ORIGINAL RESEARCH

Diabetic Retinopathy and Macular Edema in Clinical Pathology

Prakhar Kumar

Department of Opthalmology, Rama Medical College & Research Centre, Hapur, U.P, India

Corresponding Author
Prakhar Kumar
Department of Opthalmology, Rama Medical College & Research Centre, Hapur, U.P, India

Received: 13 February, 2016 Accepted: 16 March, 2016

ABSTRACT
Diabetic retinopathy and macular lump are complicated diseases. VEGF plays an important role in the pathological process of non-chronic diabetic macular lump, and VEGF blockade agents can improve vision. In chronic diabetic macular lump, inflammatory cy- tokines are the main driver of lump, and intravitreal steroids can lead to lump resolution. However, vascular part isn't always the cause of macular thickening and visual loss from non-vascular parts.

INTRODUCTION

Diabetic retinopathy and macular lump is answerable for vision loss in operating cohort thanks to symptom, once approaching patients with diabetic retinopathy, it's essential to know the underlying pathological mechanisms so as to personalized treatment as diabetic retinopathy and macular lump is complex complicated malady. loads of agents or procedures area unit offered for targeting varied pathological mech- anisms, like VEGF, inflammatory, or vitreomacular abnormality, but optimum treatment results may be achieved by exploitation the proper agent or procedure at the proper place.

MACULAR LUMP

Macular thickening and cyst formation area unit thanks to fluid accu- mulation as a {result of|thanks to|attributable to} exaggerated vascular permeableness as a result of inner blood retinal barrier break down once loss of pericytes and thickened basement membrane iatrogenic by symptom, this method is ruled by multiple and complicated factors and mechanisms like vascular , inflammatory and organic chemistry[1].

Macular lump may be iatrogenic by one or multiple factors at identical time, and it's necessary to know that pathological process mechanism may be modified from one to a different. the simplest thanks to target-pathological factors in clinical follow is to know it mechanism verities, diabetic macular lump may be iatrogenic by vascular and non-vascu- lar (vitreomacular abnormality) parts and generally mixed wherever vascular is in term may be given as anaemia or non-ischemic, wherever the latter may be as chronic or non-chronic course (Figure 1).

VASCULAR PART NON-ISCHEMIC

Non-chronic disease: once diabetic macular lump starts to develop the most mechanism is vascular disfunction, and acute inflammation in- flicting drive and so ruled by upregulated vascular epithelium protein (VEGF) and alternative inflammatory cytokines[2] like IL-1b, IL-6, IL-8, and MCP-1, wherever in non- chronic malady VEGF could play major role in pathological process and targeting it by VEGF blockade agents will cause macular lump resolution. VEGF may be targeted by obstruction the VEGF receptor exploitation being antibodies like Ranibizumab or Bevacizumab that they inhibit VEGF-A isoforms, or by housing VEGF exploitation fusion proteins like Afliber- cept, ziv-aflibercept, or conbercept that they inhabit VEGF-A VEGF-B, and PIGF.

Clinical trials have evaluated the security and effectiveness of intravitre- al VEGF-blockade agents for diabetic macular lump treatment and com- pered it head to go and with alternative treatment modalities like optical device and steroids. the most outcome of those clinical trials is that the following:- VEGF blockade agents area unit safe and effective to use for diabetic macular lump [3] (Figure 2).-VEGF blockade agents area unit superior to optical device treatment alone and to steroids in a very future follow-up [4]. -There isn't a lot of deference in visual out return once combining intravitreal VEGF blockade agents with optical device treatment in distinction to intravitreal VEGF blockade agents alone [5].

-Patients with central diabetic macular lump that

received intravitreal VEGF blockade agents as differed treatment didn't gain visual edges as those that received VEGF blockade agents at baseline perhaps thanks to permanent purposeful injury or diabetic macular lump has adopted chronic course [6]. -Patients could edges equally to any or all VEGF blockade agents once BCVA is sweet at baseline wherever Aflibercept showed additional efficacies within the first twelve months follow up once BCVA is worse at baseline [7].

This cascade of events may be shot down exploitation intravitreal ste- roids, commercially intravitreal steroids area unit offered in 3 forms: Aristopak Acetonide, corticoid zero, seven mg perishable implant and FluocinoloneAcetonide Implant zero.19 mg non- perishable implant.

A lot of trails have studied the security and effectiveness of intravitreal steroids and that they ended the subsequent Intravitreal steroids area unit safe and effective for diabetic macular lump treatment [9].-Intravitreal steroids will resolve persistent diabetic macular lump which can not re- spond well to alternative treatment modalities [10]. Intravitreal steroids induce risk of exaggerated intra ocular pressure and cataract formation
[11,12].

ISCHEMIC

Ischemic maculopathy isn't caused by exaggerated by vascular escape, it's iatrogenic by microvascular blockage and enlargement, with cap- illary loss and adjacent lump. Clinically diabetic anaemia maculopa- thy seems as feature less tissue layer and diagnosed exploitation glow in X-ray photography that seems as enlarged or irregular FAZ (foveal avascular zone) (Figure 4). In cases of considerable ischaemia, visual prognosis is poor and sadly no helpful treatment is on the market.

CHRONIC DISEASE

because the diabetic macular lump becomes long standing the fluid es- cape become diffuse and cause photoreceptor loss (Figure 3) inflam- mation ruled by mediators like MCP-1, TNF-α, IL-1b, IL-6, IL-8, and IP- ten wherever VEFG might not play a major role and so make a case for the poor response to intravitreal VEGF blockade agents in chronic DME. the method of chronic inflammation itself isn't self-resolving re- sulting in tissue stress and it any injury with exaggerated sub retinal glia accumulation which is able to cause additional fluid leak iatrogenic by leukostasis and cytotoxic impact (8).

NON-VASCULAR ELEMENT

Not all macular thickening in diabetic patients are originated from vas- cular elements sometimes non-vascular element can cause macular thickening and visual loss, the most common non vascular element is vitreomacular abnormality which cause macular traction. Macular trac- tion can be presented as anterior posterior traction due to liquefied core vitreous or tangential traction which can feature either epiretinal membrane due to vitreoschi- sis, or taut vitreous due to glial cell proliferation or contracted lamel- lae. These vitreomacular abnormalities are governed by several mech- anisms such as non-enzymatically cross linking of vitreous collagen along with glial cells and inflammatory cells infiltration and deposition of glial fibrillary acidic protein and cytokeratin.

The best way to diagnose vitreomacular abnormality is by OCT show- ing focal disturbance of inner retinal layers (Figure 5) however clinical- ly in the absence of vascular element and presence of vitreomacular ab-normalities, treatment with VEGF blockade agents, intravitreal steroids and laser may not reduce macular thickening and improve vision, as this abnormality should by be addressed surgically by performing parsplana vitrectomy with ILM peeling in cases of moderate visual loss [13].

DIABETIC RETINOPATHY

The metabolic and retinal microenvironment causes pericytes, endo- thelium and capillary damage due to agglutinated erythrocyte and th rombus, all that forms hyper cellular sacs in the capillary wall and thus forms micro aneurisms which is the main feature of non-proliferative stage of diabetic retinopathy as this process progress more micro an- eurisms forms and retinal tissue reaches state of relative ischemia and thus will trigger VEGF production and interim will induce neovascular- ization which is the main feature of proliferative stage (Figure 6)which may lead eventually to vitreous hemorrhage or/ and tractinal retinal de- tachment and blindness (Figure 6).

NON-PROLIFERATIVE STAGE

In non-proliferative stage the most options are

Microaneurisms shaped from hyper-cellular sacs within the capillary wall and because the illness progress they increase in variety and reti- nopathy become additional severe (Figure 7).

Cotton-Wool spots: anaemia causes cystic bodies changes within the RNFL and interim can cause swelling RNFL ends with neural deposits and so can kind cotton-wool spots (Figure 8) blood vessel beading, it- eration and distortion, might return proliferative stage as anaemia will increase (Figure 9). Intraretinal microvascular abnormalities (IRMA) may be a shunt runs from retinal arteriols to vena bypassing animal tissue, sometimes associated next to retinal anaemia (Figure 10).

PROLIFERATIVE STAGE

The proliferation features a cycle of 3 phases

The impending phase: VEGF is upregulated once the retinal tissue reaches the state of relative anaemia and so initiates the method of mat- uration, during this stage level of VEGF concentration is high within the vitreous [14], and this could be noted clinically as

areas of hypo insertion on resorcinolphthalein angiograms (Figure 11).

The proliferative phase: Neo-vessels ar developed as method of matu- ration began, in it's early stages modern vessel is difficult to examine however because it matures, the diameter enlarges to achieve ¼ of reti- nal vein diameter [15] during which it drains, modern vessels will grow in numerous patterns (irregular or as network forming carriage wheel), positions (flat, or anchored to the posterior hyaloid) and speed (fast or slow) (Figure12).

Clinically non proliferative diabetic retinopathy is monitored by glyce- mic management whereas proliferative diabetic retinopathy needs pan retinal surgical process treatment within the absence of diabetic mac- ular oedema whereas within the presence of diabetic macular oedema, VEGF blockade agents are often introduced to handle each macular oedema and proliferation and pan retinal surgical process treatment are often differed to patients UN agency ar exhausting to follow up or treat- ment failure

The regression stage: modern vessel seems stripped in its early stages because it starts to regress and cut back it diameter (Figure 13), fibro vascular membrane becomes additional visible forming fibro-vas- cular tissue which can contract inflicting traction detachment of the ret- ina within the areas of fibro-vascular tissue attachment with posterior hyaline [16].

Vitreous hemorrhage is one in every of the foremost com- mon complications of proliferative stage and it's induced by contrac- tion of fibro-vascular tissue or spontaneous hurt [17].

CONCLUSION

Pathology of diabetic macular oedema and retinopathy is complex, un- derstanding the involving factors is vital, to individualize the treatment for each patient by targeting the underlying mechanism, typically the one or additional mechanism is involving and typically the pathology changes the mechanism from one kind to a different. Diabetic macular oedema are often caused by vascular part or non-vascular element; but non-proliferative diabetic retinopathy options primarily microan- eurisms thanks to metabolic changes whereas proliferative diabetic retinopathy is caused by upregulated VEGF triggering the method of maturation.

REFERENCES

1. Miyamoto K, Khosrof S, Bursell SE, Moromizato Y, Aiello LP, et al. (2000) Vascular Endothelial Growth Factor (VEGF)-Induced Retinal Vascular Permeability Is Mediated by Intercellular Adhe- sion Molecule-1 (ICAM-1). Am J Pathol 156(5): 1733-1739.
2. Jonas JB, Jonas RA, Neumaier M, Findeisen P (2012) Cytokine concentration in aqueous humor of eyes with diabetic macular ede- ma. Retina 32: 2150-2157.
3. Nguyen QD, Brown DM, Marcus DM, Boyer DS, Patel S, et al. (2012) Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE. Ophthalmology 119(4): 789-801.
4. Bressler SB, Glassman AR, Almukhtar T, Bressler NM, Ferris FL, et al. (2016) Five-Year Outcomes of Ranibizumab With Prompt or Deferred Laser Versus Laser or Triamcinolone Plus Deferred Ranibizumab for Diabetic Macular Edema. Am J Ophthalmol 164: 57-68.
5. Mitchell P, Bandello F, Schmidt-Erfurth U, Lang GE, Massin P, et al. (2011) The RESTORE study: ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macu- lar edema. Ophthalmology 118(4): 615-625.
6. Boyer DS, Nguyen QD, Brown DM, Basu K, Ehrlich JS, et al. (2015) Outcomes with As-Needed Ranibizumab after Initial Monthly Therapy: Long-Term Outcomes of the Phase III RIDE and RISE Trials. Ophthalmology 122(12): 2504-2513.
7. Diabetic Retinopathy Clinical Research Network; Wells JA, Glassman AR,Ayala AR, Jampol LM, Aiello LP et al. (2015) Af- libercept, bevacizumab, or ranibizumab for diabetic macular ede- ma. N Engl J Med 372: 1193-1203.
8. Simó R, Hernández C; European Consortium for the Early Treat- ment of Diabetic Retinopathy (EUROCONDOR) (2014) Neuro- degeneration in the diabetic eye: new insights and therapeutic per-spectives. Trends Endocrinol Metab 25: 23-33.
9. Boyer DS, Yoon YH, Belfort R Jr, Bandello F, Raj K Maturi, et al. (2014) Ozurdex MEAD Study Group. Three-year, randomized, sham-controlled trial of dexamethasone intravitreal implant in pa-tients with diabetic macular edema. Opthalmology 121(10): 1904- 1914.
10. Gillies MC, Sutter FK, Simpson JM, Larsson J, Ali H, et al.(2006) Intravitreal triamcinolone for refractory diabetic macular edema: two-year results of a double- masked, placebo-controlled, random-ized clinical trial. Ophthalmology 113: 1533-1538.
11. Kiddee W, Trope GE, Sheng L, Beltran-Agullo L, Smith M, et al. (2013) Intraocular pressure monitoring post intravitreal steroids: A systematic review. Surv Ophthalmo 58(4): 291-310.
12. Gillies MC, Islam FM, Larsson J, Pasadhika S, Gaston C, et al. (2010) Triamcinolone-induced cataract in eyes with diabetic mac- ular oedema: 3-year prospective data from a randomized clinical trial. Clin Exp Ophthalmol 38(6): 605-612.
13. HallerJA, Qin H, Apte RS, Beck RR, Bressler NM et al. (2010) Vitrectomy outcomes in eyes with diabetic macular edema and vit- reomacular traction. Ophthalmology 117: 1087-1093.
14. Adamis AP, Miller JW, Bernal MT, D Amico DJ, Folkman J, et al. (1994) Increased vascular endothelial growth factor levels in the vitreous of eyes with proliferative diabetic retinopathy. Am J Ophthalmol 118: 445-450.
15. Taylor E, Dobree JH (1970) Proliferative diabetic retinopathy. Site and size of initial lesions. Br J Ophthalmol 54(1): 11-18.
16. Davis MD (1965) Vitreous contraction in proliferative diabetic ret- inopathy. Arch

Ophthalmol 74: 741-751.
17. John P Berdahl, Prithvi Mruthyunjaya (2007) Vitreous Hemor- rhage: Diagnosis and Treatment, Edited by Ingrid U. Scott, Sharon Fekrat.
18. Gross JG, Glassman AR, Jampol LM, Inusah S, Aiello LP, et al. (2015) Panretinal Photocoagulation vs Intravitreous Ranibizum- ab for Proliferative Diabetic Retinopathy: A Randomized Clinical Trial. JAMA 314(20): 2137-2146.