



Signs of Diabetic Retinopathy

A comprehensive clinical history is essential and should include the duration and type of diabetes mellitus, prior glycemic control as indicated by HbA1c levels, current medications, and the presence of associated systemic conditions such as obesity, hypertension, nephropathy, dyslipidemia, pregnancy, and kidney disease. Patients with DR may be asymptomatic during the early stages, with retinal changes often detected incidentally during fundus examination. As the disease advances, patients may experience symptoms such as blurred vision, visual distortion, floaters, and partial or complete vision loss. The signs seen in DR on fundus examination are discussed in forthcoming text.

MICROANEURYSMS

Microaneurysms represent the earliest clinically detectable lesions in DR (**Fig. 4.1**).³³ They typically first appear temporal to the fovea and may spontaneously regress over time. The diameter of microaneurysms ranges from 15 to 60 μm , generally remaining below 125 μm . Those measuring <30 μm in diameter may be undetectable through clinical examination.³⁴ The features of microaneurysms include:

- Focal saccular dilatation of the capillary wall
- Location in the inner nuclear layer
- Clinically identified by ophthalmoscopy as tiny, round, red dots with a sharp regular margin

Microaneurysms can be differentiated from dot hemorrhages using fundus fluorescein angiography (FFA). Microaneurysms



Fig. 4.1: Color fundus photograph of left eye showing microaneurysm (white arrowhead), superficial hemorrhage (black arrow), and soft exudates (black arrowheads)

appear as small hyperfluorescent punctate lesions, whereas dot hemorrhages manifest as areas of blocked fluorescence. Clinically, dot hemorrhages tend to be larger and often present with irregular margins.³⁵

HEMORRHAGES

Intraretinal hemorrhages are caused by rupture of weakened capillary walls. Superficial or flame-shaped hemorrhages arise from the precapillary arterioles located in the retinal nerve fiber layer (**Fig. 4.1**). Deep hemorrhages or dot and blot hemorrhages are located in the inner nuclear and outer plexiform layers of the retina (**Fig. 4.2**).

HARD EXUDATES

Hard exudates are composed of lipoproteins and lipid-laden macrophages localized within the outer plexiform layer of the retina (**Fig. 4.2**). They typically develop at the interface between

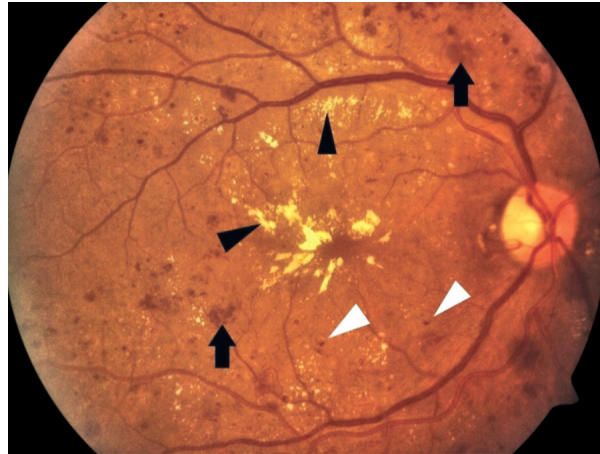


Fig. 4.2: Color fundus photograph of right eye showing dot hemorrhages (white arrowheads), blot hemorrhage (black arrows), and hard exudates (black arrowheads)

edematous and nonedematous retinal tissues. Hard exudates often form a characteristic circinate pattern surrounding leaking microaneurysms.

COTTON WOOL SPOTS/ SOFT EXUDATES

Cotton wool spots are located in the retinal nerve fiber layer and consist of accumulated axoplasmic debris (**Fig. 4.1**). They represent focal infarctions of the precapillary arterioles.

Venous Changes

- Dilatation
- Looping (**Fig. 4.3**)
- Beading
- Sausage-like segmentation

Arterial Changes

- Peripheral narrowing
- Silver-wiring
- Obliteration



Fig. 4.3: Color fundus photograph of left eye showing venous looping (black arrow)

INTRARETINAL MICROVASCULAR ABNORMALITIES

Intraretinal microvascular abnormalities (IRMAs) are collateral channels that form direct connections between retinal arterioles and venules, bypassing the capillary network. They are typically observed adjacent to areas of capillary nonperfusion. IRMAs are located within the retina, do not cross major retinal vessels, and characteristically do not exhibit leakage on fluorescein angiography (Fig. 4.4).

NEOVASCULARIZATION

Neovascularization at the disc (NVD) is defined as the growth of new blood vessels on or within one disc diameter of the optic nerve head (Fig. 4.5). Neovascularization elsewhere (NVE) refers to neovascular growth located more than one disc diameter away from the optic disc (Fig. 4.5). Neovascularization of the iris (NVI) is an indicator of poor prognosis and is strongly associated with the development of neovascular glaucoma.

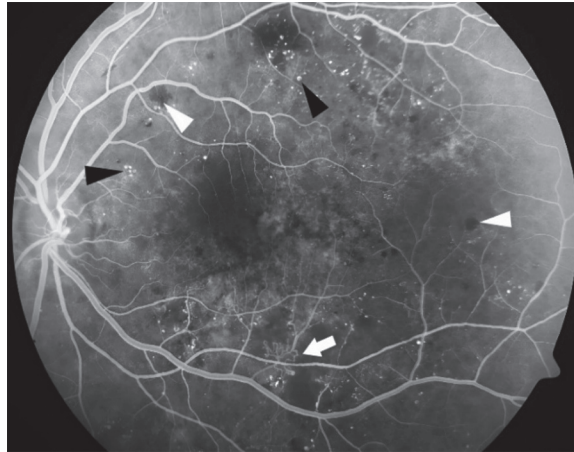


Fig. 4.4: Fundus fluorescein angiogram of left eye showing microaneurysms as hyperfluorescent dots (black arrowheads), hemorrhages seen as blocked fluorescence (white arrowheads) and intraretinal microvascular abnormalities (white arrow)

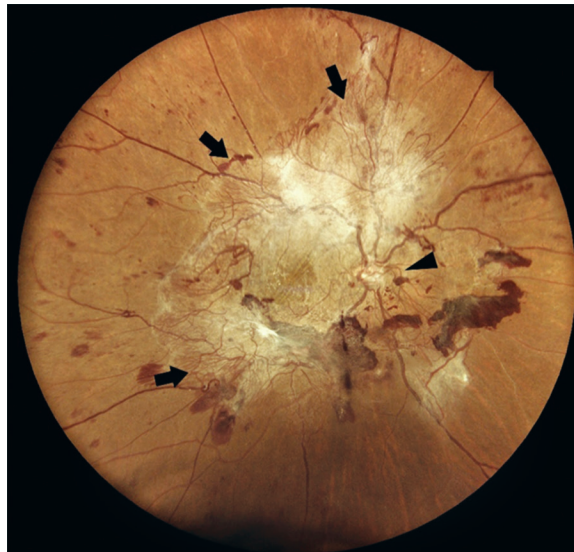


Fig. 4.5: Color fundus photograph of right eye showing neovascularization at the disc (NVD) (black arrowhead), and neovascularization elsewhere (NVE) (black arrows)

EARLY TREATMENT DIABETIC RETINOPATHY STUDY (ETDRS) CLASSIFICATION

Nonproliferative Diabetic Retinopathy (NPDR)

1. *No retinopathy*: No retinal lesions
2. *Very mild NPDR*: Microaneurysms only
3. *Mild NPDR*: A few microaneurysms, retinal hemorrhages and hard exudates
4. *Moderate NPDR*: Retinal hemorrhages (about 20 medium-large per quadrant) in 1–3 quadrants + cotton wool spots (between the grades mild and severe NPDR)
5. *Severe NPDR*: Fulfilling one rule of the 4-2-1 rule
 - Severe hemorrhages in all four quadrants
 - Venous beading in 2 or more quadrants
 - Moderate IRMA in 1 or more quadrants
6. *Very severe NPDR*: Fulfilling two or more rules of the 4-2-1 rule.^{36,37}

Proliferative Diabetic Retinopathy (PDR)

- *Mild-to-moderate PDR*: NVD or NVE insufficient to meet high-risk characteristics
- *High-risk PDR*:
 - NVD greater than ETDRS standard photograph 10A (about one-third disc area).
 - Any NVD with vitreous hemorrhage.
 - NVE >1/2 disc area with vitreous hemorrhage.
- Advanced diabetic eye disease represents the end-stage, vision-threatening complication of DR in patients with inadequate or unsuccessful treatment (**Fig. 4.6**). Clinical manifestations may include preretinal or vitreous hemorrhage, tractional retinal detachment, and rubeosis iridis.

Classification of Diabetic Macular Edema

Diabetic macular edema (DME) can be classified into the following groups:

- Focal exudative and diffuse maculopathy
- Ischemic and nonischemic maculopathy

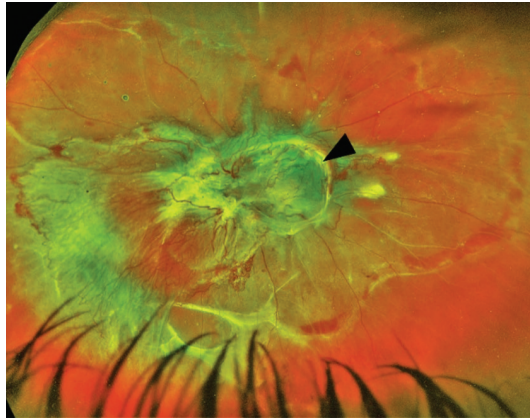


Fig. 4.6: Color fundus photograph of left eye showing advanced diabetic eye disease in the form of combined tractional and rhegmatogenous retinal detachment caused by extensive fibrovascular proliferation (black arrowhead)

- Tractional and nontractional maculopathy
- Center involving macular edema and noncenter involving macular edema

ETDRS Definition of Clinically Significant Macular Edema (CSME)

- Retinal edema within 500 μm of the center of the fovea
- Hard exudates within 500 μm of the center of the fovea if associated with adjacent retinal thickening (which may be outside the 500 μm limit) (**Fig. 4.7**)
- Retinal edema one disc area (1500 μm) or larger, any part of which is within one disc diameter of the center of the fovea^{38,39}

Optical Coherence Tomography (OCT) Classification of Diabetic Macular Edema (Fig. 4.8)

- Sponge-like thickening of retinal layers
- Large cystoid spaces
- Serous detachment of the retina
- Tractional detachment of the fovea or vitreomacular traction (VMT)



Fig. 4.7: Color fundus photograph of left eye hard exudates (black arrowhead) within 500 μm of the center of the fovea, associated with adjacent retinal thickening, qualifying as clinically significant macular edema

INTERNATIONAL CLINICAL DIABETIC RETINOPATHY DISEASE SEVERITY SCALE

- *No apparent retinopathy:* No abnormality
- *Mild NPDR:* Microaneurysms only
- *Moderate NPDR:* More than just microaneurysms and less than severe disease
- *Severe NPDR:* No signs of PDR and any of the following:
 - 20 intraretinal hemorrhages in each of the four quadrants
 - Venous beading in ≥ 2 quadrants
 - Prominent IRMA ≥ 1 quadrant
- *PDR:* One or more of the following:
 - Neovascularization
 - Vitreous or preretinal hemorrhage⁴⁰

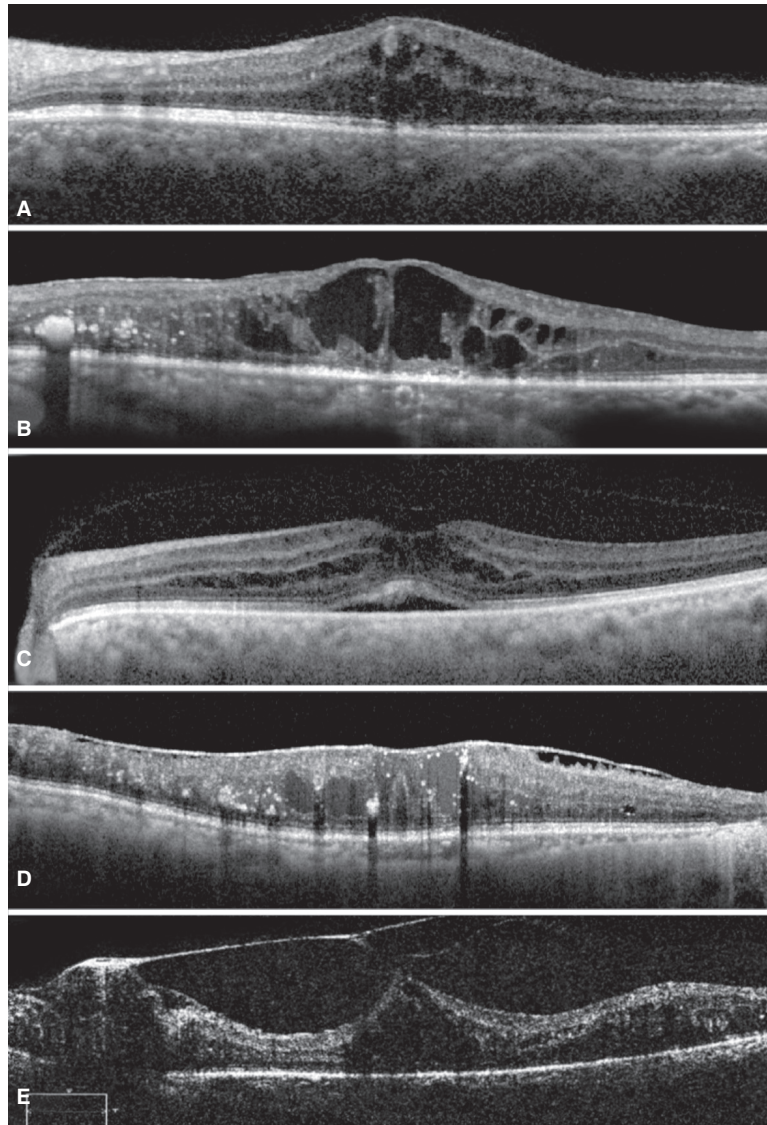


Fig. 4.8: Optical coherence tomographs showing types of diabetic macular edema. A: Spongiform edema; B: Cystoid macular edema; C: Serous detachment of the fovea; D: Tangential tractional on macula; E: Taut posterior hyaloid membrane causing macular edema

DIABETIC MACULAR EDEMA SCALE

- ***DME apparently absent:*** Apparent retinal thickening and hard exudates at the posterior pole are absent.
- ***DME apparently present:*** There is some “apparent retinal thickening and hard exudates at the posterior pole.” It can further be classified into mild, moderate, and severe based on the distance of thickening and hard exudates from the center of the fovea.
 - ***Mild DME:*** The retinal thickening or hard exudates are located far from the center of the fovea.
 - ***Moderate DME:*** Retinal thickening or hard exudates are approaching the center of the macula but not involving the center.
 - ***Severe DME:*** Hard exudate and thickening involve the center of the fovea.