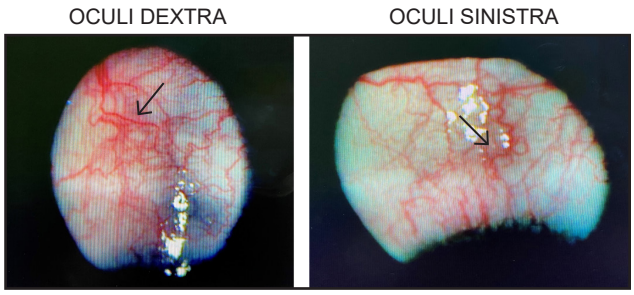

Figure 1. Presence of episcleral injection and nodule before treatment.

Differential diagnosis of nodular episcleritis are phlyctenular conjunctivitis, subconjunctival hematoma, irritated pterygium, and scleritis[3] that can be distinguished through the results of anamnesis and physical examination.

Episcleritis without systemic disease resolves spontaneously in 1-2 weeks.[6] In the absence of systemic diseases and complications, supportive therapy can be given according to symptoms, such as cold compress and artificial tears (carboxymethylcellulose 0.5%) 4-6 times a day. Topical corticosteroids are indicated to reduce inflammatory reactions, and mild topical corticosteroids (fluorometholone 0.1% or loteprednol etabonate 0.5%) could be given four times a day for one to two weeks, then tapering off. More potent corticosteroids, prednisolone acetate 1% four times a day, will be substituted if there is no improvement in clinical symptoms, and oral anti-inflammatory NSAIDs or topical (diclofenac 0.1% and ketorolac 0.5%) can be given to reduce pain.[7] If an underlying disease is found, specific therapy related to it is needed.[8] Episcleritis adjacent to the cornea leads to several complications, such as infiltration in the peripheral cornea or corneal edema.[9]

Tubercolosis (TB) is one of the systemic infectious diseases that can cause morbidity, particularly in developing countries, caused by acid-fast basil bacteria, namely Mycobacterium tuberculosis (Mtb).[10] It is an aerobic bacteria found in tissues with high oxygen content. Primarily, 80% of TB infects the lungs, and 20% can infect other organs (extrapulmonary TB), one of which is the visual organ known as ocular tuberculosis.[11] Extrapulmonary TB is 20%, of which 3.5-5.1% of ocular tuberculosis occurs mainly in human immunodeficiency virus (HIV) patients. Ocular tuberculosis is a severe disease with a long recurrence process and often leads to a significant decline in a patient's visual function and quality of life. Therefore, it is necessary to enforce the initial diagnosis and appropriate procedures.[12]

Ocular tuberculosis can manifest in anterior to posterior oculars, such as the palpebra, conjunctiva, cornea, episclera, sclera, uvea tracts, optic nerves, and eye orbit. A 2010 Indian study of pulmonary and extrapulmonary TB[10] stated that 1.4% of patients had ocular problems. Eighteen percent of patients with positive TB results in Spain had tuberculosis choroiditis, papillitis, retinitis, and vitreous.[10] Systemic abnormalities were reported to increase ocular problems by 60% significantly.[13] Ocular tuberculosis has always been considered rare; nonetheless, the incidence is elevated, correlated with the increasing population and geographical population spread.[14] As TB cases increase, the chances of ophthalmologists getting ocular tuberculosis cases daily increase.

The intraocular inflammatory process related to Mtb can lead to moderate to severe visual impairment in at least 40% of the affected eye and decrease the patient's quality of life.[8] Therefore, the enforcement of initial diagnosis and proper procedures is needed to prevent further complications. There are still few case studies that expose ocular tuberculosis, mainly tubercular episcleritis. There has not been much discussion about the incidence of nodular tubercular episcleritis, specifically in children's cases.[8],[10] Therefore, this case report aims to expose cases of nodular episcleritis in pediatric TB patients in Indonesia.

Case presentation

A 16-year-old boy presented with complaints of superior bilateral eye redness and pain in the last two weeks. The eye redness was repeated two months ago. The complaints were not accompanied by decreasing visual acuity, itching, epiphora, eye discharge, photophobic, seeing flashes of light, or shadows or black dots. The patient had treated his complaints with *tetrahydrozoline*, *hydroxypropyl methylcellulose*, and *benzalkonium chloride*, yet there was no improvement. He had a history of shrimp, dust, and cold allergies. History of fever, cough, runny nose, tightness, or joint pain was denied. There was no history of contact with TB patient. His immunization history was complete and no congenital systemic disease. He denied any previous ocular history, wearing glasses, ocular trauma, or ocular surgery. The history of smoking, asthma, hypertension, and diabetes is undeniable. The patient claimed no family member has similar eye complaints.

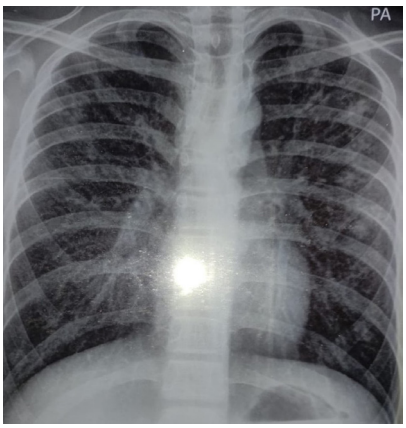

Figure 2. Chest X-ray result Pulmonary TB.

The patient was a pulmonary TB patient, who underwent advanced anti-tuberculosis treatment for nine months (isoniazid and rifampicin), curcuma, proneuron, molagit, sucralfate, lansoprazole, B-vitamins, and megazinc.

The best corrected visual acuity (BCVA) on ocular examination was 6/6. The oculi dextra (RE) results were 6/6 and 6/6F oculi sinistra (LE). SLB examination showed the dilation of blood vessels on the posterior of bulbar conjunctiva superior accompanied by a fixed pinkish nodule, firmly bordered with diameter ± 1.5 mm located at 12 o'clock in bilateral bulbar conjunctiva. The ocular movement is within normal limits. No abnormalities were found in the cornea, anterior chamber, iris, pupil, and lens. The non-contact tonometer recorded intraocular pressure on the right eye was 16 mmHg, and the left eye was 15 mmHg. The posterior segment examination obtained fundus reflex within normal limits, papil N.II were normal in color and firmly defined with cup-to-disc ratio RLE 0.3. The retina had no bleeding or exudate, and the macula reflex was positive. The phenylephrine, 10% drop test was positive (Figure 1). Blood investigations showed normal limits. Antigen SARS-CoV2 was negative, and Anti-HIV was non-reactive. The radiology examination resulted from pulmonary TB (Figure 2). Fundus photography showed the posterior chamber was within normal limits (Figure 3).

Based on clinical, physical examination, and radiological evidence, ODS Episcleritis nodular et causa Pulmonary TB was diagnosed. The mild corticosteroid topical (fluorometholone 0.1%) eye drops were given six times a day in both eyes, artificial tears every hour in both eyes, and maintenance anti-tubercular treatment with Isoniazid and Rifampicin.

Follow-up at the first week, both eye redness still persists. From the ocular examination, the visual acuity of both eyes remain. There was still obtained conjunctival injection under the bulbar conjunctiva superior, but the nodules inflammation vanished. The patient got prednisolone acetate (1%) six times a day in both eyes and continued artificial tears every hour in both eyes, then re-evaluated one week later.

Following up in the second week, the complaints were improved. The examination results obtained showed that the BCVA was 6/6. There was a decrease in conjunctival injections under the superior bulbar conjunctiva without any nodules. The corticosteroid treatment in both eyes were tapering off four times a day, artificial tears on both eyes six times a day, and anti-tubercular treatment was continued.

After five weeks of treatment, there were no complaints from the patient. The examination showed visual acuity in both eyes, with the best correction being 6/6. The conjunctival injection under superior bulbar conjunctiva and nodules were no longer available (Figure 4). The treatment of corticosteroid eye drop was stopped, artificial tears and anti-tubercular treatment were continued.

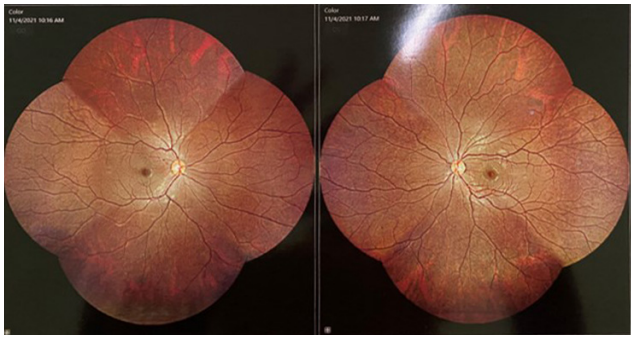

Figure 3. Normal fundus photography of both eyes.

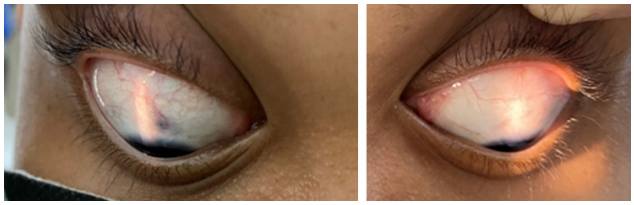

Figure 4. Absence of episcleral injection and nodule after treatment.

Discussion and conclusions

Episcleritis is an acute non-granulomatous inflammation of vascular connective tissue between the conjunctiva and the surface of the sclera that can heal spontaneously for about 2-21 days (self-limiting).[3] Episcleritis is often in young adults but rarely in children. Some cases of nodular episcleritis are closely related to systemic diseases related to infection, immunology, and TB.[15] The acute inflammatory process involves activating lymphocytes and macrophages that make inflammatory mediators appear, leading to vasodilation, increased vascular permeability, and migration of leucocytes and macrophages.[3]

Ocular tuberculosis develops because Mtb enters the respiratory tract through droplets and reaches the alveolus, macrophages, and dendritic cells. Furthermore, there is the process of phagocytosis Mtb which causes the production of pro-inflammatory cytokines (IL-12 and IL-18). The inflammatory process triggers the arrival of monocytes and phagocytosis of living germs. In macrophages, Mtb inhibits the encounter between phagosomes and lysosomes, so macrophages are destroyed while Mtb grows. TNF-α is formed and triggers a slow-type hypersensitivity response that will destroy macrophages with Mtb in them. As a result, central caseous necrosis is surrounded by active macrophages, T cells, and other immune cells. If the immune response is weak, Mtb can replicate, and some will enter the lymphatic system and circulate to other organs, including the eyes. Once in the eye, Mtb can be instantly active and cause clinical symptoms, but it can also enter a dormant phase for many years and become active at any time. Conversely, if the immune response is good, T cells eat Mtb before replicating and spreading.[16]

In our 16-year-old boy's case, nodular episcleritis was a liability related to systemic disease, TB. Clinical conditions obtained bilateral eye redness and pain in the superior of the eyes since two weeks ago, without visual impairment. Following the explanation of the American Academy of Ophthalmology (AAO) guidelines in 2020[7], the most typical symptoms of episcleritis are eye discomfort, accompanied by mild pain without a decrease in visual acuity.

On physical examination, the dilation of blood vessels appears on the posterior of the bulbar conjunctiva superior, accompanied by a pinkish nodule, firmly bordered, fixed, diameter ± 1.5 mm at the 12 o'clock position of the bulbar conjunctiva . This dilation of blood vessels faded after being tested with phenylephrine (10%); this examination aims to eliminate the differential diagnosis of scleritis. The complaints of eye redness and pain with normal visual acuity were also found in the tubercular nodular episcleritis case study[15] on a 12-year-old girl from India. Bathula et al.[17] also reported a similar case in a 12-year-old boy with unilateral eye redness, pain, epiphora, and blurred vision accompanied by pinkish nodules. The clinical appearances and physical examination of the cases above[15],[17] are not much different from ours.

Several cases of tubercular nodular episcleritis found in boys may relate to the immune system and immunological response[15], influenced by many endogenous and exogenous factors. Research by Rao[18] stated that men tend to be more susceptible to TB infection by a 2:1 ratio to women, possibly at a young and productive age. It may be related to the human sex chromosome, chromosome XX in females and XY in males. The innate and adaptive immune systems are associated with the X chromosome. Some effectors controlling the transcription and translation processes to activate cytokine receptors are also on the X chromosome. Because the immune system is regulated by X-coded genes on chromosomes, causing females to have more CD4+ T cells and lower IL-6 production than males, antibodies are formed more and last longer in circulation. Therefore, women tend to be more resistant to inflammation, viral infections, bacteria, and parasites than men.

In addition, sex hormones such as estrogen, progesterone, and testosterone affect immune cells quantitatively and qualitatively. Dihydrotestosterone (DHT) and testosterone, which increase concentration in post-pubertal males, have an immune system inhibition effect through increased regulation of anti-inflammatory cytokines (IL-10). In vivo research, testosterone exposure also reduced the activity of natural killer (NK) cells in mice.[14] These factors may cause male susceptibility to TB infection.

Due to the limitations of tools and regiments, our diagnostic examination merely used a biomicroscopic slit lamp and fundus photography to determine abnormalities in the posterior segment. In addition, diagnosis can also be made through the patient's clinical response to anti-tubercular treatment. Studies from Abdisamadov and Tursunov suggested that the positive clinical response to anti-tuberculosis therapy also supports the diagnosis of ocular tuberculosis, wherein our patients, clinical response improved after getting pulmonary TB therapy. The definitive diagnosis can be made by isolating Mtb bacteria from ocular tissue or ocular fluid from nodule biopsy or cotton swab through the microbiological and histopathological examination of M. tuberculosis (direct removal of acid-resistant bacteria or Mtb cultures from ocular samples), tuberculin tests, interferon-gamma release assays (IGRA) and polymerase chain reaction (PCR). In adult nodular tuberculosis cases in India, a cotton swab examination of ocular fluid for acid-resistant bacterial culture obtained negative results. Nodule biopsy is possibly done; nevertheless, it is not recommended because it can injure the sclera[19], thus not recommended to be applied to children.

In this case, we provide mild corticosteroid eye drops (fluorometholone 0.1%) six times a day, artificial tears every hour, and continuing the anti-tubercular treatment. Hand and eye hygiene education is also suggested for minimizing contamination. In the following week, the eye redness still remained then; the mild corticosteroids were replaced using prednisolone acetate eye drops were 1% six times a day and tapering off each week, artificial tears every hour, and symptoms improved after five weeks of therapy. The procedures follow AAO 2020 guidelines[7], shown that episcleritis with inflammatory reactions requires mild topical corticosteroid therapy (fluorometholone 0.1% or loteprednol etabonate 0.5%) 4 times a day for 1 to 2 weeks, then tapering off. If there is no improvement, it can be replaced with more potent corticosteroid eye drops, prednisolone acetate (1%) four times a day, and oral or topical anti-inflammatory drugs if needed. Although the signs and symptoms of episcleritis can be effectively reduced with topical steroid use, this agent requires supervision, particularly in recurrent episcleritis, associated with complications due to long-term corticosteroid use, such as glaucoma, cataracts, and infection.[3]

Uveitis (11.4%) and glaucoma (7.8%) are the most common complications, especially in recurrent episcleritis patients.[2] As much as 0.3% of episcleritis can develop into scleritis. Therefore, it is necessary to follow up periodically to prevent ocular complications, particularly in recurrent episcleritis patients. It is necessary to investigate the cause of episcleritis by eliminating any underlying systemic diseases, including the cause of allergies or irritation, which are also removed in atopic patients.

Based on the results and discussion, episcleritis can occur at any age, generally in young adults. Nodular episcleritis can be associated with a systemic infectious disease related to immunology, TB infection. Indonesia is an endemic area of TB infection whose clinical manifestations has impact to the eye organ (ocular tuberculosis) due to hematogenous spread and delayed hypersensitivity reactions of Mtb. Delays in therapy can result in severe complications, decreased visual acuity, and quality of life. The lack of research literature, case discussion, and diagnostic tools is still our problem. Therefore, ophthalmologists in Indonesia focus on the suspicion of adolescent episcleritis cases related to systemic diseases, particularly TB infection.

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