IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 24, Issue 11 Ser. 2 (November. 2025), PP 85-89
www.iosrjournals.org

Bull's Eye Maculopathy In An HIV-Positive Patient Receiving Tenofovir (TFV: T), Lamivudine (3TC: L), And Dolutegravir (DTG: D) – TLD – A Case Report

Omaka A.U., Ezeigbo A
Department Of Optometry, Abia State University, Uturu

Abstract
Bull's Eye Maculopathy (BEM) is a rare but serious ocular complication that has been associated with certain antiretroviral therapies used in the treatment of HIV/AIDS. We present a case of a 53-year-old HIV-positive male who developed BEM after taking Tenofovir, Lamivudine, and Dolutegravir (TLD) regimen for 36 months. The patient presented with complaints of progressive central visual blurring and metamorphopsia in both eyes. Fundus examination revealed characteristic findings of BEM, including a central bull's eye pattern of pigmentary changes in the macula. Optical coherence tomography (OCT) confirmed the presence of outer retinal layer changes consistent with BEM. Upon further investigation, the patient had no history of other retinal diseases or macular toxicities. This case highlights the importance of monitoring patients on TLD therapy for ocular side effects and the need for prompt recognition and management to prevent irreversible visual impairment.
Keywords: *Bull's eye maculopathy, metamorphopsia, tenofovir, lamivudine, dolutegravir*

Date of Submission: 01-11-2025 Date of Acceptance: 10-11-2025

I. Introduction

Bull's Eye Maculopathy (BEM) is a rare but potentially sight-threatening condition that has been associated with various underlying etiologies, including the human immunodeficiency virus (HIV) infection. HIV infection can lead to a range of ocular manifestations, with BEM being one of the less common presentations. The exact pathogenesis of BEM in HIV remains unclear, but it is believed to involve a combination of direct viral effects, immune-mediated mechanisms, and the side effects of antiretroviral therapy (ART). BEM in HIV-infected individuals typically presents as a bilateral, symmetrical, and well-demarcated area of retinal pigment epithelial (RPE) atrophy, giving rise to a characteristic bull's eye pattern on fundoscopic examination. This pattern is caused by the preferential loss of RPE cells in the macular region, leading to disruption of the overlying photoreceptor layer and subsequent visual impairment. The clinical course of BEM in HIV disease can vary, with some patients experiencing gradual progression of macular changes and others remaining stable over time. Early detection and management are crucial in preventing irreversible vision loss in affected individuals. This case report aims to provide a comprehensive overview of BEM in the context of HIV infection, including its clinical features, pathogenesis, diagnostic considerations, and management strategies.

II. Case Report

JJ, a 53-year-old male oil worker presented to the eye clinic at Moorfield Optometry specialist Eye Centre with complaints of gradual reduction in his vision in both eyes of 6 months duration, with inability to see clearly at far and near, vision is worse in the evenings. He is a known RVD patient with a consistent compliance to his HAART treatment with TLD (Tenovir, Lamivudine, Dolutegravir). Prior to presentation to our clinic, the patient had received treatment in a clinic where his prescription glasses were changed without any commensurate improvement in his vision. He had been classified as a glaucoma suspect and commenced on glaucoma treatment with an unspecified oral medication. His family history was unremarkable for hypertension and diabetes, ocular history was remarkable for a refractive error (myopic astigmatism/presbyopia). Aside his HAART medication (TLD) he was not on any other medication.

Clinical findings
Visual Acuity
Entry Visual Acuity (VA): Right eye (OD): 6/60, Left eye (OS): 6/36+1, Both Eyes (OU): 6/24
Near VA: OD: N24, OS: N24, OU: N24

External examination

Pupils: Equal and round in both eyes with no afferent pupillary defect
Eyelids and Periorbital Area: No signs of ptosis, lid edema, or erythema.
Conjunctiva and Sclera: No signs of injection, hemorrhage, or chemosis, but sclera had a dirty brown appearance.
Cornea: Bilateral corneal arcus senilis otherwise clear cornea
Anterior Chamber: No signs of inflammation (cells, flare) or neovascularization seen
Iris: No signs of neovascularization, rubeosis, or heterochromia seen
Lens: no signs of opacities,
Extraocular Movements: No restrictions in the movement of the extraocular muscles in all directions of gaze.
Proptosis: No protrusion of the eye balls noted.
Fundoscopic Examination: A dilated fundoscopic examination was performed to assess the retina, optic nerve, and macula for any signs of retinal vein occlusion, including retinal hemorrhages, cotton-wool spots, macular edema, and optic disc swelling (papilledema) areas of hypopigmentation measuring 4DD around the macula area in both eyes

Retinal Photography:

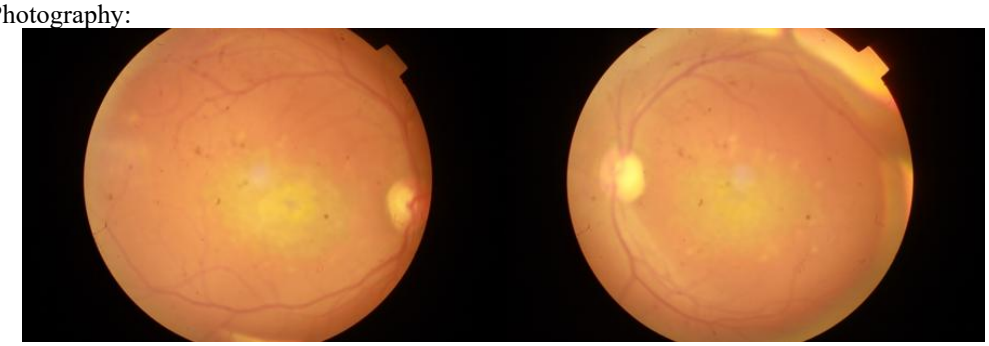

Fig 1: A fundus photograph of the Right and Left eye with Bilateral Bull's eye Maculopathy

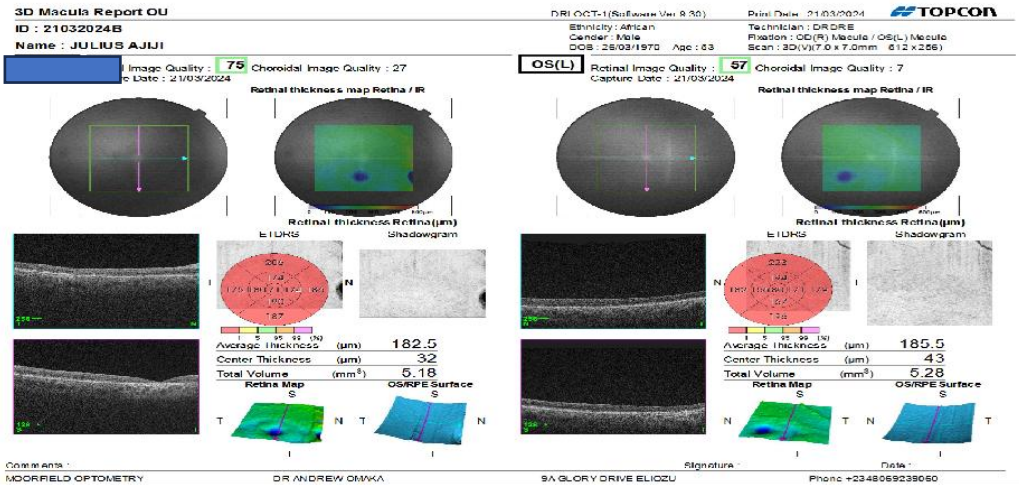

Fig 2: OCT macula report depicting maculopathy consistent with bull's eye maculopathy

Diagnosis: A tentative diagnosis of BULL'S EYE MACULOPATHY was made.

Treatment:

The treatment regimen for Bull's Eye Maculopathy (BEM) associated with retroviral diseases, such as HIV, focuses on managing the underlying condition, minimizing further retinal damage, and preserving vision. Since there is no specific treatment for BEM itself, the approach often involves:

I. Antiretroviral Therapy (ART): Optimal control of HIV with ART is crucial to prevent further progression of ocular manifestations, including BEM.
II. Regular Ophthalmic Monitoring: Close monitoring of visual function and retinal changes is essential to detect any progression of macular damage and adjust treatment accordingly.
III. Vitamin Supplements: Some studies suggest that supplements containing antioxidants and vitamins (e.g., vitamin C, vitamin E, lutein, zeaxanthin, and zinc) may help slow the progression of macular degeneration, which is similar to the pathology seen in BEM.

IV. Anti-inflammatory Therapy: In cases where there is evidence of inflammation contributing to macular damage, anti-inflammatory medications, such as corticosteroids, may be considered.
V. Lifestyle Modifications: Encouraging patients to adopt a healthy lifestyle, including a balanced diet rich in antioxidants, regular exercise, and avoidance of smoking, can support overall ocular health.
VI. Low Vision Rehabilitation: For patients with significant visual impairment, low vision rehabilitation services can help improve quality of life by maximizing the use of remaining vision through visual aids and training.
VII. Patient Education: Providing education about the condition, its management, and the importance of regular follow-up can help patients understand and cope with the disease better.

It is important to tailor the treatment regimen to each individual patient based on the severity of BEM, underlying retroviral disease, and other comorbidities. Close collaboration between ophthalmologists and infectious disease specialists is crucial for the comprehensive management of patients with BEM and retroviral diseases. Early-stage detection remains challenging, and too often the imaging findings are symptomatic. Diagnostic imaging such as fundus photographic imaging, Optical Coherence Tomography (OCT), Spectral-Domain OCT, enhanced depth imaging optical coherence tomography, Multicolor and Autofluorescence imaging allow early-stage detection. In addition, analyzing the accompanying symptoms along with imaging features may help improve understanding towards causes, associations and management in future cases of this potentially reversible and treatable condition[7].

III. Discussion

Human immunodeficiency virus (HIV) infects over 40 million individuals worldwide and cells of the immune system, primarily CD4+ T cells, macrophages, and dendritic cells. Cases of non-infectious HIV retinopathy, that is, retinal pathology in otherwise immunocompetent, non-infectious clinically apparent individuals are relatively rare. However, such cases have been reported both prior to and after the advent of highly active antiretroviral therapy (HAART) 2. With HAART, HIV viremia is suppressed and patients generally respond positively to therapy; however, some individuals develop bull's-eye maculopathy (BEM), defined as localized atrophy of the retinal pigment epithelium (RPE)/choroid in a characteristic pattern resembling a bull's-eye target. BEM is a form of non-infectious maculopathy and in HIV-positive individuals can occur as a result of viral infection, therapy, or other mechanisms. Although cases of HIV-associated BEM due to more than 10 different classes of antivirals have been reported, it typically occurs in individuals receiving the nucleotide analog reverse transcriptase inhibitors, tenofovir (TFV) or a combination therapy (TFV and lamivudine). In BEM, areas of RPE atrophy allow visualization of underlying choroidal vessels and may rarely progress to geographic atrophy. Subsequently, photoreceptor apoptosis and degeneration lead to profound vision loss, refractoriness to therapy, and an end-stage condition referred to as atrophy of the macula (AM).

Differential Diagnosis

The differential diagnosis in this case should focus on common entities that can mimic the current findings. These include acute retinal necrosis, sarcoid, and other infectious and inflammatory conditions. In addition, drug-induced retinopathy needs to be excluded. Acute retinal necrosis (ARN) is characterized by well-defined patches of necrotic retina classically in a posterior-chorioretinal location with secondary associated peripheral atrophic lesions, which is less seen in the index case. There may also be vitreous abscesses and a significant amount of inflammatory exudates, which are absent in the current case[8].

In the case of the patient with bull's eye maculopathy, the treatment regimen included tenofovir, lamivudine, and dolutegravir. Tenofovir is a nucleotide analogue reverse transcriptase inhibitor used to treat HIV infection. Its efficacy and tolerability have led to it becoming widely used in first-line antiretroviral therapy regimens. Because of the low renal toxicity of second-generation tenofovir, tenofovir alafenamide has gained a place in first-line antiretroviral therapy regimens, potentially reducing the risk of tenofovir-related nephrotoxicity. Nonetheless, given the widespread use of tenofovir, clinicians should be aware of the possibility of adverse effects. Virologically suppressed patients taking tenofovir who develop focal bone pain may present a rare but serious adverse event. Tenofovir induces a modest, sustained decline in the glomerular filtration rate, leading to proximal tubular dysfunction with tubular proteinuria, glucosuria, phosphaturia, and hypophatemia[6]. After being introduced to treatment with tenofovir, HIV-positive patients should be carefully monitored for possible local inflammatory bone lesions, particularly if they present with focal bone pain and evidence of localized swelling and/or inflammation. In this case report Clinical examination and optical coherence tomography showed bilateral foveo-macular atrophy and star-shaped foveal lesions. Despite the patient refusing to stop the ART, knowledge of the adverse effect of ART allowed early detection of the eye disorder[1] that would progressively deteriorate until significant visual loss. Antiretroviral medications are typically utilized to manage human immunodeficiency virus (HIV) infection, and most of them have been related to various ocular problems. A HIV-positive woman was referred for a routine ophthalmologic examination after a fundus screening revealed sickles in her mid-periphery fundus. Twelve years ago, she began a treatment regimen consisting of two antiretrovirals and one

integrative inhibitor. A diagnosis of tenofovir-related retinal toxicity was made based on the drug-efficacy profile[5]. As a result of scientific study and the introduction of medications, the survival time of HIV-positive patients has considerably lengthened. Most antiretroviral medications have relatively few side effects. Many new anti-HIV drugs are safer and better tolerated than those of earlier generations. The majority of anti-HIV drugs are safe for the retina. Zidovudine was related to pigmented retinopathy and maculopathy such as zebra lines long ago. Fortunately, it is rarely used now. The most likely antivirals to cause retinal toxicity either presently or in the future are 2 NRTIs: didanosine and tenofovir. Tenofovir is the first nucleotide analogue, and in combination with lamivudine, it has been the most widely prescribed[2]. Didanosine was the second nucleoside analogue approved for the treatment of HIV infection. Toxicity has been known since its early promotional days. Most primary effects were retinal. It was evident in patients after a latent period of years and presented as bilateral, symmetrical peripheral atrophy of the retinal pigment epithelium detectable on fundus examination. While spared, the naked fovea simulates a bull's eye pattern. Scattered mid-peripheral atrophy of the RPE gradually expanded to a bull's eye, and symptoms such as night blindness progressively developed. This case was about these dialatogenic/reticular toxicities after seven years of use. The long latent period was unexpected. No patient previously treated with didanosine for more than three years was reported.

IV. Implications Of Findings

HIV still presents as a major public health challenge even in the antiretroviral therapy era. In addition to the improvement of life expectancy, several long-term complications, not directly related to opportunistic infections, have been discovered. In particular, noninfectious retinopathy, HIV retinopathy, with resulting vision abnormalities is the most common complication not directly related to opportunistic infections[2]. It has been estimated that 6-25% of all HIV-positive patients present electroretinogram (ERG) abnormalities due to noninfectious processes. The possible causes include retinal toxicity of commonly used medications for treatment of HIV, HIV-related vascular dysregulation, and direct effects of HIV itself. HIV-retinopathy, the most prevalent ocular complication of HIV associated HIV/AIDS disease, is a degenerative retinal process with a characteristic fundus appearance. These characteristics include presence of ischemic retinopathy, retinal hemorrhages, retinal edema, and cotton wool spots. However, little is known about the clinical and pathophysiological characteristics of maculopathy in HIV-positive subjects. This is a report of a maculopathy resembling a bull's eye maculopathy in an HIV-positive patient receiving Tenofovir 300mg + Lamivudine 300 mg + Dolutegravir 50 mg treatment. In this clinical case of an HIV-positive patient who received a combination of Tenofovir, Lamivudine, and Dolutegravir for 3 months, a retinal affliction resembling bull's eye maculopathy found on optical coherence tomography and perimetric findings is depicted. Most conjunctival or retinal segmental lesions are reversible upon the cessation of antiretroviral drugs. On the other hand, bull's eye maculopathy is rarely reversible. Importantly, whether the fundoscopic changes or degree of vision abnormality are reversible or not is still unclear[1].

V. Review Of Similar Cases In Literature

In the search of literature, the electronic database was searched for articles in the past 25 years published in English regarding "Bull's eye maculopathy" & "HIV." The first significant work showing the association of maculopathy (specifically, Bull's Eye maculopathy) with HIV infection was published in 2013 on a previously healthy 43-year-old female who was diagnosed with HIV infection and began on treatment with Lamivudine, Atazanavir, and Tenofovir. After one year of treatment, she noted gradually worsening central vision in both eyes (BE). Examination revealed BCVA of 20/25 and 20/30 in the right and left eyes respectively, and the patient exhibited macular atrophy that was well outside the arcades similar to chloroquine or Hydroxychloroquine toxicity. The patient had only a slight paracentral scotoma, and her visual acuity remained sufficient for most daily activities[2]. The central fovea was spared in this case and the patient had maintained more than 20/25 vision[5].

Another similar case was published in January 2022 describing a 61-year-old female with a history of HIV, chronic hepatitis B & C infections, genotype 1, Raymond's syndrome with intractable headaches and bilateral retinopathy. The patient was suspected to have Bull's eye maculopathy and underwent further evaluation which showed choroidal atrophy surrounding the fovea with ill-defined inner retinal cyst. It was concluded later that tenofovir was the most likely drug to cause these changes, although the retinopathy was atypical. Prior to 2013, there were other cases of retinopathy due to different medications associated with HIV infection were documented but Bull's eye maculopathy in association with HIV infection was reported for the first time in 2013, and 4 other similar cases were independently reported later.

VI. Recommendations For Clinicians

While screening for age-related maculopathy is commonplace in resource-rich countries, it is nevertheless uncommon to detect bull's eye maculopathy in patients with HIV. The current patient received regular monitoring for signs of maculopathy with no abnormalities noted during prior consultations. Clinicians

should therefore be cognizant of the possibility of bilaterally-symmetric maculopathy even if the patient's ocular examination demonstrates no signs of such disease. To that end, any point-of-care assessment for HIV-related immunosuppression, such as an unexplained increase in CD4 count, should prompt broader assessment for previous tenofovir or EFV exposure. The axial pericentral field loss with preservation of fixation and inferior temporal visual field loss due to maculopathy is more consistent with bull's eye maculopathy than advanced hypertensive retinopathy. While the patient had been at high risk of developing toxic maculopathy for the past decade, the absence of bilateral dot-fleck retinopathy diminishes the suspicion of its presence. However, less common toxic maculopathies, such as those secondary to hydroxychloroquine and ethambutol, should be requested to exclude alternatives, especially if fundus examination findings are subtle. The emergence of HIV/AIDS in Nigerian youth needing multi-drug antiretroviral therapy thus provides CDC experts an opportunity to increase awareness and a case for screening in resource-enhanced settings. Moreover, with the increasing off-patent use of Tenofovir AF/DF, Lamivudine, and Dolutegravir, higher prevalence of toxic maculopathy cases can be anticipated in other settings that have been slow to adopt RDRF/RDRI screening[5], reinforcing the inextricable link between HIV and human rights.

VII. Conclusion

Bull's Eye maculopathy (BEM) is a type of retinal toxic morphology that can occur in patients treated with anti-HIV or retroviral drug regimens. To the best of the authors' knowledge, this is the first report of BEM in a patient treated with the nucleoside reverse transcriptase inhibitors (NRTIs) tenofovir DF and lamivudine along with the integrase strand transfer inhibitor dolutegravir in his clinic. In this case, even after the immediate cessation of both NRTIs and the introduction of monitoring on a protease inhibitor and a non-nucleoside reverse transcriptase inhibitor, there has been a gradual deterioration of vision with consequential persistent retinal toxicity[5]. This report and its accompanying discussion will highlight the critical clinical, anatomical, and physiological evidence for HIV-associated retinal toxicity and retinopathy, the role of pharmacovigilance in the post-marketing surveillance of antiretroviral drugs, and the current recommendations for the monitoring, management, and screening of patients receiving long-term anti-HIV therapy[1].

The current study underlines that BEM can occur with the latest generation of NRTIs. This has an important relevance given the widespread use of tenofovir DF for both the treatment and pre-exposure prophylaxis of HIV. It reaffirms the importance of clinic and optical coherence tomography screening even in the absence of complaints or sight threatening symptoms. Ocular and retinal toxicities can worsen even after the cessation of NRTIs and patients should be made aware of this risk. Increasing awareness amongst optometrists and routine retinal screening may allow for early diagnosis of NRTI-associated retinal toxicities. Lastly, concern surrounding this case highlights the growing importance to addiction to highly effective antiretroviral therapy and the need to continue monitoring for ocular side effects despite the wide-ranging safety profiles of antiretrovirals in use today.

References:

[1]. Mangioni, D., Bandera, A., Muscatello, A., Squillace, N., Crivellaro, C., Guerra, L., Messa, C., & Gori, A. Focal Bone Lesions In HIV-Positive Patient Treated With Tenofovir. BMC Infectious Diseases,2014: 14, 131. Https://Doi.Org/10.1186/1471-2334-14-131

[2]. Kozak, I., Sasik, R., Freeman, W. R., Sprague, L. J., Gomez, M. L., Cheng, L., El-Emam, S., Mojana, F., Bartsch, D. U., Bosten, J., Ayyagari, R., & Hardiman, G. A Degenerative Retinal Process In HIV-Associated Non-Infectious Retinopathy. Plos One, 8(9), E74712. Https://Doi.Org/10.1371/Journal.Pone.0074712

[3]. Kitagaki, T., Sato, T., Hirai, J., Kimura, D., Kakurai, K., Fukumoto, M., Tajiri, K., Kobayashi, T., Kida, T., Kojima, S., & Ikeda, T. A Case Of Proliferative Diabetic Retinopathy With HIV Infection In Which HAART Possibly Influenced The Prognosis Of Visual Function. Case Reports In Ophthalmology,2016: 7(3), 239–244. Https://Doi.Org/10.1159/000452789

[4]. Wong, K. L., Pautler, S. E., & Browning, D. J. Near-Infrared Reflectance Bull's Eye Maculopathy As An Early Indication Of Hydroxychloroquine Toxicity. Clinical Ophthalmology (Auckland, N.Z.),2015: 9, 521–525. Https://Doi.Org/10.2147/OPTH.S76963

[5]. Joharjy, H., Pisella, P. J., Audo, I., & Le-Lez, M. L. A Rare Case Of Didanosine-Induced Mid-Peripheral Chorioretinal Atrophy Identified Incidentally 11 Years After The Drug Cessation. Medicina (Kaunas, Lithuania),2022: 58(6), 735. Https://Doi.Org/10.3390/Medicina58060735

[6]. Hamzah, L., Jose, S., Booth, J. W., Hegazi, A., Rayment, M., Bailey, A., Williams, D. I., Hendry, B. M., Hay, P., Jones, R., Levy, J. B., Chadwick, D. R., Johnson, M., Sabin, C. A., & Post, F. A Treatment-Limiting Renal Tubulopathy In Patients Treated With Tenofovir Disoproxil Fumarate. Journal Of Infection, 2017: 74(5), 492–500. Https://Doi.Org/10.1016/J.Jinf.2017.01.010

[7]. Barteselli, G., Chhablani, J., Gomez, M. L., Doede, A. L., Dustin, L., Kozak, I., Bartsch, D. U., Azen, S. P., Letendre, S. L., & Freeman, W. R. Visual Function Assessment In Simulated Real-Life Situations In HIV-Infected Subjects. Plos ONE, 2014: 9(5). Https://Doi.Org/10.1371/Journal.Pone.0097023

[8]. Latif, N., Janani, M. K., Sudharshan, Selvamuthu, P., & Dutta Majumder, P. Triple Trouble: A Case Of Retinochoroiditis In A Patient With Syphilis, Tuberculosis, And Human Immunodeficiency Virus Infection. Indian Journal Of Ophthalmology,:2020 68(9), 1995–1997. Https://Doi.Org/10.4103/Ijo.IJO_2170_19