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**Case Report**

# A Rare Case of Newly Diagnosed Type 2 Diabetes with Bilateral Cystoid Macular Edema Treated with Intravitreal Ranibizumab

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**Abstract:**
Diabetic macular edema is caused by retinal vasculature alterations. Diagnosis involves binocular slit-lamp biomicroscopy, FA leakage, and OCT data. Macular edema is a complex and multifaceted disease. Disruption of the blood-retinal barrier can lead to fluid accumulation in the macula. An anti-VEGF drug, intravitreal ranibizumab, inhibits blood vessel growth by interrupting VEGF's receptor interface. In our case, though the patient is denovo diabetic, chronic hypertension and hyperlipidemia are significant risk factors for macular edema. The patient is taking metformin, telmisartan, and atorvastatin. High blood glucose levels, poor adherence to oral hypoglycemic agents, and an inappropriate diet are the reasons for the repeated administration of intravitreal ranibizumab injections, which lead to financial burden and poor quality of life in patients.
**Keywords:** Diabetes, anti-VEGF drug, diabetic macular edema, nonproliferative diabetic retinopathy.

## Introduction

The number of people with diabetes mellitus (DM) is approximately 347 million. By 2030, 430 million people would likely have DM worldwide, according to predictions **(**Varma R *et al*., 2014**)**. When the retina thickens within two disc diameters of the foveal center, the condition is known as diabetic macular edema.

Macular edema (ME), which is defined by vascular leakage and fluid accumulation brought on by pathologic alterations in the retinal vasculature, can cause irreparable structural damage and result in lifelong blindness. It is diagnosed using binocular slit-lamp biomicroscopy, leakage on FA, and, more recently, OCT (optical coherence tomography) data that provides both qualitative and quantitative data on retinal structure and thickness **(**Tawfek AZ, 2022**)**.

The underlying pathophysiology of ME is complicated, poorly understood, and multifaceted **(**Vujosevic S, 2015**)**. Based on a number of clinical studies, the inner barrier is where most vascular leakage that causes degenerative (DME) occurs. When the blood-retinal barrier (BRB) is disrupted, there is an aberrant inflow of fluid into the neurosensory retina that may be greater than the outflow, which can result in fluid accumulation in the intraretinal layers of the macula. (Simons M, 2016).

The blood-retinal barrier is breached and capillary permeability is increased when vascular endothelial growth factor (VEGF) is upregulated in response to hypoxia (Hwang TS *et al*., 2016). The retina contains a variety of cells, including capillary endothelial cells, pericytes, pigment epithelial cells, neurons, and astrocytes, which all produce VEGF. VEGF affects various types of retinal cells, although its main target is the capillary endothelial cell. Intravitreal ranibizumab, a recombinant humanized IgG monoclonal antibody fragment that adheres to and suppresses VEGF, is the first anti-VEGF drug to receive FDA approval. Ranibizumab, approved for treating macular edema and diabetic macular edema, inhibits the growth of new blood vessels by interrupting VEGF's receptor interface (Smiddy WE, 2012).

Most recently, it was approved in 2015 for patients with diabetic retinopathy(Kebede*et al*., 2017).Clinical studies have shown that anti-VEGF medication ensures the best increase in visual acuity (VA), despite the fact that patients' socioeconomic burden increases. Actually, compared to other standard therapies for DME, the cost per quality-adjusted life year is significantly higher. Although rare but severe, the negative effects of anti-VEGF therapy, such as endophthalmitis and life-threatening atherothrombotic disorders, outweigh the positive effects. Three main regimens, namely fixed monthly or biweekly, pro re nata (PRN), and treat-and-extend (TAE), can be used to treat DME, taking into account the half-lives of the drug in the vitreous humor. According to the research, anti-VEGF medications affect the disturbed BRB quickly and directly while acting on the resolution of DME slowly and indirectly **(**Almutairi NM, 2021**).**

## Case Report

A 52-year-old male patient who is non-alcoholic and vegetarian visited the endocrinology department for a second review. He had a known case of denovo diabetes for 2 months and hypertension and hyperlipidemia for 12 years, using metformin 500mg twice a day, telmisartan 40mg once a day (OD), and atorvastatin 40 mg OD. During the patient interview by the clinical pharmacist, we came to know he frequently skipped the doses due to his busy lifestyle and poor knowledge of the complications of diabetes. Patient complained of blurred vision and floaters. As per endocrinologist advice, he consulted a retina specialist, who suggested an optical path difference analyzer (OPD), revealed macula hemorrhages, microaneurysms, and hard exudates found in the fundus of both eyes, and a retina specialist suggested OCT (optical coherence tomography), and this test revealed clinically significant macular edema (CSME), mild nonproliferative diabetic retinopathy in both eyes, and advised intravitreal anti-VEGF injection in the left eye and glycemic control to prevent the disease progression. After the first intravitreal ranibizumab injection, the OCT results showed that the left eye's macula hemorrhages, microaneurysms, and hard exudates had somewhat improved. It was advised to consult an endocrinologist for better glycemic control.

Metformin (500 mg), glimepiride (2 mg), and Vidagliptin (50 mg) were recommended by the endocrinologist, along with clinical pharmacist consultation for a diet chart, patient counseling for medication, and an efficient, balanced diet for better glycemic management. The patient continued the same treatment and diet for 1 year with frequent monitoring of FBS and HbA1C.

The patient was apparently normal for 1 year, and then he developed the same complaints of blurred vision. Upon being asked by a retinal specialist, he answered that he missed the medication and was not continuing a balanced diet due to his busy lifestyle. OCT findings of the left eye revealed macula-microaneurysms, altered foveal reflex, diffuse thickening of the fundus, and moderate nonproliferative diabetic retinopathy (NPDR) changes. Right eye also had moderate NPDR changes; patients had bilateral NPDR changes, worsening of left eye disease progression. This shows the importance of glycemic control and medication adherence in chronic disease patients. Retina specialists are advised to take a second intravitreal ranibizumab

injection and to have frequent retinal checkups with RBS and HbA1c monitoring.

After one month, the patient re-visited the retina specialist with RBS and HbA1c reports, which revealed poor glycemic control with HbA1c of 8.4%. Upon OCT, the doctor advised the patient to take a third intravitreal ranibizumab injection and to follow a low-carbohydrate diet with regular exercise and regular monitoring of capillary blood glucose with a CBG kit at home. The patient has received seven intravitreal ranibizumab injections so far; despite poor glycemic control and noncompliance with oral hypoglycemic medicine, the patient's condition has not improved. All these factors contributed to the economic burden on patient due to the high cost of ranibizumab and compromised quality of life.

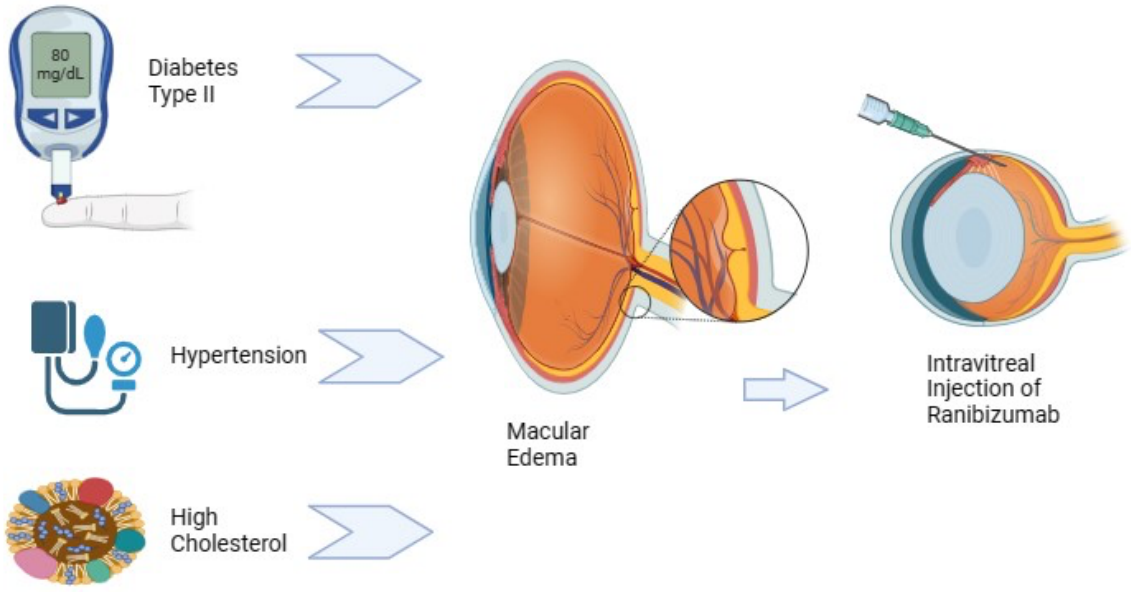


**Fig 1: Graphical representation of case report**

## Discussion

In this case, the patient was diagnosed with cystoid macular edema, clinically significant macular edema, and non-proliferative diabetic retinopathy. The most fascinating thing in this case is that the patient was de novo diabetic and had chronic, uncontrolled hypertension and chronic hyperlipidemia with elevated total cholesterol, triglyceride, and LDL levels. A few studies revealed that approximately half (51%) of diabetic retinopathy (DR) develops in the first five years, especially in young adults (Padhy S, 2018). Another study showed the cutoff HbA1C of 6.6% with a duration of 8.2 years is the average time to develop diabetic retinopathy (Ehrlich R, 2008**).**

In our case, the patient has had chronic, uncontrolled hypertension with an average blood pressure of 175 mmHg for 2 months. This indicates that elevated blood pressure is a significant risk factor for developing macular edema. In this case, an acute rise in blood pressure may lead to exudative changes in the form of macular edema, hemorrhages, and serous macular detachment that can lead to visual decline. Persons with hypertension at baseline were approximately two to three times more likely to develop neovascular macular degeneration after 10 years. (Chen CH, 2023)

Few studies have shown that anti-hyperlipidemic medications will reduce the incidence of age-related macular degeneration (AMD) (Zhang YP *et al*., 2022). Patients with hyperlipidemia had a considerably higher risk of

age-related macular degeneration (AMD) than patients without hyperlipidemia. We address hyperlipidemia as the second important risk factor for CME, as the patient in our case had chronic hyperlipidemia and poor diet control. In our case, we identified three major risk factors contributing to the development of CME, NPDR, and AMD: hyperlipidemia, hypertension, and, though the patient has denovo diabetes, elevated blood glucose levels are also one of the established reasons for NPDR with poor glycemic control.

## Conclusion

All three major risk factors were preventable in this case if they were diagnosed early and managed. This proves that early detection of lifestyle disorders and treatment with both pharmacological and non-pharmacological therapy will prevent complications. Reduce economic burden because the cost of ranibizumab intravitreal injection is around 30000 INR, reduce the length of hospital stay, and improve the quality of life of patients.

## Limitations

Unfortunately, after few months patient haven't visited the hospital so we missed the disease progression.

## Author Contributions

All authors contributed equally in case collection, case interpretation, and regular follow ups, Nikitha designed the case report draft and scrutinized for corrections.

## List Of Abbreviations

OCT: Optical coherence tomography; VEGF: Vascular Endothelial Growth Factor,ME: Macular edema; PRN: Pro renata, TAE: Treat-and-extend; NPDR: Non proliferative diabetic retinopathy; CBG: Capillary blood glucose; LDL: Low Density Lipoprotein;OPD: Optical path difference analyzer; CSME: clinically significant macular edema;AMD:Age-related macular degeneration.

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## Ethical Approval

Patient consent is obtained prior to case collection and manuscript submission.

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