FUNDUS FLUORESCEIN ANGIOGRPAHY (FFA) IN DIABETIC RETINOPATHY (DR)

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Role of FFA in Diabetic Retinopathy

One of the most common application of FFA is in diabetic retinopathy. It may be used to identity the stages of DR, to study the progression of disease through these stages, to indicate the need for intervention; to assess the visual prognosis, and to follow up the natural course of the disease or the efficacy of treatment.

a. Stages and progression of DR

FFA clearly highlights not only the presence of new vessels and hence proliferative DR (PDR) in doubtful cases of non-proliferative DR (NPDR) but also indicates the risk of progression of NPDR to PDR by the following lesions: capillary dilatation, fluorescein leakage and capillary loss or non-perfusion (CNP).

b. Indication for treatment and visual prognosis

In the presence of clinically significant macular oedema (CSME), FFA is fundamental for the detection of treatable lesions and thus the pattern of laser treatment to be applied, depending on the extent of leakage - focal or diffuse. In doubtful cases of diabetic maculopathy, FFA indicates the need for treatment by detecting the presence or absence of significant leakage. Moreover where cystoid macular oedema (CME) or macular ischemia is seen, poor visual progrnosis is evident with or without treatment.

c. Follow up

On one hand, by indicating the risk of progression of DR (esp from NPDR to PDR) FFA indicates need for more frequent follow ups (2-3 months). On the other, it helps in assessing the efficacy of laser treatment or the natural course of disease on subsequent follow ups, calling for additional treatment when new vessels or CNP are seen in lasered eyes.

II. Angiographic plan for FFA in DR

a. Red-free photographs of dise and macula of Both Eyes

b. Control photograph : With fluorescein filters in place but before fluorescein injection. This checks the dual filter system for autofluorescence and pseudo fluorescence.

c. Primary eye disc and macula : 6 photographs, at interval of 1.5 to 2 seconds. Start 8-12 seconds after fluorescein injection, depending on patient's age.

d. Quadrants of the primary eye : The next 4 photograps (20-30 sec after injection) are for the quadrants. For orientation, nasal, superior and inferior photographs are taken with the edge of the opticdisc at the edge of the photograph and the temporal photograph with the fovea at the edge of the photograph.

e. Second eye disc and macula

f. Quadrants of the second eye

g. Late photographs : Primary eye macula and disc; second eye macula and disc.

This plan yields maximal information about PDR and NPDR. The referring physician should also preferably indicate the specific areas of interest so that pertinent information is not missed.

INTERPRETATION OF FFA IN DR

Hypofluorescence

1. Blocked retinal fluorescence
   - Vitreous haemorrhage
   - Subhyaloid haemorrhage
   - Retinal haemorrhage
2. Blocked Choroidal fluorescence

Deep retinal material

- Edema fluid (eg CME) also causes late leak
- Hard exudates

- Hemorrhages - dot and bolt

As the capillary bed, source of the above, lies in inner nuclear layer, outer plexiform layer most often accumulates these materials. They block neither superficial large vessels, nor deep capillary bed; rather make these vessels more prominent by increased contrast with blocked choroidal fluorescence.

3. Vascular filling defects (VFD)

a. Retinal VFD - Capillary non-perfusion (CNP) i.e. an area of hypofluorescence not corresponding to any visible (deep retinal) blocking material ophthalmoscopically. They are generally encircled by dilated retinal vessels and may also cause blocked choroidal fluorescence due to associated retinal edema. When occuring in macula, a CNP manifests as either enlarged FAZ or macular ischaemia.

b. Optic disc VFD : Seen only when anterior ischemic optic neuropathy (AION) is present. Sectoral CNP is of ciliary origin and so is seen in early phase followed by leakage from adjoining capillaries in late phase.

Hyperfluorescence

1. Abnormal retinal and disc vessels

a. Anastomosis

The type of anastomosis seen in DR is an arteriovenous collateral, i.e. (intraretinal microvascular abnormality (IRMA) seen adjacent to a CNP area. They herald the onset of neovascularisation. They are differentiated from new vessels by lack of profuse leakages, situation within retina and failure to cross over major blood vessels.

b. Neovascularisation - new vessels are hallmark of PDR

i) Neoascularisation at disc (NVD)

- Defined as new vessels at / within 1 disc diameter of disc
- Fill up before retinal arteries, suggesting that the choroid is the source of blood for these vessels.
- A feeder vessel is sometimes evident at the disc
- Start leaking in the arteriovenous (AV) phase
- In some patients, the neovascular fronds fill slowly
- Marked leakage into vitreous coulds the disc in late phases.

ii. Neovascularisation elsewhere (NVE)

- Defined as new vessels more than 1 DD away from disc. Generally occur within 3 DD of arcade vessels
- Tend to occur at the junction of perfused and non-perfused retina
- Leak profusely tend to bleed too, resulting in associated blocked fluorescence

c. Aneurysms

- Capillary micro aneurysms herald the onset of DR (mild NPDR)
- Adjacent to CNP areas / soft exudates in advanced cases.
- Fill up in arterial or early AV phase.
- Some leak in late phase other don't. Depends on the extent of endothelial damage.

2. Leak

a. Retinal leak

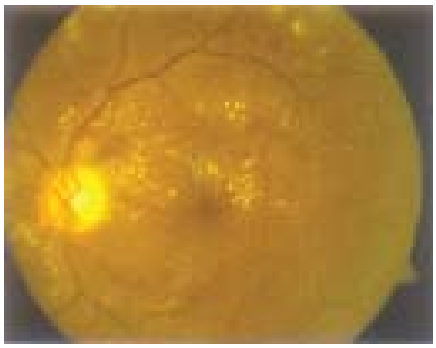
Any extravascular retinal fluorescence in late phases is abnormal and indicates either cystoid or non cystoid retinal edema. In context of DR, only macular oedema is relevant. In context of macula, nonrstoid edema is milder from of cystoid edema, ie leakage is insufficient to collect in discrete cystic aces and appears as ?

5. Early PDR with early NVE / NVD / both.

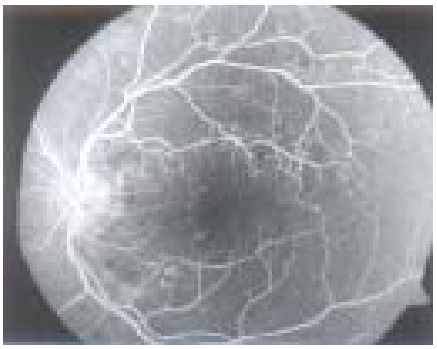
6. High risk PDR, with NVD more than 1/3 disc area or NVD/NVE associated with pre-retinal vitreous hemorrhage.

c. DR lesions in various stages of FFA

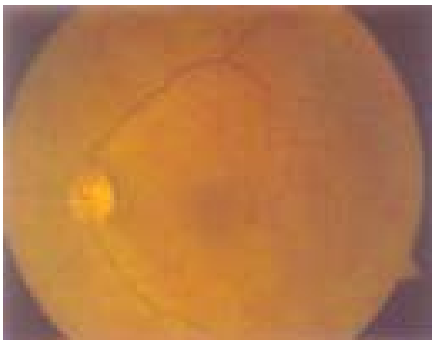
Finally it is essential to know the time of appearance of various diabetic lesions as one records various phases



Fundus photograph of the left eye showing hard exudates arranged in a loose circinate pattern in the superior part of the macula

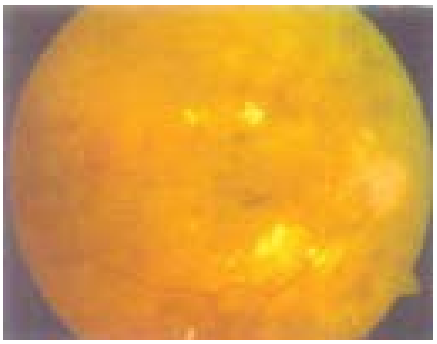


Arteriovenous phase showing the multiple hyperfluorescent points caused by microaneurysms. These are seen boarding the areas of capillary non-perfusion

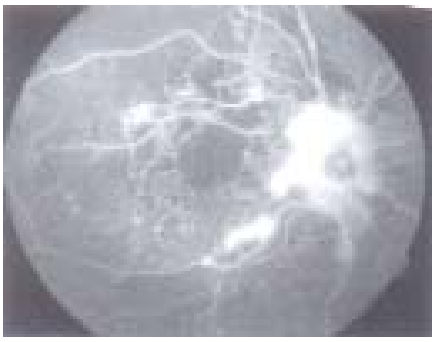


Fundus photograph of the left eye. Retinal thickening was noted in the macular region. Note the absence of hard exudates or retinal hemorrhages

Late film shows accumulation of the dye in cystoid spaces around the fovea. Non-cystoid collection of the dye is also noted in the other parts of the macula. The leakage from the neovascular frond has also increased



A large neovascular frond is seen at the disc. Hard exudates are seen in the upper and lower part of the macula while the foveal area has dull washed out appearance



Marked leakage of the dye is seen from the NVD. A large area of capillary non-perfusion is seen in the upper part of the macula involving the fovea; dialated capillaries are seen around this

of the angiogram so that no lesions are missed or wrongly interpreted.

1. Pre-arterial phase

No typical lesions of DR are evident in this phase

2. Arterial Phase

Neovascularisation, either NVD/NVE. Feeder vessel may be evident in NVD

3. Arteriovenous phase

Most lesions of DR are evident in this phase as it is a microangiopathy

- Microaneurysms
- Hemorrhages
- IRMAs
- Venous beading
- Exudates
- CNP areas
- Macular ischemia
- Abnormality in FAZ (foveal avascular zone)

Most of the above pathologies are more distinctly evident in the early AV phase

4. Venous phase

The two main lesions manifesting with leakage in late venous phases are; new vessels and macular edema. The former can be easily diagnosed in early phases but a photograph of each macula is essential in late venous phase to establish the diagnosis of macular edema and its pattern.