Jurnal Oftalmologi 2020, Vol. 2, No. 2.
E-ISSN.2541-4283

BENZATHINE PENICILLIN G INTRAMUSCULAR SUCCESSFUL TREATMENT OF OCULAR SYPHILIS WITH HUMAN IMMUNODEFICIENCY VIRUS POSITIVE : A CASE REPORT

Marco Angelo Liwan[1], Sitti Soraya Taufik[1], Hasnah B Eka[1], Safrudin Amin[2]
[1]Department of Ophthalmology,Faculty of Medicine,Hasanuddin University,Makassar,Indonesia
[2]Department of Dermatovenerology,Faculty of Medicine,Hasanuddin University,Makassar,Indonesia
*Corresponding author: Marco Angelo Liwan, E-mail : marcoliwan@gmail.com

ABSTRACT

Introduction: Ocular Syphilis is a manifestation of multisystemic chronic infection caused by the spirochete *Treponema pallidum,* it can affect all structures and may present as anterior uveitis, posterior uveitis, panuveitis, retinitis, papillitis, making it “a great masquerader”.
Objective : To report successful treatment of ocular syphilis co infection with human immunodeficiency virus positive with Benzathine Penicillin G intramuscular.
Case Presentation : A 28 year old man (heterosexual) presented with painless blurring of his eyes of three month’s duration. His visual acuity was hand movement in his right eye and 1/60 in the left with no dermatology lesion, funduscopy finding papillitis and vitreous cells in both eyes with retinal vasculitis and intraretinal hemorrhage in inferior region in left eye, serological tests revealed VDRL and TPHA test positive with ELISA was positive for human immunodeficiency virus. The patient immediately treated with benzathine penicillin G 2.4 million units intramuscularly once weekly for three consecutive weeks and antiretroviral. After three weeks, his visual acuity showed improvement and decreased VDRL titer three months later.
Conclusion: Ocular Syphilis with HIV positive is curable with Penicillin G Intramuscular, with early detection and treatment are important for a good visual outcome.

Keywords : benzathine, ocular, penicillin, syphilis.

INTRODUCTION

Ocular Syphilis is a manifestation of multisystemic chronic infection caused by the spirochete *Treponema pallidum,* transmission occurs most often through sexual contact (acquired syphilis) with infectious lesions of the mucous membrane or abraded skin, via blood transfusion; however, transplacental infection of the fetus (congenital syphilis) may occur after the tenth week of pregnancy.[1,2] In 2012, there are about 18 million (0,5%) prevalent cases of syphilis among 15-49 year old world wide, with 5.6 million of new cases. The natural history of untreated acquired syphilis has been well described.[3]

Syphilis can involve all parts of the eye and may be the only manifestation of syphilis. Ocular syphilis is a rare manifestation of syphilis (6-9%) and was reported to have a prevalence rate of 0.6% in HIV-infected patients. It can result in visual loss if it is unrecognized or if it is mistreated as a noninfectious ocular inflammation. It can affect various parts of the eye and may present as anterior uveitis, posterior uveitis, panuveitis, focal retinitis, vasculitis, papillitis, vitritis and even scleritis, making it a “great masquerader”.[3]

A high level of clinical suspicion is required for the appropriate diagnosis of syphilitic uveitis, due to its variable clinical presentation and atypical presentation in

HIV-infected individuals. Appropriate laboratory studies can aid in confirming the diagnosis and rule out other disease entities. Penicillin G is the preferred treatment for all stages of syphilis The dose, route of administration, and duration of therapy are determined by the stage and clinical findings.[2,3]

CASE PRESENTATION

A 28-year-old man (heterosexual) presented with painless blurring of vision in his left eye of three month's duration and followed with his right eye. His right-eye vision at presentation was hand movement (HM) and 1/60 in his left eye. Firstly, he complained with blurry vision with glare, and get worse. Slitlamp examination showed 1+ cell and keratic precipitate in the anterior chamber of bilateral eyes. Funduscopy examination showed papillitis and vitreous cell +2 both eyes with retinal vasculitis and intraretinal hemorrhage in inferior region in left eye **(Figure 1).**

Physical examination showed general weakness and good nutrition. His body weight had decreased by 10 kg in the last year. The clinical examination revealed no dermatology lesion as confirmed by dermatologist, chest roentgenography and abdominal sonography both showed no pathologic lesions. The patient treated with prednisolone acetate and methylprednisolone for two weeks but no significant improvement.

Two weeks later, Complete blood counts revealed 7,700 white blood cells/mm3 with 66% neutrophils, 26,2% lymphocytes, 6,8% monocytes and 0,5% eosinophils. Subsequent serologic tests confirmed the diagnosis of syphilitic infection. Venereal disease research laboratory (VDRL) test and *T. pallidum* hemagglutination (TPHA) test were all positive : VDRL with the titer 1:512 and TPHA with the titer 1:2560. Neurologic examinations were all within normal limits. Lumbar puncture for cerebrospinal fluid (CSF) study was suggested, but the patient refused.

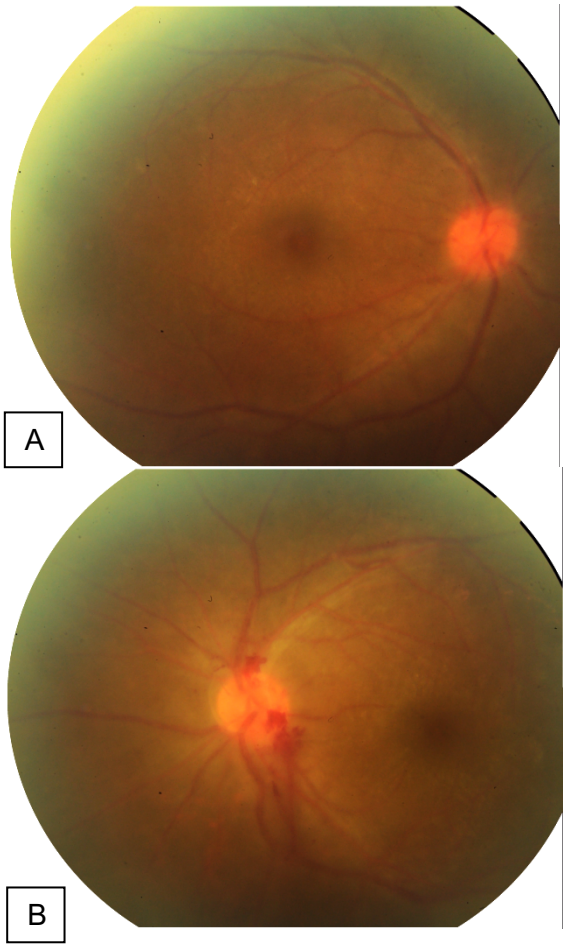

Figure 1. Fundus Photograph (A) Right eye showed papillitis and retinal vasculitis (B) Left eye showed papillitis and intraretinal hemorrhage.

After completing examination, the patient referred to Dermatovenerology outpatient clinic and was treated with benzathine penicillin G 2.4 million units intramuscularly once weekly for three consecutive weeks. After one week of therapy, his visual acuity improved to 4/60 in right eye and 20/120 in the left, the patient also reported decreased floaters and glare with fever and malaise.

Then, the patient consulted to *Voluntary*

Counseling and Treatment and also being diagnosed with human immunodeficiency virus positive after the serologic tests confirmed with positive with enzyme-linked immunosorbent assay (ELISA) and CD_4^+ T-lymphocytes count was 330cells/µl (normal, 470-1298 cell/µl). One week later, the patient feels better with improvement visual acuity 20/120 on right eye and 20/60 in the left.

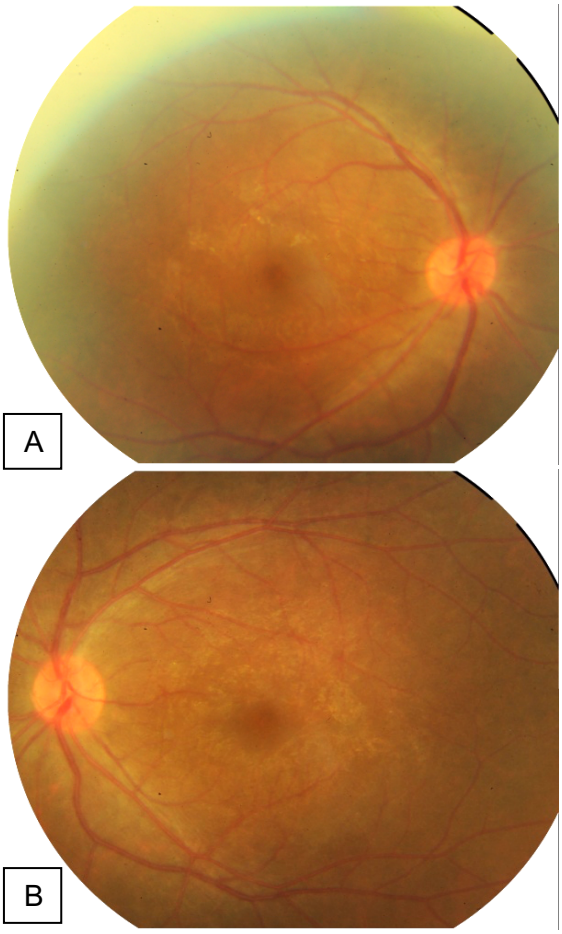

Figure 2. Fundus Photograph 3 months after treatment (A) Right eye showed decreased of papillitis (B) Left eye showed decreased of intraretinal hemorrhage with demyelinating of nerve fiber layer.

On third week after therapy, his visual acuity improved 20/60 on right eye and remained 20/60 on left eye. The patient also treated with tenofovir 300mg/ lamivudine 150mg/ efavirenz 600mg daily for six months. Three months post treatment, the visual acuity improved 20/30 in both eyes. The hemorrhage also reduced **(Figure 2).** Serologic test revealed decreased in VDRL test with the titer 1: 128.

DISCUSSION

Ocular syphilis is a rare manifestation of syphilis (6-9%) and was reported to have a prevalence rate of 0.6% in HIV-infected patients. It is an uncommon disease. Ocular syphilis is more rapidly progressive and more extensive in HIV infected patients in comparison to HIV uninfected patients. It is usually bilateral and more common in males. The resurgence of syphilis in recent years has also seen a global increased reporting of ocular syphilis. Known as the great masquerader, syphilis can involve all ocular structures throughout the different stages of infection, although typically occurs during the secondary or latent stage. [3,5,7]

Primary syphilis follows an incubation period of approximately 3 weeks and is characterized by a chancre, a painless, solitary lesion that originates at the site of inoculation, resolving spontaneously within 12 weeks regardless of treatment. The central nervous system (CNS) may be seeded with treponemes during this period, although there is an absence of neurologic findings. Secondary syphilis occurs 6–8 weeks later and is heralded by the appearance of lymphadenopathy and a generalized maculopapular rash that may be prominent on the palms and soles. Tertiary syphilis refers to gummas and cardiovascular syphilis and neurosyphilis including Ocular Syphilis if the patient being untreated. Latent syphilis is defined as syphilis characterized by seroreactivity without other evidence of primary, secondary, or tertiary disease. Persons who

have latent syphilis and who acquired syphilis during the preceding year are classified as having early latent syphilis, a subset of latent syphilis.[4,5,6,7]

The local and systemic response to *T. pallidum* is complex, and is initiated as the bacteria enter the body through intact mucosa. Local invasion of the tissues ensues, and dissemination occurs via blood and the lymphatic system. On the microscopic level, lymphocytic infiltration is seen, either diffuse or focal, surrounding the blood vessels of affected organs. In the eye, this can be found in the iris, ciliary body, and choroid, along with chronic granulomatous inflammation, including epithelioid histiocytes and multinucleated giant cells. Mononuclear cells, sensitized T-lymphocytes, macrophages, and plasma cells can also be seen. This inflammation and the resulting adaptive immune response cause the tissue destruction characteristic of syphilis. Local antibodies are also produced against the lipid, protein, and lipoprotein components of *T. pallidum*. The majority of bacteria are eradicated by opsonization and phagocytosis by macrophages.[6,7]

Centers for Disease Control and Prevention released guideline that presumptive diagnosis of syphilis requires use of two tests: a nontreponemal test (i.e., Venereal Disease Research Laboratory [VDRL] or Rapid Plasma Reagin [RPR]) and a treponemal test (i.e., fluorescent treponemal antibody absorbed [FTA-ABS] tests, the *T. pallidum* passive particle agglutination [TP-PA] assay, various enzyme immunoassays [EIAs], chemiluminescence immunoassays, immunoblots, or rapid treponemal assays). Use of only one type of serologic test is insufficient for diagnosis and can result in false-negative results in persons tested during primary syphilis and false-positive results in persons without syphilis.[5] However, VDRL or RPR are more useful to obtain information on disease activity and therefore for therapeutic monitoring. It is recommended to check serum nontreponemal titers at intervals of 1 month, 2, 3, 5, 9 and 12 months to ensure that titers are declining appropriately (at least four fold in three to five months).[6,7,8]

The CDC recommends that all patients with any syphilitic ophthalmic manifestations should diagnosed with neurosyphilis and undergo CSF evaluation to identify those with abnormalities who should have follow-up CSF examinations to assess treatment response but the patient declined. Then should be treated as neurosyphilis, because the retinal and optic neuroepithelial structures are embryologically derived from the brain. According to the clinical appearance and laboratory findings, the patients diagnosed with Ocular Syphilis with late latent syphilis and human immunodeficiency virus positive because the titer for VDRL was positive with 1: 512 and TPHA 1:2560 with ELISA positive for HIV.

To manage ocular syphilis, European (International Union against Sexually Transmitted Infections) and United States (Centers for Disease Control and Prevention (CDC)) and World Health Organization guidelines recommend standard use of intravenous benzyl penicillin at a dose of 12–24 million units per day, with 3-4 million units given every 4 h, for 10–21 days because benzyl penicillin can penetrate blood ocular barrier and penicillin G doesn't. The recent World Health Organization sexually transmitted infection (STI) guidelines recommend benzathine penicillin G administered intramuscularly at a dose of 2.4 million units once weekly for three consecutive weeks to treat late syphilis

(including ocular syphilis).[3] Penicillin G is in class of beta-lactam antibiotics which inhibits biosynthesis of the cell wall peptidoglycan during the stage of active multiplication. This results in an osmotically unstable cell wall, leading to lysis of the cell wall, subsequent destruction of the bacterial cell, and death.[1,4,9,10]

The patient received treatment with benzathine penicillin G 2.4 million units intramuscularly once weekly for three consecutive weeks as World Health Organization recommendation in 2016 because the availability of the the regiment and gives good response with improvement for his visual acuity. His visual acuity improved to 20/60 in both eyes and 20/30 both eyes three months later. The Jarisch-Herxheimer reaction, usually experienced within the first 24 hours after initiation of therapy, results from a hypersensitivity reaction of the patient to treponemal antigens that are released in large number as spirochetes are killed. Symptoms include fever, myalgia, headache, and malaise. Supportive care and observation are all that is required in most cases. This reaction is not an indication for discontinuation of treatment.

The treatment can give good respond to this patient. Successful therapy achieved when after treatment, the titers should decline fourfold (i.e., a titer of 1:32 decreases to 1:8) or lower within 6 months in primary or secondary syphilis, and within 24 months in latent syphilis. The patient showed good response for the treatment which three months after treatment the VDRL titer decreased 1:128 (before 1:512).[7]

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