Retinal vascular disease

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Reviewed and Modified
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Signs of retinal vascular disease

- Two changes to the retinal capillary microcirculation:
  1. Vascular leakage
  2. Vascular occlusion.
Signs of retinal vascular disease

- Retinal vascular disease
  - Occlusion of capillaries
    - Ischaemia
      - Cotton-wool spots
      - Irregular retinal veins
    - New vessels
      - Lipid exudates
      - Oedema
      - Haemorrhages
  - Leakage from capillaries
Leakage from the microcirculation

- Hemorrhages caused by leakage of blood from damaged vessels;
- Edema of the retina, result of fluid leakage from damaged vessels;
- Exudates formed by lipids, lipoprotein and lipid-containing macrophages – these are yellow in color, with well defined margins.
Leakage from the microcirculation

- Edema of the retina, result of fluid leakage from damaged vessels;
- Exudates formed by lipids, lipoprotein and lipid-containing macrophages – these are yellow in color, with well defined margins.
Occlusion of the microcirculation

**Cotton-wool spots (soft exudates)**

- Fluffy white focal lesions with indistinct margins.
- They occur at margins of an ischemic retinal infarct due to obstruction of axoplasmic flow and build-up of axonal debris in the nerve fiber layer of the retina.
- Their visibility depends on nerve fiber layer thickness at that site, so they are seen close to optic disc, where nerve fiber layer is thick, and not in periphery, where nerve fiber layer is thin. They are white in color because accumulated axoplasmic particles scatter light, whereas normal nerve fiber is transparent.

**New vessels**

- An ischemic retina releases vasogenic factors (e.g. VEGF) which result in growth of abnormal blood vessels and fibrous tissue onto retinal surface and forwards into the vitreous.
- These intravitreal vessels are much more permeable than normal retinal vessels, so that they leak dye during retinal fluorescein angiography.
- Their abnormal location predisposes them to break and bleed.
Figure 12.2 The signs of retinal vascular disease: (a) haemorrhage and exudate; (b) cotton-wool spots, note the yellowish nature and distinct margin to the exudates, compared to the less distinct and whiter appearance of the cotton-wool spots; (c) new vessels, here particularly florid and arising at the disc: (d) this fluorescein angiogram demonstrates the occlusion of the retinal capillary circulation (the dark areas (arrow)), the bright areas indicate leakage from new vessels.
Diabetic retinopathy

- **Epidemiology**
  - **Type I diabetes**
    Onset is relatively acute and diabetic retinopathy begins to appear about 5 years after onset.
  - **Type II diabetes**
    Retinopathy may be found at presentation because type II diabetes may be present for several years prior to diagnosis.

- **Diabetes is associated with the following ocular events:**
  1. retinopathy
  2. cataract: a rare ‘snowflake’ cataract in youth, and a greater frequency and earlier onset of age-related cataract;
  3. glaucoma (e.g. rubeotic glaucoma, but an association with chronic open angle glaucoma is disputed);
  4. extraocular muscle palsy due to microvascular disease of the third, fourth or sixth cranial nerves.
Factors important in development of diabetic retinopathy include:

- duration of diabetes: 80% have retinopathy after 20 years of disease
- poor diabetic control
- coexisting diseases: e.g. hypertension
- smoking.
- Pregnancy development of retinopathy may be accelerated
Diabetic Retinopathy: Pathology

Retinal damage results from damage to the circulation. Pathological studies show:
  – a decrease in # of pericytes
  – development of microaneurysms on capillary network,
  – patchy closure of capillary net, (capillary non-perfusion),
Diabetic retinopathy should be diagnosed before it is symptomatic.

All diabetics should have fundoscopy performed at least yearly.

Screening for sight-threatening retinopathy (maculopathy and proliferative retinopathy) 5 years after diagnosis type I

At time of presentation in type II

5 years after diagnosis type I

Younger patients likely to develop proliferative disease

Older patients more likely to develop maculopathy and proliferative DR (due to it is more common than type I)

Visual acuity may be reduced gradually by a maculopathy, or suddenly by a vitreous hemorrhage.
**Diabetic Retinopathy**

*Nonproliferative retinopathy*

- Microaneurysms (earliest sign)
- “Dot-and-blot hemorrhages”
  - Damaged capillary → leakage of fluid
- Cotton-wool spots
  - Nerve infarctions
  - Occlusion of precapillary arterioles
  - Also seen in hypertension

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**Diabetic Retinopathy**

*Nonproliferative retinopathy*

- Hard exudates/macular edema
  - Macular swelling
  - Yellow exudates of fatty lipids
  - **Can lead to blindness in diabetics**

*Image credit: National Eye Institute, National Institutes of Health Public Domain*
Diabetic Retinopathy

Proliferative retinopathy

- Vessel proliferation ("proliferative retinopathy")
  - Retinal ischemia $\rightarrow$ new vessel growth
  - "Neovascularization"
  - Abnormal vessels: friable, grow on surface of retina
  - Can lead to retinal detachment
  - Can cause macular edema $\rightarrow$ blindness
Treatment

1. The mainstay of treatment for sight-threatening diabetic retinopathy is Anti-VEGF therapy (anti-vascular growth factor inhibitors) and laser therapy.
2. A vitrectomy is performed to remove the vitreous gel and blood and to repair any of the detached retina.
3. Indications of vitrectomy:
   - vitreous hemorrhage does not clear after a few weeks
   - fibrous traction on the retina causing detachment from the overlying pigment epithelium (traction retinal detachment)
Diabetic Retinopathy Classification

**NPDR 4 stages**
- **Mild**: bleeding in 1 quadrant
- **Moderate**: bleeding in 2 quadrant
- **Sever**: bleeding in 3 quadrant
- **Sever (pre-proliferative)**: Bleeding in 4 quadrant

**Small bleeding**
- Leaked blood (hemorrhage)

**PDR**
- New blood vessels

**And bleeding**
A ➞ sever NPDR, bleeding in 3 quadrant
B ➞ white on the left is white exudate with central microanyrism and hemorrhage
C ➞ pre-proliferative or PDR
D ➞ PDR (new thin blood vessel) with hemorrhage
To differentiate between the laser burns and navis

- **Laser** ➔ hyper-pigmented center, hypo-pigmented peripheries (away from blood vessels)
- **Navis** ➔ pigmented peripheries and black center

Figure 12.4 Typical appearance of retinal laser burns.
Hard exudates: Lipids, ring pattern, defined edges, bright

Soft eudates (cotton-wool): neural fibers damage, indistinct margin, pale, near optic disc
Macular Edema and Hard Exudates
Subhyaloid Hemorrhage
Vitrectomy completed with 23-gauge
Arterial occlusion

Pathogenesis...

Central and branch retinal artery occlusions are usually embolic in origin.

- Three types of emboli are recognized:
  1. fibrin – platelet emboli, commonly from diseased carotid arteries;
  2. cholesterol emboli, commonly from diseased carotid arteries (Figure 12.5);
  3. calcific emboli, from diseased heart valves.

Figure 12.5 The clinical appearance of a cholesterol embolus (arrow). They appear to sparkle when viewed with a direct ophthalmoscope.
Arterial occlusion
History

- The patient complains of a sudden painless loss of all or part of the vision.
- Fibrin – platelet emboli typically cause a fleeting loss of vision as the emboli pass through the retinal circulation (amaurosis fugax). This may last for some minutes, and then it clears.
- Cholesterol and calcific emboli may result in permanent obstruction with no recovery in vision (they may also be seen in the retinal vessels of asymptomatic individuals).
- In young patients, transient loss of vision may be caused by migraine.

Signs

- Occasionally, a series of white platelet emboli can be seen passing rapidly through a vessel; more often a bright yellow, reflective cholesterol embolus is noted occluding an arterial branch point. The acutely affected retina is swollen and white (oedematous), while the fovea is red (cherry - red spot) because the choroid can be seen through the thin retina of the fovea. After several weeks the disc becomes pale (atrophic) and the arterioles attenuated.

- The condition may also occasionally be caused by vasculitis, such as giant cell arteritis.
Investigation
• Patients require a careful vascular work-up, since disease in the eye may reflect systemic vascular disease. A search for carotid artery disease should be made by assessing the strength of carotid pulsation and listening for bruits. Ischaemic heart disease, peripheral claudication and HTN may present.

Treatment
• Acute treatment of central and branch artery occlusions is aimed at dilating the arteriole to permit the embolus to pass more distally and limit the damage.
• The patient is referred to an eye unit, where the following measures may be tried:
  I. lowering the intraocular pressure with intravenous acetazolamide;
  II. ocular massage;
  III. paracentesis (a needle is inserted into the anterior chamber to release aqueous and lower the intraocular pressure rapidly);
  IV. asking the patient to rebreathe into a paper bag firmly applied around the mouth and nose to use the vasodilatatory effect of raised carbon dioxide levels.

Prognosis
• Full visual recovery occurs with amaurosis fugax, but more prolonged arterial occlusion results in severe, unrecoverable visual loss.
Venous occlusion

Pathogenesis

- Central retinal vein occlusion (CRVO) may result from:
  - abnormality of the blood itself (the hyperviscosity syndromes and abnormalities in coagulation);
  - an abnormality of the venous wall (inflammation);
  - an increased ocular pressure.

History

- The patient complains of a sudden partial or complete loss of vision, although onset may be less acute than that of arterial occlusion.

Signs

- There is marked haemorrhage and great tortuosity and swelling of the veins.
- The optic disc appears swollen. Branch retinal vein occlusion may originate at the crossing point of an arteriole and a vein where the arteriole has been affected by arteriosclerosis associated with hypertension (A/V nipping).
  - Subsequently:
    - Abnormal new vessels may grow on the retina and optic disc, causing vitreous haemorrhage. This happens if the retina has become ischaemic as a result of the vein occlusion (an ischaemic retinal vein occlusion).
    - In ischaemic retinal vein occlusion abnormal new vessels may grow on the iris, causing rubeotic glaucoma.
Figure 12.6 The contrast between: (a) an inferior branch retinal artery occlusion (note the white appearance of the affected retina) and (b) a superior branch vein occlusion.
Investigation

- Investigation of a CRVO includes vascular and haematological work - up to exclude increased blood viscosity. CRVO is also associated with raised ocular pressure, diabetes and hypertension and smoking.

Treatment

- Retinal laser treatment is given if the retina is ischaemic, to prevent the development of retinal and iris new vessels may improve vision by reducing macular oedema which may also be treated with intravitreal steroid therapy.
- There is also increasing interest in the use of anti-VEGF agents.

Prognosis

- The vision is usually severely affected in central, and often in branch, vein occlusion and usually does not improve. Younger patients may fare better, and there may well be some visual improvement.
<table>
<thead>
<tr>
<th><strong>CRAO</strong></th>
<th><strong>CRVO</strong></th>
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<tbody>
<tr>
<td><strong>CENTRAL RETINAL ARTERY OCCLUSION</strong></td>
<td><strong>CENTRAL RETINAL VEIN OCCLUSION</strong></td>
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<tr>
<td><strong>“eye stroke”</strong></td>
<td><strong>“eye cvt”</strong></td>
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<tr>
<td><strong>CLINICAL</strong></td>
<td><strong>Variable - blurred vision to sudden vision loss</strong></td>
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<tr>
<td>Sudden, profound vision loss</td>
<td>Painless</td>
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<td>Painless</td>
<td>Monocular</td>
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<td><strong>ETIOLOGY</strong></td>
<td><strong>Risk factors include:</strong></td>
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<tr>
<td>Embolism</td>
<td>Typical stroke risk factors</td>
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<tr>
<td>Vasculitis</td>
<td>Hypercoagulable states</td>
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<td>Vasospasm</td>
<td>Glaucoma</td>
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<tr>
<td>Sickle Cell</td>
<td>Compression of the vein in thyroid or orbital tumors</td>
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<td>Trauma</td>
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<tr>
<td>Glaucoma</td>
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<tr>
<td><strong>DIAGNOSIS</strong></td>
<td><strong>Optic disk edema</strong></td>
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<tr>
<td>Retinal pallor</td>
<td>Diffuse retinal hemorrhages</td>
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<tr>
<td>Macular cherry red spot</td>
<td>(&quot;blood-and-thunder&quot;)</td>
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<tr>
<td>+/- Afferent pupillary defect</td>
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<td><strong>TREATMENT</strong></td>
<td><strong>Consult ophtho + neurology</strong></td>
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<td>Consult ophtho + neurology</td>
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<tr>
<td>Case reports of intra-arterial TPA</td>
<td>No specific treatment</td>
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<td>Limited evidence for treatment: possibly digital massage, lowering intraocular pressure</td>
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Giant cell arteritis (GCA)

**Most Common Form of Vasculitis That Occurs in Adults.**

**Almost All Patients Are Over the Age of 50.**

**GCA Commonly Causes Headaches, Joint Pain, Facial Pain, Fever, and Difficulties with Vision, and Sometimes Permanent Visual Loss in One or Both Eyes.**

**Because Disease Is Relatively Uncommon and Because Disease Can Cause So Many Different Symptoms, Diagnosis of GCA Can Be Difficult to Make.**

**With Therapy, GCA Is Treatable, Controllable, and Curable Disease.**
Giant Cell Arteritis

Age associated:
- Mean > 70yo
- Not often seen < 50yo
- Female predominance

Most associated with a (+) biopsy

Fever, Fatigue, Weight Loss, Headaches, Jaw Claudication, Transient Vision Loss

ESR CRP

Can progress to permanent vision loss

No vision loss:
- Prednisone 1mg/kg daily PO
  (up to 60mg)
- With vision symptoms:
  Methylprednisolone 500-1000mg IV daily x 3 days

Large vessel (Aorta) may be involved
Temporal Arteritis

Easy to diagnose and treat -- if you think of it.

Tender temporal arteries
Jaw gets tired chewing.

Physical exam and labs are otherwise nonrevealing.

Ask me about my grandchildren!

Granulomatous thickening of the inner portions of the branches of the external carotid arteries.

Easily mistaken for "tension headaches" -- until one or both eyes suddenly go blind.

Most patients also have polymyalgia rheumatica, muscle aches easily mistaken for "rheumatism."
Stages Of Hypertensive Retinopathy

Arteriosclerosis:
attenuation of retinal arterial vessels:

Copper and silver wiring (first stage)

Presence of nipping (second stage) of retinal vein where it is crossed by arteriole.

If severe, retina demonstrates signs of capillary occlusion (cotton-wool spots) (third stage).

Very high blood pressure cause swelling of optic nerve head—papilledema—(fourth stage)

Copper and silver wiring (first stage)
Arteriosclerosis and hypertension
stages of hypertensive retinopathy

• First stage: Arteriosclerosis can be visualized in the eye as an attenuation of the retinal arterial vessels - copper and silver wiring
• Second stage: AV nipping
• Third stage: signs of capillary occlusion (cotton - wool spots)
• Fourth stage: swelling of the optic nerve head – papilledema

Hypertension in addition may cause focal arteriolar narrowing and a breakdown in the blood – retinal barrier, resulting in the signs of vascular leakage. These are particularly prominent if the hypertension is of renal origin.
Hypertensive Retinopathy

A-Stage 1; B-Stage 2; C-Stage 3; D-Stage 4
Treatment of the hypertension results in the resolution of the retinal signs over some months. A rapid reduction of systemic blood pressure is avoided, because it may precipitate vascular occlusion.

Figure 12.7 The fundus in malignant hypertension. The disc is swollen, and there are retinal haemorrhages and cotton wool spots.
Hypertensive Retinopathy – Diagnostic Techniques & Signs

Focal narrowing of the retinal arterioles – Copper and Silver Wiring
Hypertensive Retinopathy – Classification Grade 2
Hypertensive Retinopathy – Classification Grade 3
Hypertensive Retinopathy – Classification Grade 4
Retinopathy of prematurity is a vascular response of the retina occurring predominantly in low-birth weight premature infants exposed to oxygen therapy in the early weeks of life.
• **Roth spots** *(haemorrhages have white centres)* can be caused by Leukaemia with a greatly raised white cell count. These may also be a feature of bacterial endocarditis and autoimmune diseases associated with vasculitis.

![White-centred haemorrhages](image-url)
Multiple choice questions

1. Assign each of these signs of retinal vascular disease to either leakage or occlusion.
   A) Hemorrhage.
   B) New vessels.
   C) Cotton-wool spot.
   D) Exudate.
   E) Edema.
Multiple choice questions

2. A central retinal vein occlusion
   A) Does not usually cause loss of vision.
   B) May be associated with the formation of new vessels.
   C) May be a cause of rubeotic glaucoma.
   D) May be associated with hypertension.
   E) Produces few abnormal signs in the retina.
3. Diabetic retinopathy

A) Is seen in 80% of patients who have had diabetes for 20 years.
B) Control of systemic hypertension is important in reducing the severity of the retinopathy.
C) The number of pericytes around the capillaries is increased.
D) Vitreous hemorrhage is associated with formation of new vessels on retina or optic nerve head.
E) Circinate patterns of exudates are treated with scattered laser.
4. Match pictures with diagnoses

I. Diabetic retinopathy.
II. Sickle cell retinopathy.
III. Bacterial endocarditis.
IV. Retinal vein occlusion.
V. Retinopathy of prematurity.
VI. Retinal artery occlusion.
VII. Retinal arteriole embolus.
GIANT CELL ARTERITIS

31. All is true about Giant cell arteritis except-

(PGMEE 2012-13)

a. Segmental nature of the involvement
b. Involves large to small sized arteries
c. Most commonly involved artery is abdominal aorta
d. Granulomatous inflammation

[Ref: Robbin's 8th/e pg. 512-513]
32. True about Giant cell arteritis is all EXCEPT:

   (PGMEE 2014-)

   a. High dose of steroid is drug of choice
   b. ESR is usually raised
   c. Intracranial ICA is particularly susceptible
   d. Mainly affects people of >70 years

   [Ref: Harrison’s 18th ed. ch.14, Pg. 112, Harrison’s 19th/e pg 2189]
33. Giant cell arteritis causes which of the following in the eye:

(PGMEE 2014-15)

a. Episcleritis
b. Anterior ischemic optic neuropathy
c. Neuroparalytic keratitis
d. Band keratitis

[Ref: Harrison’s 18th ed. ch.14, Pg. 112]
34. What is feature of temporal arteritis? (PGME)

a. Giant cell arteritis
b. Granulomatous vasculitis
c. Necrotizing vasculitis
d. Leucocytoclastic Vasculitis