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Review Article

Clinical Presentation of Diabetic Retinopathy

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Abstract

Diabetic retinopathy (DR) is a multifaceted ocular complication of diabetes, classified into non-proliferative and proliferative stages based on the presence of abnormal blood vessels. Macular edema, involving retinal thickening, is a significant subtype. Regular screening for early detection is crucial due to the often asymptomatic nature of DR, and individualized treatment strategies are essential given the unique combination of findings and progression rates in each patient. The complex pathogenesis involves abnormal permeability and vascular occlusion, leading to ischemia and neovascularization. Early intervention is vital to preserve vision and manage this prevalent diabetic complication.

Key words: Macular edema, Neovascularization, Proliferative

INTRODUCTION

Diabetic retinopathy (DR) stands out as a significant contributor to global visual impairment, being the primary cause of compromised vision among individuals aged 25–74. The visual decline associated with DR can result from various factors, including macular edema (ME), hemorrhage from new vessels, retinal detachment, or neovascular glaucoma. DR often remains asymptomatic until its advanced stages. Due to the potential for rapid progression and the effectiveness of therapy in enhancing vision, preventing further visual deterioration, and slowing disease advancement, regular screening of diabetic patients for retinal disease is crucial. This discussion will delve into the classification, clinical characteristics, and natural progression of DR. Additionally, it is worth noting that cataracts linked to diabetes represent a significant cause of visual impairment, particularly in individuals with type 2 diabetes.

CLASSIFICATION

Diabetic retinopathy (DR) manifests in two primary forms: Non-proliferative and proliferative, distinguishing between the absence and the presence of abnormal new blood vessels originating from the retina. Severity further categorizes DR, and diabetic ME can arise at any stage, from mild non-proliferative disease to proliferative DR. These classifications serve as valuable tools for assessing treatment efficacy in the literature and offering general guidelines for treatment approaches. However, each individual with DR presents a distinctive combination of findings, symptoms, and progression rates, necessitating a personalized treatment approach to preserve vision effectively.

Non-proliferative DR (NPDR) encompasses a range of features, including nerve-fiber layer infarcts (cotton wool spots), intra-retinal hemorrhages, hard exudates, and microvascular abnormalities (such as microaneurysms, occluded vessels, and dilated or tortuous vessels). These manifestations primarily occur in the macula and posterior retina. Visual impairment in NPDR is primarily linked to the development of diabetic ME. NPDR can be further categorized into mild, moderate, and severe stages. This classification is crucial for assessing the risk of progression to proliferative retinopathy and influencing decisions on follow-up intervals and treatment approaches. The one-year risks of progressing to proliferative retinopathy are 5% and 15% for mild and moderate NPDR, respectively, while the severe and very severe categories carry higher respective 1-year risks of 52% and 75%, respectively.[1]

Proliferative DR (PDR) is characterized by the emergence of neovascularization (abnormal new vessels) originating

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from the disc and/or retinal vessels. The consequences of this neovascularization include pre-retinal and vitreous hemorrhage, subsequent fibrosis, and traction retinal detachment. PDR may develop in conjunction with severe non-proliferative changes or independently of substantial NPDR. Diabetic ME can also occur in the presence of PDR.

Visual impairment in PDR can occur suddenly if bleeding from the abnormal vessels obstructs the light path to the retina. However, the blood is often reabsorbed, and vision spontaneously clears over several weeks to months. Permanent vision loss may occur through retinal detachment, macular ischemia, or a combination of these factors.

In early PDR, new vessels appear as fine loops or networks, not meeting criteria for the high-risk category. High-risk PDR is characterized by moderate to severe neovascularization of the optic disc (greater than one-third to one-half disc area), any neovascularization of the optic disc with concurrent vitreous or pre-retinal hemorrhage, or moderate to severe neovascularization elsewhere on the retina (at least one-half disc area) in the presence of vitreous or pre-retinal hemorrhage. Untreated high-risk PDR poses a 60% risk of severe vision loss within 5 years.[1] The presence of ME should be considered in the overall treatment strategy for any degree of PDR.

ME is a potential occurrence at any stage of DR. It is characterized by retinal thickening and edema affecting the macula. Detection can be achieved through specialized fundus examination with stereoscopic viewing, fluorescein angiography, and, most directly, by optical coherence tomography (OCT), which is a non-invasive imaging technology utilizing low-energy lasers. Diabetic ME is classified as center involved when retinal thickening in the macula affects the central subfield zone or non-center involved when it occurs in other areas.

CLINICAL MANIFESTATIONS

Visual Symptoms

Visual symptoms in DR often go unnoticed by many patients until the advanced stages when effective treatment may be challenging. Given the potential for rapid progression and the beneficial impact of therapy on symptom alleviation and disease progression, regular screening of diabetic patients for retinal disease is crucial. In later stages of DR, symptoms may manifest, depending on the specific eye problem. Examples include a curtain-like sensation with a vitreous bleed, floaters during the resolution of vitreous bleeds, and decreased visual acuity that cannot be corrected with refraction in the presence of ME.

Opthalmological Features

The development of clinical DR is a complex process influenced by various interrelated factors, resulting in damage to the retinal neurovascular unit. The neurovascular unit emphasizes the functional connectivity between retinal neural cells and the retinal vasculature.[2] Clinically observable features primarily stem from two fundamental changes within the retinal vessels: Abnormal permeability and vascular occlusion leading to ischemia and subsequent neovascularization. Numerous studies have shown that reduced retinal neural function can be measured before the onset of clinical retinopathy.[3,4] The retina, being one of the most metabolically active organs, is particularly vulnerable to substrate imbalance or ischemia.[5] In the early stages of diabetes, there is a loss of retinal pericytes and microvascular endothelial cells. Another early change in DR is the thickening of the retinal basement membrane, a similarity observed in glomeruli. The death of retinal pericytes and microvascular cells, along with impaired basement membrane function, is linked to the formation of retinal capillary microaneurysms and excessive vascular permeability. Microaneurysms, characterized by hypercellular outpouchings of retinal capillaries with weakened walls, partially due to pericyte loss, and the leakage of lipid and proteinaceous material (manifesting as "hard" exudates), represent the initial clinical signs of DR.

Neovascularization

The initial phase of cell death and increased capillary permeability may undergo cycles of renewal and further cell death, resulting in progressive microvascular obliteration and ischemic injury. This leads to the subsequent release of vasoproliferative factors, including vascular endothelial growth factor, erythropoietin, and others, in the ischemic retinal area.[6-15] These diffusible factors stimulate the development of new vessels (neovascularization) from adjacent retinal vessels in an unsuccessful attempt to revascularize the diseased tissue. This process is associated with various clinical changes.

- Intraluminal cell proliferation, alterations in platelet function, erythrocyte and leukocyte aggregation, and elevated plasma fibrinogen concentrations result in vascular occlusion and rupture. This can lead to small flame-shaped and blot hemorrhages proximal to the occlusion and intraretinal infarcts ("cotton wool" or "soft exudates") distal to the occlusion.[16-18]
- Proliferation of endothelial cells in retinal veins causes marked changes in vein caliber, forming tortuous loops.

- More severe ischemia results in vasoproliferation, leading to the formation of new vessels (neovascularization or proliferative DR [PDR]).[19-24]

Although PDR can be diagnosed through fundus examination, fluorescein angiography (a photographic study recording the transit of intravenously injected fluorescein dye by photography with a special camera) is useful for documenting capillary non-perfusion and leakage from new blood vessels. An alternative, rapid, and dye-free non-invasive technique called OCT angiography can also be used to document retinal circulatory abnormalities, but it is less widely used and less sensitive than fluorescein angiography.

New vessels in PDR are categorized based on four variables: Presence, location, severity, and associated hemorrhagic activity. In PDR, the vessels initially grow along the plane of the retina under the posterior hyaloid, or outermost layer, of the vitreous body. However, as the vitreous gradually pulls away and detaches from the retina, the new vessels grow out of from the retina plane and into the vitreous cavity.

The consequences of neovascularization are severe, as the delicate new vessels invariably rupture, resulting in the development of intraocular (usually vitreous) hemorrhage. Alternatively, they can create a fibrovascular overgrowth of the retina, causing distortion and tractional retinal detachment, especially if forward-growing vessels have attached to the posterior pole of the vitreous body and pull the retina anteriorly when they contract. New vessel proliferation can also occur on the surface of the iris (rubeosis or neovascularization of the iris) and in the anterior chamber. The latter change can obstruct the outflow path for aqueous humor in the eye, leading to acute glaucoma (neovascular glaucoma).

Retinal Thickening and Edema

Capillary leakage is linked to retinal thickening and edema, a condition known as ME. When the central macula is involved, ME can lead to a loss of visual acuity.[25-32] ME can develop at any stage of retinopathy and typically manifests with a gradual onset of blurred vision at both near and distant distances, particularly in patients exhibiting other signs of microvascular eye disease, such as perimacular microaneurysms.

The yellow exudates observed in association with ME in DR represent a residual product of extensive leakage that has undergone reabsorption, leaving behind the least soluble lipid components. These hard exudates often display a "circinate" pattern, forming an arc-like appearance due to the demarcation of areas with damaged retinal vessels from adjacent, more normal areas capable of reabsorbing the edema.

CONCLUSION

DR is categorized into two main forms: Non-proliferative and proliferative denoted by the absence or presence of abnormal new blood vessels originating from the retina. Further classification by severity is possible. ME, involving retinal thickening and edema in the macula, represents a visually significant type of DR and can occur at any stage of the condition. While these classifications are beneficial for analyzing treatment efficacy and establishing general treatment strategies, each patient with DR presents a unique combination of findings, symptoms, and progression rates, necessitating an individualized treatment approach to preserve vision. Clinical manifestations are often absent in the majority of patients who develop DR, and due to the potential for rapid progression, regular screening of diabetic patients is crucial for the early detection of retinal disease. The development of clinical DR is a complex process influenced by various interconnected factors, resulting in two fundamental changes within the retinal vessels: Abnormal permeability and vascular occlusion leading to ischemia and subsequent neovascularization.

REFERENCES

1. Aiello LM. Perspectives on diabetic retinopathy. Am J Ophthalmol 2003;136:122-35.
2. Gardner TW, Davila JR. The neurovascular unit and the pathophysiologic basis of diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol 2017;255:1-6.
3. Nian S, Lo AC, Mi Y, Ren K, Yang D. Neurovascular unit in diabetic retinopathy: Pathophysiological roles and potential therapeutical targets. Eye Vis (Lond) 2021;8:15.
4. Simó R, Stitt AW, Gardner TW. Neurodegeneration in diabetic retinopathy: Does it really matter? Diabetologia 2018;61:1902.
5. Frank RN. Diabetic retinopathy. N Engl J Med 2004;350:48.
6. Mizutani M, Kern TS, Lorenzi M. Accelerated death of retinal microvascular cells in human and experimental diabetic retinopathy. J Clin Invest 1996;97:2883.
7. Sharma S, Rashid A, Ashraf M, Ismail M, Tanvir M, Sharma P, *et al*. Clinical profile of acute coronary syndromes (ACS) in North Indian population: A prospective tertiary care based hospital study. Ann Int Med Dent Res 2017;3:ME50-3.
8. Ismail M, Andrabi SM, Rashid A, Jan A, Ashraf M, Kumar R, *et al*. Coronary artery profile on coronary angiography in TMT positive female patients. J Evol Med Dent Sci 2015;4:16510-2.
9. Latif M, Rashid W, Kaur B, Aggarwal A, Rashid A. Sex determination from mandibular canine index for the age group of 17-40 years in North Indian population. Int J Sci Stud 2016;4:1-7.
10. Ismail M, Gul I, Rashid A, Tanvir M, Jehangir M, Gul S, *et al*. Coronary CT angiography in asymptomatic diabetes mellitus. Ann Int Med Dent Res 2016;2:133-8.
11. Wani MI, Rashid A, Tanvir M. Demographic and behavioural determinants of hepatitis B disease transmission. Ann Int Med Dent Res 2017;3:ME68-71.
12. Mir AM, Rashid S, Rashid A, Maqbool R, Ahmad M, Rashid W, *et al*. Serum fibrinogen levels and its relation to diabetic retinopathy. J Evol Med Dent Sci 2015;4:16036-44.

13. Ashraf M, Sharma S, Rashid A, Ismail M, Tanvir M, Sharma P, *et al*. Prevalence of undiagnosed diabetes mellitus in acute coronary syndrome patients: A hospital-based study. Int J Sci Stud 2016;4:179-84.
14. Rashid A, Ajaz S, Ajaz S, Rasool N. Echo and electrocardographic profile of CKD patients. Int J Curr Res 2015;7:23123.
15. Rashid W, Lone I, Mir AM, Rashid A, Latif M. Fuchs heterochromic iridocylitis: Clinical characteristics and outcome of cataract extraction with intra ocular lens implantation in a Kashmiri population- a hospital based study. J Clin Diagn Res 2016;10:NC13-6.
16. Majeed A, Rashid A, Maqbool R, Rashid W, Ahmed M, Gulzar U. Serum fibrinogen levels and its relation to hypertension. Int J Sci Stud 2016;3:72-5.
17. Shaheen N, Rashid W, Rasool F, Mir AM, Saleem T, Rashid A. Intraocular pressure control in post trabeculectomy patients with pseudoexfoliation syndrome: A prospective study. Int J Sci Stud 2016;4:228-30.
18. Kawoosa AR, Khan FP, Rashid A, Sheikh NA, Khan BA. Association of metabolic syndrome with fatty liver. Int J Curr Res 2015;7:23359-61.
19. Rashid A, Rasool N, Ajaz S, Wani MI. Clinical profile and predictors of mortality of myocarditis in tertiary care hospital. Int J Sci Stud 2017;5:242-4.
20. Wani MI, Aamir A, Tanvir M, Ajaz S. Prevalence of hepatitis B in Kargil, Ladakh; Community based study from a rural area of Jammu and Kashmir. Ann Int Med Dent Res 2017;3:ME63-7.
21. Kawoosa AR, Khan FP, Rashid A, Sheikh NA. Prevalence of metabolic syndrome in Kashmiri local population. Analysis of age and gender. Int J Curr Res 2015;9:45272-5.
22. Rashid A, Ajaz S, Ajaz S, Rasool N. Cardiovascular manifestations of newly diagnosed hypothyroid patients. Int J Curr Res 2015;7:23356-8.
23. Kawoosa AR, Khan FP, Rashid A. Differences in prevalence of metabolic syndrome in urban and rural Kashmiri population. Int J Sci Res (IJSR) 2017;6:2534-7.
24. Zaffar S, Afroz F, Rashid A, Lone M, Ashraf M, Sidiqui M, *et al*. Association of epstein barr virus with mucosal squamous cell cancers of head and neck. J Evol Med Dent Sci 2015;4:14392-400
25. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. Arch Ophthalmol 1984;102:527.
26. Diabetes Control and Complications Trial Research Group; Nathan DM, Genuth S, Lachin J, Cleary P, Crofford O, *et al*. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329:977-86.
27. Tramboo ZM, Ahmad N, Rashid A. Clinicoechocardiographic profile of paediatric pulmonary artery hypertension patients. Ann Int Med Dent Res 2019;5:PE09-13.
28. Tramboo ZM, Rashid A, Ahmad N. Survival in paediatric pulmonary arterial hypertension. Int J Contemp Med Res 2019;6:D3-5.
29. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;352:837.
30. Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Research Group, Nathan DM, Zinman B, Cleary PA, Backlund JY, Genuth S, *et al*. Modern-day clinical course of type 1 diabetes mellitus after 30 years' duration: The diabetes control and complications trial/epidemiology of diabetes interventions and complications and Pittsburgh epidemiology of diabetes complications experience (1983-2005). Arch Intern Med 2009;169:1307.
31. Lecaire T, Palta M, Zhang H, Allen C, Klein R, D'Alessio D. Lower-than-expected prevalence and severity of retinopathy in an incident cohort followed during the first 4-14 years of type 1 diabetes: The Wisconsin Diabetes Registry Study. Am J Epidemiol 2006;164:143-50.
32. LeCaire TJ, Palta M, Klein R, Klein BE, Cruickshanks KJ. Assessing progress in retinopathy outcomes in type 1 diabetes: Comparing findings from the Wisconsin Diabetes Registry Study and the Wisconsin Epidemiologic Study of Diabetic Retinopathy. Diabetes Care 2013;36:631-7.

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