MEDICUS

ISSN 1409-6366 UDC 61 Vol · 28 (1) · 2023

Original scientific paper

Profesional paper

Review

Case report

DIABETIC MACULAR EDEMA (DME)

Gazmend Mehmeti[1], Vesna Cheleva[1,2], Jana Nivicka Kjaeva[1,2], Hristian Duma[1,2]

[1]University Clinic for Eye Disease - Skopje
[2]Ss. Cyril and Methodius University - Medical Faculty - Skopje

Corresponding address:
Dr.Gazmend Mehmeti
University Clinic for Eye Disease - Skopje,
Republic of North Macedonia
e-mail: mendi750@hotmail.com

Medicus 2023, Vol. 28 (1): 120-124

ABSTRACT

Diabetic macular edema (DME) is a common complication of diabetes and a leading cause of vision loss among diabetic patients. It is characterized by the accumulation of fluid in the macula, the central part of the retina responsible for sharp and detailed vision. DME occurs when high blood sugar levels damage the tiny blood vessels that supply nutrients to the retina, leading to leakage of fluid and other substances into the macula.

DME can cause blurred or distorted vision, making it difficult for patients to read, drive, or perform other activities that require sharp vision. The condition can also lead to permanent vision loss if left untreated. Treatment options for DME include lifestyle changes such as controlling blood sugar levels, managing blood pressure and cholesterol, and administering medications such Anti-VEGF, to reduce swelling in the macula. In some cases, laser therapy may also be used to treat the condition.

Early detection and treatment of DME are crucial to prevent permanent vision loss. Diabetic patients should receive regular eye exams to detect any signs of DME, and those diagnosed with the condition should work closely with their healthcare providers to manage their diabetes and prevent further damage to the retina. Ongoing research aims to develop new treatments for DME that may improve outcomes for patients with this condition.

INTRODUCTION

Diabetic Macular Edema (DME) is a retinal disorder that results from the accumulation of fluid in the macula due to increased vascular permeability and breakdown of the blood-retinal barrier in patients with diabetes mellitus. This can lead to swelling and thickening of the macula, which may cause vision impairment and, in severe cases, permanent vision loss. DME is a common complication of diabetes and is associated with chronic hyperglycemia, hypertension, and dyslipidemia. (2)

Chronic hyperglycemia is a key factor in the development of DME, which leads to disruption of the blood-retinal barrier (BRB), resulting in leakage of fluid and other molecules into the retina. The loss of pericytes and breakdown of endothelial cell junctions within the BRB contribute to this process. In addition, inflammation and oxidative stress play important roles in the development and progression of DME, with multiple cytokines and chemokines implicated in the disease. The neurovascular unit, which consists of various retinal cells, also undergoes significant changes in DME. Chronic hyperglycemia and inflammation, can lead to upregulation of VEGF expression in the retina. The overproduction of VEGF

in the retina can cause abnormal blood vessel growth and leakage of fluid and other molecules into the macula, leading to DME. VEGF also contributes to the inflammation and oxidative stress associated with DME, exacerbating the damage to retinal cells. (2,9)

The prevalence of DME varies depending on the population and the diagnostic criteria used. According to the World Health Organization (WHO), the global prevalence of diabetic retinopathy (DR), which includes DME, is estimated to be 34.6% among people with diabetes aged 20-79 years. The prevalence of DME is known to increase with longer duration of diabetes and poor glycemic control. Other factors that may increase the risk of DME include hypertension, hyperlipidemia, and impaired renal function. The risk factors for DME include, diabetes mellitus, poor glycemic control - high levels of hemoglobin A1c (HbA1c), duration of diabetes, hypertension, hyperlipidemia, obesity, smoking, genetics, gender and age, kidney disease. (1)

SIGNS

The signs of DME can include:

Blurred or distorted vision, or reduced central vision. Straight lines may appear wavy, and colors may appear less vibrant. Reduced color sensitivity. Dark spots or shadows to appear in the central field of vision. Difficulty reading or recognizing faces other activities that require detailed vision. Rapid changes in vision. It is important to note that in some cases, DME may not cause any noticeable symptoms in the early stages. That is why it is crucial for diabetic patients to have regular eye exams to detect any signs of DME early and prevent vision loss. (2,1,9)

PREVENTION

Preventing DME involves managing the underlying condition of diabetes and its associated risk factors. Here are some ways to prevent DME:

Control blood sugar levels through a combination of diet, exercise, and medication. Control blood pressure and cholesterol levels through lifestyle changes and medication. Quit smoking. Regular eye exams can prevent further damage and vision loss. Maintain a healthy weight through a balanced diet and regular exercise. (8)

DIAGNOSIS

DME can be diagnosed through a comprehensive eye exam, which may include the following: best visual acuity test using an eye chart, dilated eye exam, optical coherence tomography (OCT). Three basic structural changes can be seen: retinal swelling, cystoid macular edema, subretinal fluid. (10)

These types are center-involved DME and non-center involved DME. Center-involved DME is defined as the presence of fluid within 1,000 µm of the fovea. Non-center involved DME, is characterized by fluid accumulation in areas of the macula outside of the central 1,000 µm.

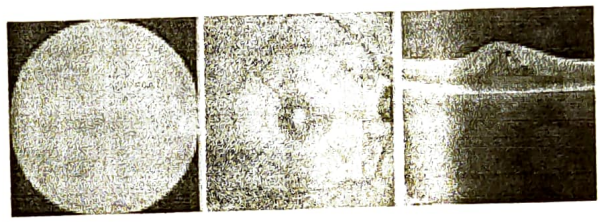

Image 1: Center-involved DME

Image 2: Non-center involved DME

Fluorescein angiography (FA): This test involves injecting a special dye into a vein in the arm and taking pictures of the retina as the dye flows through the blood vessels. FA can help to detect leaking blood vessels and areas of abnormal blood flow in the retina.

Tonometry: This test measures the pressure inside the eye and can help to detect glaucoma, which is a potential complication of DME.

DIFFERENTIAL DIAGNOSIS

The following conditions may be considered in the differential diagnosis of diabetic macular edema (DME): Age-related macular degeneration (AMD), Central serous chorioretinopathy (CSC), Retinal vein occlusion (RVO), Uveitis, Epiretinal membrane (ERM), Vitreomacular traction (VMT)

TREATMENT

Medical therapy is an important part of the management of diabetic macular edema (DME). The following are some of the medical therapies used to treat DME:

Intravitreal injections: The most commonly used medication for DME is anti-vascular endothelial growth factor (anti-VEGF) agents, such as bevacizumab, ranibizumab, and aflibercept. These medications help reduce inflammation and improve macular edema by blocking the activity of VEGF, which is a key contributor to the development of DME. Here are some key points about anti-VEGF treatment for DME:

Frequency of injections: The frequency of injections depends on the specific anti-VEGF medication used and the individual patient's response to treatment. In general, injections are given at regular intervals, typically every 4-8 weeks, until the macular edema is resolved or stabilized.

Potential side effects: The most common side effects of anti-VEGF injections include eye pain, redness, and inflammation. There is also a small risk of more serious side effects, such as infection or retinal detachment, although these are rare.

Efficacy: Anti-VEGF injections have been shown to be highly effective in reducing macular edema and improving visual outcomes in patients with DME. In clinical trials, a significant proportion of patients treated with anti-VEGF injections experienced improvement in visual acuity and reduction in macular edema. (4,5)

Corticosteroids: Corticosteroids are another class of medications that can be used to treat DME. They work by reducing inflammation in the eye and reducing fluid accumulation in the macula, leading to improved vision. Examples of corticosteroids used to treat DME include triamcinolone acetonide and dexamethasone. Here are some key points about corticosteroid treatment for DME:

Frequency of injections: The frequency of corticosteroid injections depends on the specific medication used and the individual patient's response to treatment. In general, injections are given at regular intervals, typically every 4-6 months for sustained-release implants, and every 4-8 weeks for other types of injections.

Potential side effects: Corticosteroids can have side effects, such as increased intraocular pressure (IOP), cataract formation, and infection. Regular monitoring of IOP and other side effects is necessary during treatment. (11,12)

Laser photocoagulation: This is a procedure that uses a laser to create small burns in the retina. The burns help seal leaking blood vessels and reduce macular edema. Laser photocoagulation is typically used in cases of focal DME, where the edema is confined to a specific area of the retina. Here are some key points about laser photocoagulation treatment for DME:

Frequency of treatment: The frequency of laser photocoagulation treatment depends on the severity and location of the macular edema. In general, one or more sessions of laser treatment may be necessary to achieve the desired reduction in macular edema.

Potential side effects: Laser photocoagulation can cause side effects such as mild discomfort, blurry vision, and decreased color vision. Rarely, more serious side effects such as retinal detachment or scarring can occur. (6)

Combination therapy: Some cases of DME may require combination therapy, which involves using two or more treatments together. For example, anti-VEGF injections may be combined with laser photocoagulation or corticosteroid injections to achieve better outcomes. Here are some of the combination therapies that may be used to manage DME: Anti-VEGF injections plus laser photocoagulation, Anti-VEGF injections plus corticosteroids, Anti-VEGF injections plus vitrectomy and triple therapy. (5,6,11)

Glycemic control and blood pressure management: Tight control of blood glucose and blood pressure levels is important in preventing and managing DME.

There are several future directions for the management for diabetic macular edema (DME) that show promise in improving visual outcomes for patients. Here are some of the modern and futuristic treatments: Personalized medicine: Advances in genetic and biomarker testing may enable the development of personalized treatment plans for patients with DME. Sustained-release drug delivery systems: such as implants or hydrogels, can be used to deliver medications directly to the retina over an extended period of time. This approach may reduce the need for frequent injections and improve treatment adherence. Nanoparticle-based therapies: can be used to deliver drugs directly to cells in the retina, increasing the effectiveness of treatment and reducing side effects. Stem cell therapies: involve using stem cells to regenerate damaged retinal cells and promote healing. This approach has shown promise in preclinical studies for treating

DME. Advances in artificial intelligence and machine learning may enable more precise and efficient diagnosis and treatment of DME. Machine learning algorithms may be used to analyze imaging data and guide treatment decisions, as well as to develop predictive models for treatment response. Ongoing research is focused on the development of new drugs for the treatment of DME, including novel anti-inflammatory agents, gene therapies, and sustained-release drug delivery systems. (7)

TREATMENT COMPLICATION

Like any medical treatment, there are potential complications associated with the treatment of diabetic macular edema (DME). The most common side effects of anti-VEGF injections include eye pain, redness, and inflammation. There is also a small risk of more serious side effects, such as infection, retinal detachment, or an increase in intraocular pressure (IOP), although these are rare. Corticosteroids can have side effects, such as an increase in IOP, cataract formation, and infection. Regular monitoring of IOP and other side effects is necessary during treatment. Laser photocoagulation can cause side effects such as mild discomfort, blurry vision, and decreased color vision. Rarely, more serious side effects such as retinal detachment or scarring can occur. Vitrectomy is a surgical procedure that involves removing the vitreous gel in the eye. This procedure carries risks such as bleeding, infection, and retinal detachment.

The potential complications associated with DME treatments are relatively low, and most can be effectively managed with close monitoring and appropriate medical management. Patients undergoing DME treatment should be aware of the potential risks and discuss any concerns with their ophthalmologist. (3,4,5,6,11)

PROGNOSIS

The prognosis for diabetic macular edema (DME) depends on several factors, including the severity of the edema, the duration of diabetes, the presence of other medical conditions, and the response to treatment. In general, the earlier DME is detected and treated, the better the prognosis for visual outcomes.

Patients with mild to moderate DME who receive timely treatment with anti-VEGF injections, corticosteroids, laser photocoagulation, or a combination of these therapies, can expect significant improvement in visual acuity and reduction in macular edema. However, in cases of advanced or refractory DME, visual outcomes may be less favorable.

In addition, patients with DME who have poor glycemic control or uncontrolled hypertension may be at higher risk for progression of the disease and poor visual outcomes. Regular monitoring of blood glucose, blood pressure, and other medical conditions is important in managing DME and improving prognosis.(2,9)

CONCLUSION

Diabetic macular edema (DME) is a common complication of diabetes mellitus that affects the macula, the central part of the retina responsible for fine visual acuity. It is characterized by the accumulation of fluid in the macula, which can result in vision loss and distortion.

DME is caused by the disruption of the blood-retinal barrier due to chronic hyperglycemia, which leads to endothelial cell junction breakdown and pericyte loss. This results in interstitial fluid accumulation within and underneath the retina through leakage of molecules dependent on intact cell-to-cell junctions.

Risk factors for DME include longer duration of diabetes, poor glycemic control, hypertension, hyperlipidemia, and impaired renal function.

Diagnosis of DME involves a comprehensive eye exam, including a dilated fundus exam, optical coherence tomography (OCT), and fluorescein angiography.

Treatment options for DME include anti-vascular endothelial growth factor (VEGF) injections, corticosteroids, laser photocoagulation, and combination therapies. Tight glycemic and blood pressure control, as well as lifestyle modifications, are also important in preventing and managing DME.

The prognosis for DME depends on several factors, including the severity of the edema, duration of diabetes, and response to treatment. Ongoing research is focused on developing new treatments and improving existing therapies to better manage and prevent DME.

REFERENCES

1. Yau JWY, Rogers SL, Kawasaki R, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35(3):556-564. doi: 10.2337/dc11-1909
2. Solomon, S. D., Chew, E., Duh, E. J., Sobrin, L., Sun, J. K., VanderBeek, B. L., Wykoff, C. C., & Gardner, T. W. (2017).

Diabetic retinopathy: a position statement by the American Diabetes Association. Diabetes Care, 40(3), 412-418. Link: https://care.diabetesjournals.org/content/40/3/412

3. Schmidt-Erfurth, U., Garcia-Arumi, J., Bandello, F., Berg, K., Chakravarthy, U., Gerendas, B. S., ... & Wolf, S. (2017). Guidelines for the management of diabetic macular edema by the European Society of Retina Specialists (EURETINA). Ophthalmologica, 237(4), 185-222. Link: https://www.karger.com/Article/FullText/478732
4. Jaffe GJ, Burton TC, Kuhn E, Prescott A, Hirsch J. Anti-VEGF therapy for diabetic macular edema: 2019 update. Ophthalmology. 2020;127(1):1-2. doi: 10.1016/j.ophtha.2019.09.012.
5. Korobelnik JF, Do DV, Schmidt-Erfurth U, et al. Intravitreal aflibercept for diabetic macular edema. Ophthalmology. 2014;121(11):2247-2254. doi: 10.1016/j.ophtha.2014.05.006.
6. Early Treatment Diabetic Retinopathy Study Research Group. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Arch Ophthalmol. 1985;103(12):1796-1806. doi: 10.1001/archopht.1985. 01050120030015.
7. Published 2020. Accessed March 15, 2023. Nicholson L, Ramu J, Triantafyllopoulou I, Taylor SRJ. New and future treatments for diabetic macular oedema. Eye. 2021;35(6):1667-1677. doi: 10.1038/s41433-021-01410-6.
8. American Diabetes Association. Standards of medical care in diabetes--2022. Diabetes Care. 2022;45(Suppl 1):S1-S220. doi: 10.2337/dc22-S001.
9. Bandello, F., Lattanzio, R., Zucchiatti, I., & Del Turco, C. (2013). Pathophysiology and treatment of diabetic retinopathy. Acta Diabetologica, 50(1), 1-20. Link: https://link.springer.com/article/10.1007%2Fs00592-012-0449-3
10. Otani, T., Kishi, S., & Maruyama, Y. (1999). Patterns of diabetic macular edema with optical coherence tomography. American Journal of Ophthalmology, 127(6), 688-693. Link: https://www.sciencedirect.com/science/article/pii/S0002939499001403
11. Haller, J. A., Bandello, F., Belfort, R., Blumenkranz, M. S., Gillies, M., Heier, J., ... & Li, J. (2010). Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. Ophthalmology, 117(6), 1134-1146. Link: https://www.sciencedirect.com/science/article/pii/S0161642010000914
12. Campochiaro, P. A., Brown, D. M., Pearson, A., Chen, S., Boyer, D., Ruiz-Moreno, J., ... & FAME Study Group. (2012). Sustained delivery fluocinolone acetonide vitreous inserts provide benefit for at least 3 years in patients with diabetic macular edema. Ophthalmology, 119(10), 2125-2132. Link: https://www.sciencedirect.com/science/article/pii/S0161642012006853