Utility of Fundus Fluorescein Angiography and Efficacy of Ranibizumab Intravitreal Therapy in Peripheral Retinal Vascular Abnormalities of Diabetic Patient: A Case Report

Suganya M.^{1*}, Maragatham S.²

¹Department of Sociology, Saveetha College of Nursing, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai, Tamil Nadu, India ²Department of Medical and Surgical Nursing, Saveetha College of Nursing, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai, Tamil Nadu, India

Abstract

Diabetes predominantly affects the microvascular circulation of the retina. Diabetic retinopathy is a severe complication of diabetes mellitus and a leading cause of diminution of vision. Preventing irreversible vision loss requires early diagnosis of retinal vascular abnormalities. Fundus fluorescein angiography (FFA) is the gold standard for assessing retinal vascular abnormalities and optical coherence tomography confirms the diagnosis. The purpose of this case report was to examine the effectiveness of ranibizumab intravitreal therapy in diabetic patients as well as the usefulness of FFA in evaluating peripheral retinal vascular abnormalities. A 67-year-old adult presented to the emergency department in a tertiary care hospital in Chennai, India, with the sudden onset of painless vision loss in the left eye. Due to irregular medication, he developed diabetic macular oedema. Optical coherence tomography confirmed the presence of macular edema in the left eye and consent was obtained for unilateral pan-retinal photocoagulation (PRP). Despite grid laser, the macular edema persisted and after PRP it was reduced. FFA assisted in treating macular oedema by detecting peripheral retinal ischaemia and administering anti-vascular endothelial growth factor injection (Ranibizumab). The patient's best-corrected visual acuity was improved from 6/36 to 6/9 in the left eye. Research are needed to improve glycaemic management and prompt therapies to help patients with diabetic retinopathy see better and live better lives.

Keywords: Diabetic Patient, Fundus Fluorescein Angiography, Intravitreal Therapy, Peripheral Retinal Vascular, Ranibizumab.

Introduction

Diabetic retinopathy (DR) is a severe complication of diabetes mellitus and a leading cause of diminution of vision [1]. Around the world, 700 million adults between the ages of 20 to 79 are predicted to have diabetes by the end of 2045 [2]. In DR, maintaining a balanced diet and managing self-care activities appropriately is essential [3]. The accumulation of comorbidities makes the ageing diabetic more fragile, especially in adults, and is linked to increased hospitalisation and death rates. Preventing irreversible vision loss requires early diagnosis of retinal vascular abnormalities [1]. Fundus fluorescein angiography (FFA) is the gold standard for assessing retinal vascular abnormalities in the macula and providing guidance for different treatments, while optical coherence tomography (OCT) confirms the diagnosis [4]. To lessen macular oedema, FFA detects peripheral retinal ischaemia. It induces retinal oedema, breaks down blood-retinal barriers, and releases vascular endothelial growth factor (VEGF) into the eyes [4].

Intravitreal anti-VEGF therapy is the highest standard for treating Diabetic Macular Edema (DME). Aflibercept and Ranibizumab are the two intravitreal anti-VEGF medications that the US FDA currently approves for the treatment of DME [5]. There are currently a few treatment options for diabetic retinopathy, such as anti-VEGF medications and laser photocoagulation, which are promising new therapeutics still in development. The Early Treatment Diabetic found Retinopathy Study that laser photocoagulation reduced the risk of moderate vision loss by up to 50% [6]. The purpose of this case report was to examine the effectiveness of ranibizumab intravitreal therapy in diabetic patients as well as the usefulness of FFA in evaluating peripheral retinal vascular abnormalities.

Case Report

A 67-year-old adult presented to the emergency department in a tertiary care hospital in Chennai, India, with the sudden onset of painless vision loss in the left eye associated with lower-extremity weakness. He had been diagnosed with type 1 diabetes mellitus (T1DM) twenty-five years ago. He did not have DR at the baseline. Oral hypoglycemic agents were prescribed for him to prevent the disease. At the beginning of 2024, due to irregular medication, he developed DME and his best-corrected visual acuity (BCVA) was 6/36 in the left eye which was to counting fingers (CF) at a 1m distance.

Fundus examination by direct ophthalmoscope revealed that he had visual complaints such as dot, blot haemorrhages and photophobia. OCT confirmed the presence of macular oedema in the left eye and showed areas of retinal leakage from numerous microaneurysms in the macular area (Fig. 1). DR was developed and progressed to PDR. The patient was prescribed to be under insulin therapy. The condition was explained to the patient and informed consent was obtained for unilateral pan-retinal photocoagulation (PRP). An initial grid laser treatment followed by two sessions of PRP was performed in the left eye. Despite grid laser, the macular edema persisted and after PRP it was reduced.



Figure 1. Horizontal (A, B, C) and Vertical (D) Sections and Maps on Optical Coherence Tomography (OCT) at A&B Baseline, and C&D after 2 Months. Sequential OCT Images Showing Gradual Reduction in Diabetic Macular Edema

A non-invasive imaging method called fundus fluorescein angiography enables physicians to identify minute vascular alterations in the macula and offers dynamic visualisation of the retinal blood vessels (Fig. 2). Because FFA can detect macular ischaemia, leaks, and neovascularisation, it has become a vital tool in the evaluation and treatment of diabetic maculopathy. A digital fundus camera fitted with a fluorescein filter was used to perform FFA. During the arterial, venous, and late phases, serial pictures of the retinal vasculature were taken following an intravenous injection of 5 ml of 10% sodium fluorescein dye. (Fig 2) FFA assisted in treating the macular oedema by detecting peripheral retinal ischaemia and administering anti-VEGF injections.

The ophthalmologist recommended the anti-VEGF medication (Ranibizumab) for the patient, and it was administered two weeks later. Ranibizumab is a monoclonal antibody fragment directed towards all isoforms of VEGF-A [7]. The unique structure of ranibizumab was specifically engineered for ocular disease. The patient's best-corrected visual acuity (BCVA) was improved from 6/36 to 6/9 in the left eye.



Figure 2. Colour Fundus Photography at Baseline Showing Retinal Hemorrhage and Cotton Wool Spots. At the Baseline, the early and Late Phases of Fluorescein Angiography Showing Retinal Leakage and Areas of Retinal Capillary Non-perfusion

Discussion

This case report describes in detail the utility of FFA and the efficacy of anti-VEGF injection (Ranibizumab) in the treatment of Peripheral Retinal Vascular Abnormalities in Diabetic Patients [8, 9]. FFA plays a significant role in the investigation of the peripheral retina, especially when the clinical manifestation is not evident. Peripheral retinal ischaemia can be detected with FFA, which aids in diagnosis, monitoring, and treatment by peripheral photocoagulation. The first biosimilar to ranibizumab in the world, Razumab, is approved for several macular conditions, including wet age-related macular degeneration (AMD) [10]. The safety and effectiveness of biosimilar ranibizumab in wet AMD were assessed by Sharma et al. In all, 126 patients from 16 Indian locations were recruited, given biosimilar ranibizumab, and added to the safety and immunogenicity groups. From the beginning to the completion of the trial, there was a considerable improvement in the Visual Functional Questionnaire (VFQ-25) scores [11, 12].

According to research, a 52-year-old male driver in Iran was initially diagnosed with type 2 diabetes mellitus five years prior but did not have diabetic retinopathy. Within a year of receiving a diagnosis of proliferative retinopathy, he lost his left eye's vision. In this instance, proliferative retinopathy has advanced due in large part to occupational stress brought on by the nature of the profession [13].

The Treat-and-Extend (T&E) regimen produced a clinically significant improvement in BCVA that was not worse than monthly therapy, according to the CANTREAT research. Compared to monthly dosage, the T&E dosing regimen with ranibizumab achieved these benefits with fewer injections and visits, potentially increasing convenience and lowering costs to the healthcare system [14]. Researches are needed to improve glycaemic management and prompt therapies to help patients with diabetic retinopathy see better and live better lives. To fully comprehend the underlying mechanisms and risk factors causing peripheral retinal vascular abnormalities, more investigation and largerscale studies are required.

References

[1]. Raka, M., Daigavhane, S., & Patil, A. A., 2022, Clinical case report of diabetic retinopathy. *Asian J Biomed Pharmaceut Sci*, 12(90),128. https://www.alliedacademies.org/articles/a-clinicalcase-report-of-diabetic-retinopathy.pdf

[2]. International Diabetes Federation, 2019, IDF Diabetes Atlas, 9th ed. Brussels, Belgium, *International Diabetes Federation*, https://dnet.idf.org/en/library/542-idf-diabetes-atlas-2019-9th-edition.html

[3]. Suganya, M., & KalaBarathi, S., 2024, Association of body mass index with dietary intake and self-care health activities of mothers after postpartum: A mixed-method research in Chennai City, India. *Int J Nutr Pharmacol Neurol Dis*, 14, 52-7. https://doi.org/10.4103/ijnpnd.ijnpnd_71_23

[4]. Sultana, A., 2023, Role of fundus fluorescein angiography in identifying the unexplained visual loss due to macular edema in peripheral retinal diseases. *Indian J Clin Exp Ophthalmol*, 9(1), 53-59. https://doi.org/10.18231/j.ijceo.2023.011

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Conflict of Interest

The authors declare that they have no conflict of interest that could have appeared to influence the work reported in this paper.

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[5]. Farheen, Naz., & JenilaRani, D., 2022, Detection and Comparison of Diabetic Retinopathy using Thresholding Algorithm and CMeans Clustering Algorithm, *Journal of Pharmaceutical Negative Results*, 14(4). https://www.pnrjournal.com/index.php/home/articl e/view/899

[6]. Bhuvaneswari, R., Diviya, M., Subramanian, M., Maranan, R., & Josphineleela R., 2023, Hybrid generative model for grading the severity of diabetic retinopathy images. *Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization*, 11(7). https://doi.org/10.1080/21681163.2023.2266048

[7]. Woo, S. J., Cho, G. E., & Cho, J. H., 2019, Short-term Efficacy and Safety of Ranibizumab for Neovascular Age-related Macular Degeneration in the Real World: A Post-marketing Surveillance Study. *Korean J Ophthalmol.* 33(2), 150-166. https://doi/10.3341/kjo.2018.0081

[8]. Ramakrishnan, A., Veeramani, P. A., & et al, 2024, Association of Various Optical Coherence Tomographic Patterns of Diabetic Macular Edema with Central Subfield Thickness and Visual Acuity: A Cross-Sectional Observational Study. *Cureus*. 19,16(9). https://doi/10.7759/cureus.69731

[9]. Suganya, M., & Kalabarathi, S., 2024, Efficacious Maintenance-Electroconvulsive Therapy (m-ECT) and Antipsychotic Medication for Schizophrenia Spectrum Disorder in a Young Adult Woman in Chennai, India: A Case Report. International Journal of Nutrition, Pharmacology, Neurological Diseases, 14(3),390-392. https://doi.org/10.4103/ijnpnd.ijnpnd_42_24

[10]. American Academy of Ophthalmology, 2020,Age-relatedmaculardegeneration.https://www.aao.org/bcscsnippetdetail.aspx?id=9711f063-ed7b-452b-8708-c4dad0d893e8.

[11]. Sharma, S., Gupta, V., Maiti, A., & et al., 2021, Safety and efficacy of RazumabTM (world's first biosimilar ranibizumab) in wet age-related macular degeneration: a post-marketing, prospective ASSET study, *Int J Retin Vitr.* 24(7). https://doi.org/10.1186/s40942-021-00293-w

[12]. Suganya, M., & Maragatham, S., & Sheela, P., 2024, Assessment on Health Status of Adult Patients with Osteoarthritis of the Lower Limb by Western Ontario and McMaster's Universities Osteoarthritis Index (WOMAC): A Study in Chennai City. *Texila International Journal of Public Health*. Special Issue:1-8.

https://doi.org/10.21522/TIJPH.2013.SE.24.02.Art 007

[13]. Ebrahimi, M. H., & Gharibi, H., 2016, A case study of a patient with diabetic retinopathy. Diab Met Syndr: *Clin Res Rev.* http://dx.doi.org/10.1016/j.dsx.2016.01.022

[14]. Kertes, P. J., Galic, I. J., Greve, M., & et al., 2020, Efficacy of a Treat-and-Extend Regimen with Ranibizumab in Patients with Neovascular Age-Related Macular Disease: A Randomized Clinical Trial. *JAMA Ophthalmol.* 138(3), 244–250. https://doi/10.1001/jamaophthalmol.2019.5540