Vascular diseases of the nervous system

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Clinical Neurology

Ischemic stroke

- Sudden loss of blood supply to an area of the brain resulting in loss of neurological functions of that area.
- It results from arterial cerebral thrombosis or embolus.
- It is more common than haemorrhagic stroke (80% ischemic to 20% haemorrhagic).

Causes of ischemic Stroke

a.30% are due to small-artery occlusion

b. 30% are due to large-artery thromboembolism

c. 20% are due to cardioembolism

d. 20% are due to other mechanisms or are cryptogenic

Anterior cerebral artery

The ACA arises from the internal carotid artery. The ACA supplies:

- The medial aspect of the frontal lobe
- The medial aspect of the parietal lobe
- The anterior part of the internal capsule
- The anterior portion of the basal ganglia

Middle cerebral artery

The MCA supplies:

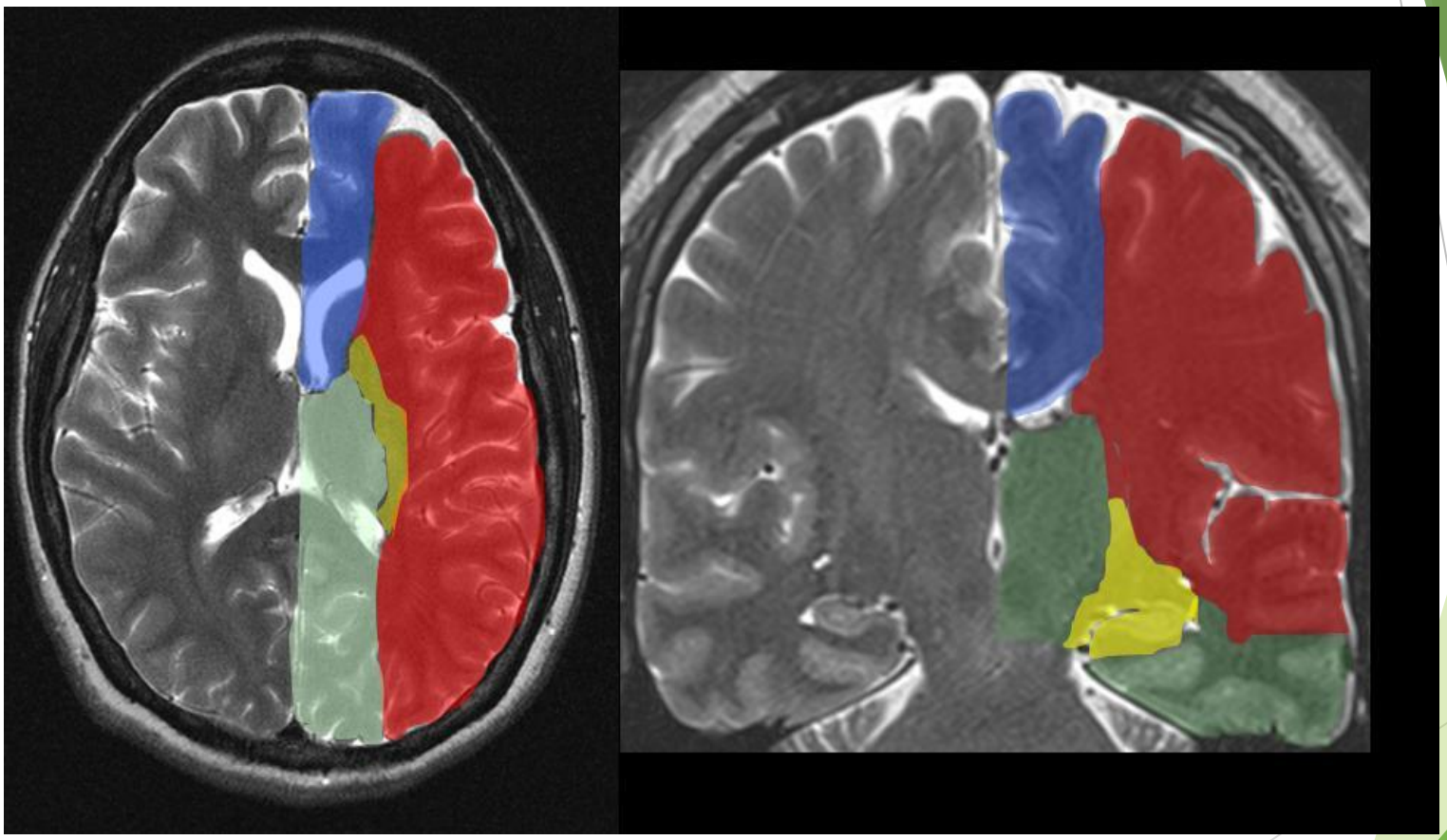
- The lateral portion of the frontal lobe
- The anterior and lateral portions of the parietal lobe
- The internal capsule, globus pallidus and putamen.

Posterior cerebral artery

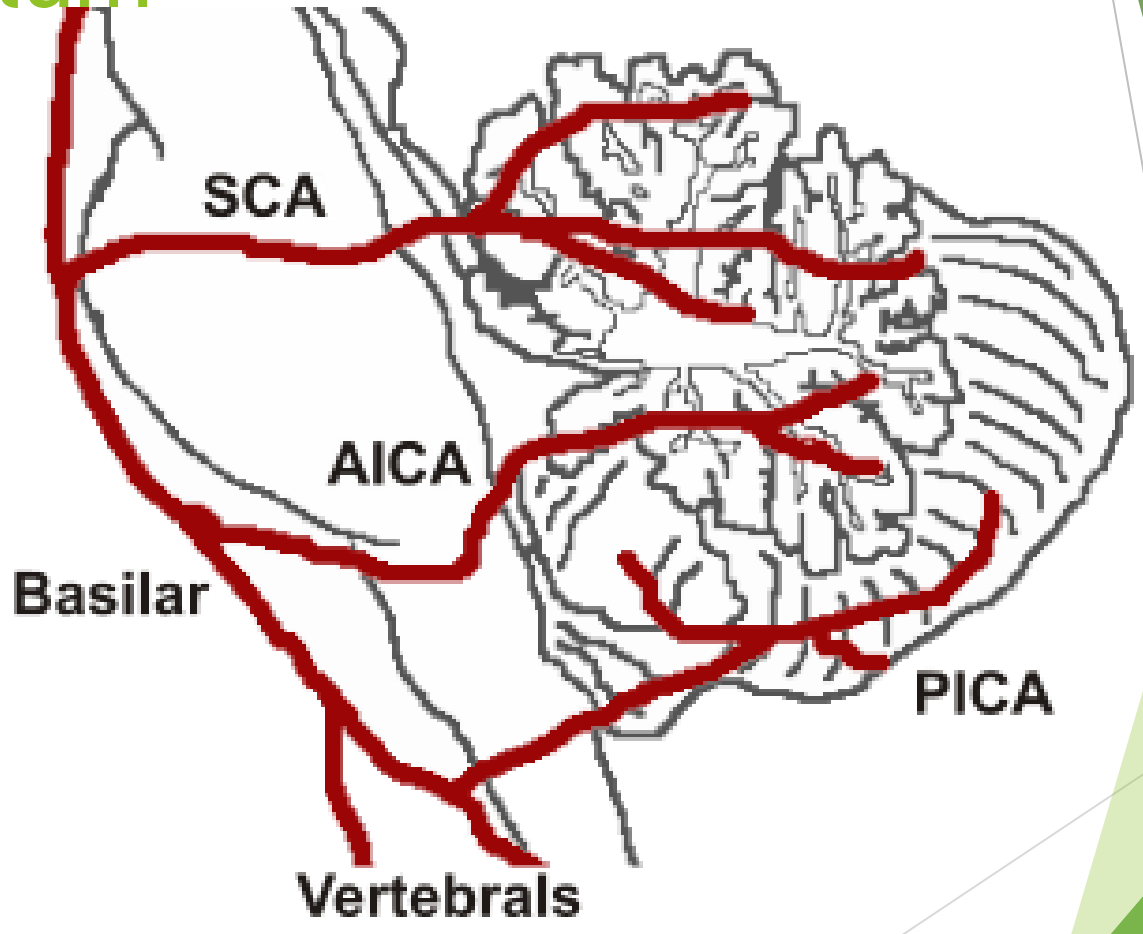
- It branches from the basilar artery.
- It forms the posterior circulation of the brain and supplies:

1. The thalami
2. The posterior and medical portion of the temporal lobe
3. The brain stem
4. The occipital lobe

Red: MCA, blue: ACA, green: PCA. Yellow



Arterial supply of the cerebllum



Ischaemic stroke pathophysiology

- Initially blood flow to the area is significantly reduced.
- Energy supplements are therefore reduced.
- Available ATP is not enough to maintain the functions of the membrane pumps including Na-K pumps and Ca+ pumps.
- Consequently the membrane depolarizes and Na and Ca+ accumulate intracellularly.

Ischaemic stroke pathophysiology

- The is will results in cytotoxic edema, which occurs early in the process of infarction.
- The central area has the lowest perfusion and usually dies within minutes and called the core.
- Peripheral areas usually receive collaterals and therefore they have reduced perfusion and may stay viable for hours after the stroke. This area is called the penumbra.

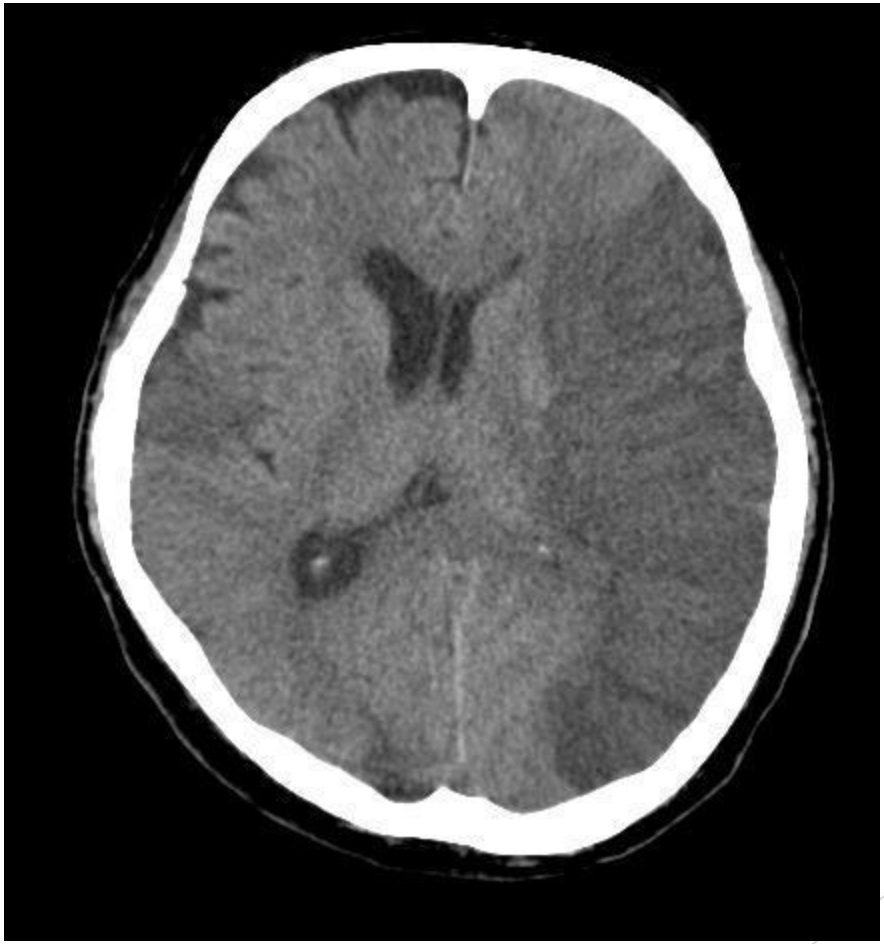
Ischaemic stroke pathophysiology

- Ca+ usually stimulates other enzymes that create more damage.
- Ischemia usually results in disruption of the BBB. This results in diffusion of fluids, substances and macrophages. This usually causes vasogenic oedema and starts after hours and peak at 3-5 days and resolves after several weeks.

Ischaemic stroke pathophysiology

- The infarcted core produces destructive cytokines after hours. These will produces further damage to the penumbra. Therefore reperfusion should be within 3-4.5 hours.
- In the core, astrocytes and oligodendrocytes are destructed and phagocytosed by macrophages that invaded through the disrupted BBB. This results in liquefaction necrosis and the area appears cystic with density similar to CSF density.

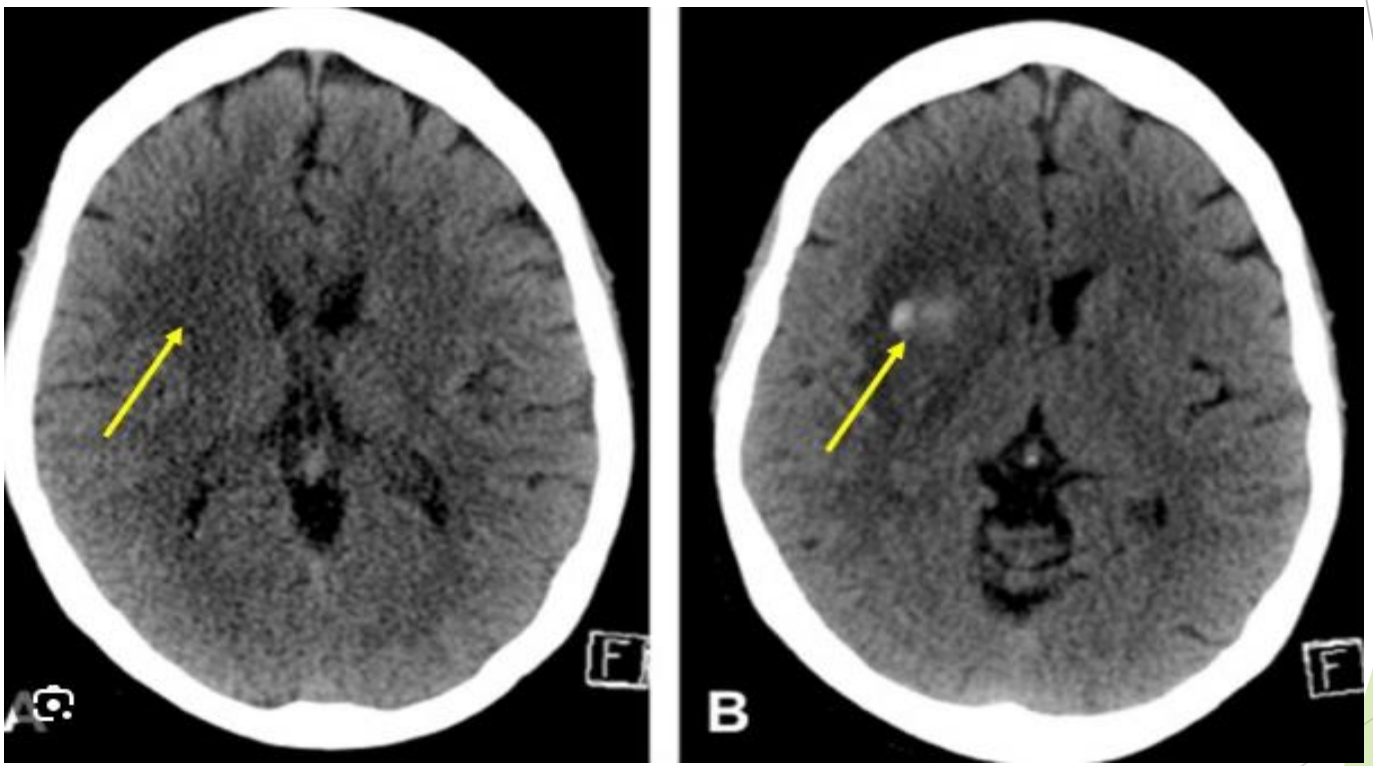
Stroke appears as cystic after liquefaction necrosis



Ischaemic stroke pathophysiology

- Haemorrhagic transformation can occur in 5% of strokes that did not receive rt-PA.
- This happens more with cardioembolic strokes and in large infarctions.
- This is due to either reperfusion with collateral or recanalization or from BBB disruption.
- Usually haemorrhage occurs with 2-14 days and may be in the form of petechial haemorrhage that is not associated with neurological decline or large haemorrhage that may need evacuation.
- It is more likely to occur with rt-PA

Hemorrhagic transformation



Ischaemic stroke

- In large infarction, cerebral edema and herniation may occur. This is rare
- Seizures can occur in up to 2-23% of patients.
- Seizures can occur within few days and can become chronic.

Ischemic stroke

- Cardiogenic emboli are common source for recurrent strokes. They are associated with higher mortality.
- Within 60 minutes, aim is to stabilise patient, assess his status, evaluate physical examination, perform CT scan and consider reperfusion if appropriate.

Ischemic stroke aetiology

- Non modifiable risk factors:

1. Age
2. Sex (more common in male but death rate is 26% in males and 39% in females)
3. Race (1.5 times more in black)
4. Ethnicity
5. Migraine with aura
6. Family history or genetic factors
7. Fibromuscular dysplasia (narrowing of medium sized arteries)

Ischemic stroke aetiology

- Modifiable risk factors

1. hypertension
2. Smoking
3. Obesity
4. Diabetes
5. Carotid artery stenosis
6. Cardiac diseases such as atrial fibrillation, valvular heart disease, ASD, VSD, cardiac aneurysm, atrial myxoma)
7. Hypercholeserolemia
8. TIAs
9. Hyperhomocystenaemia, homocystinuria
10. Oral contraceptive pills
11. Sickle cell disease.

Other risk factors

hyperhomocysteinemia and homocystein urea

- Autosomal recessive
- Most common cause of death in these individuals is thormboembolic events including stroke and MI.
- Risk of vascular event in age of 30 is 50% in homozygote's
- Heterozygote's have also increased risk of vascular events.
- High blood homocyteinuria in heterozygote's can be treated by giving folic acid.

Other risk factors

Amyloid angiopathies

- Can cause stroke and dementia
- Autosomal dominant
- Onset 3rd or 4th decade

CADASIL

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy.

- Affects small arteries mostly
- Stroke like episodes around age of 46
- White matter changes occurs early and continues for life
- Learning difficulties

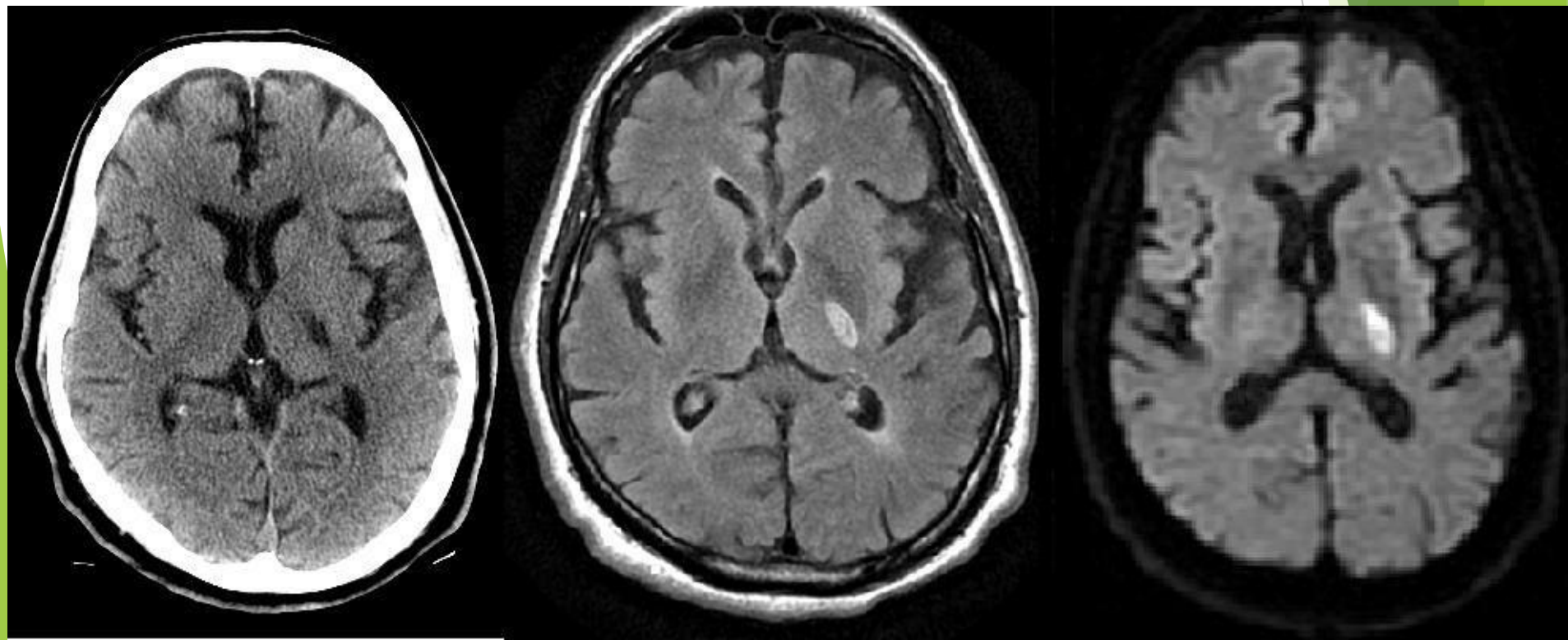
Large artery occlusion

- Mostly due to embolization from the carotid arteries or from the heart
- Less common due to in situ thrombosis or ruptured atheroma.
- Most commonly involved artery is the MCA and to a lesser extent the ACA.

Lacunar strokes

- Lacunar infarcts account for up to 20% of ischemic strokes
- It is due to embolic or thromboembolic events affecting perforating arteries of the MCA, lenticulostriate, vertebral, basilar, and the arteries of circle of Willis.
- Majority of lacunar infarcts are related to hypertension

Lacunar infarct affecting the posterior limb if the internal capsule
CT, MRI FLAIR, apparent diffusion coefficient

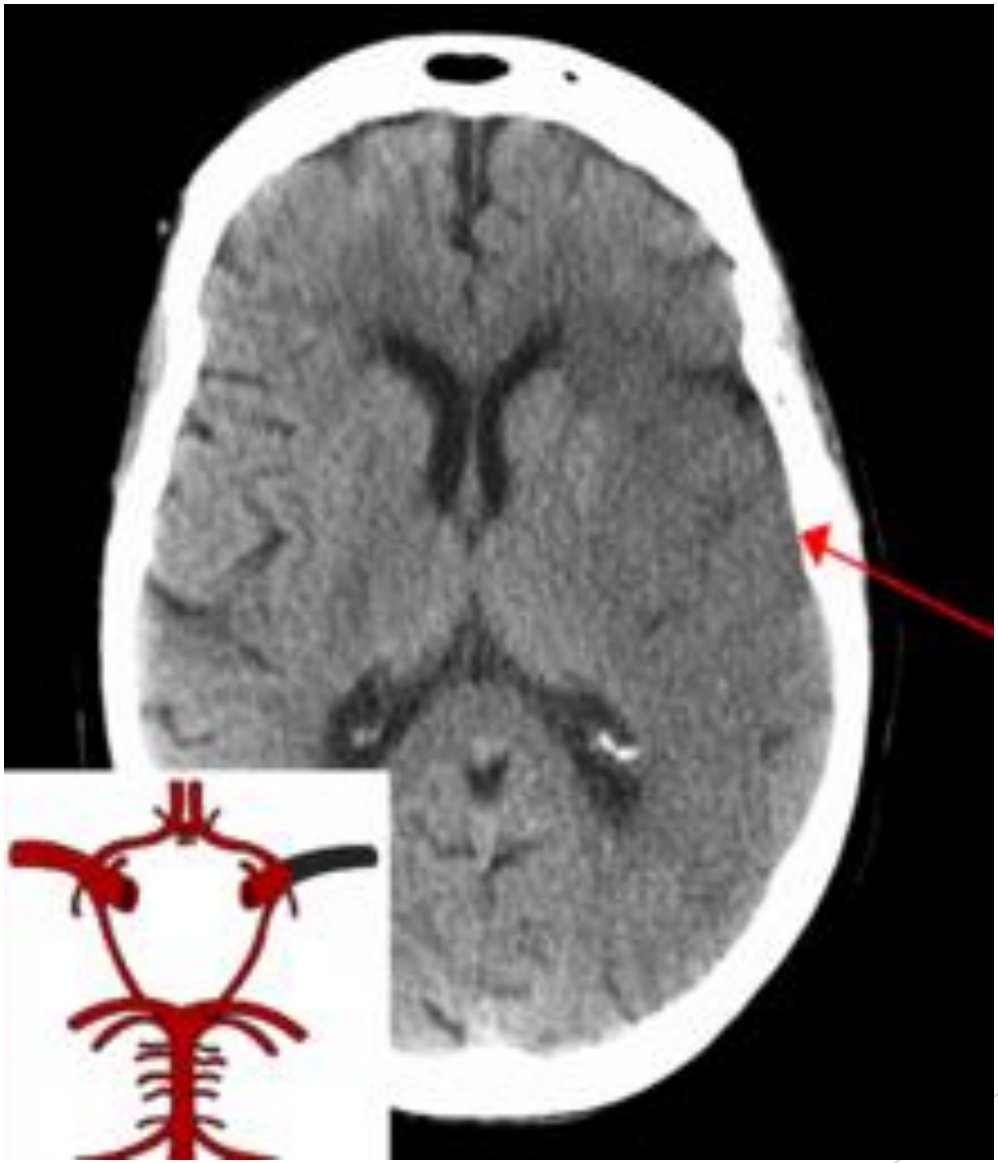


symptoms

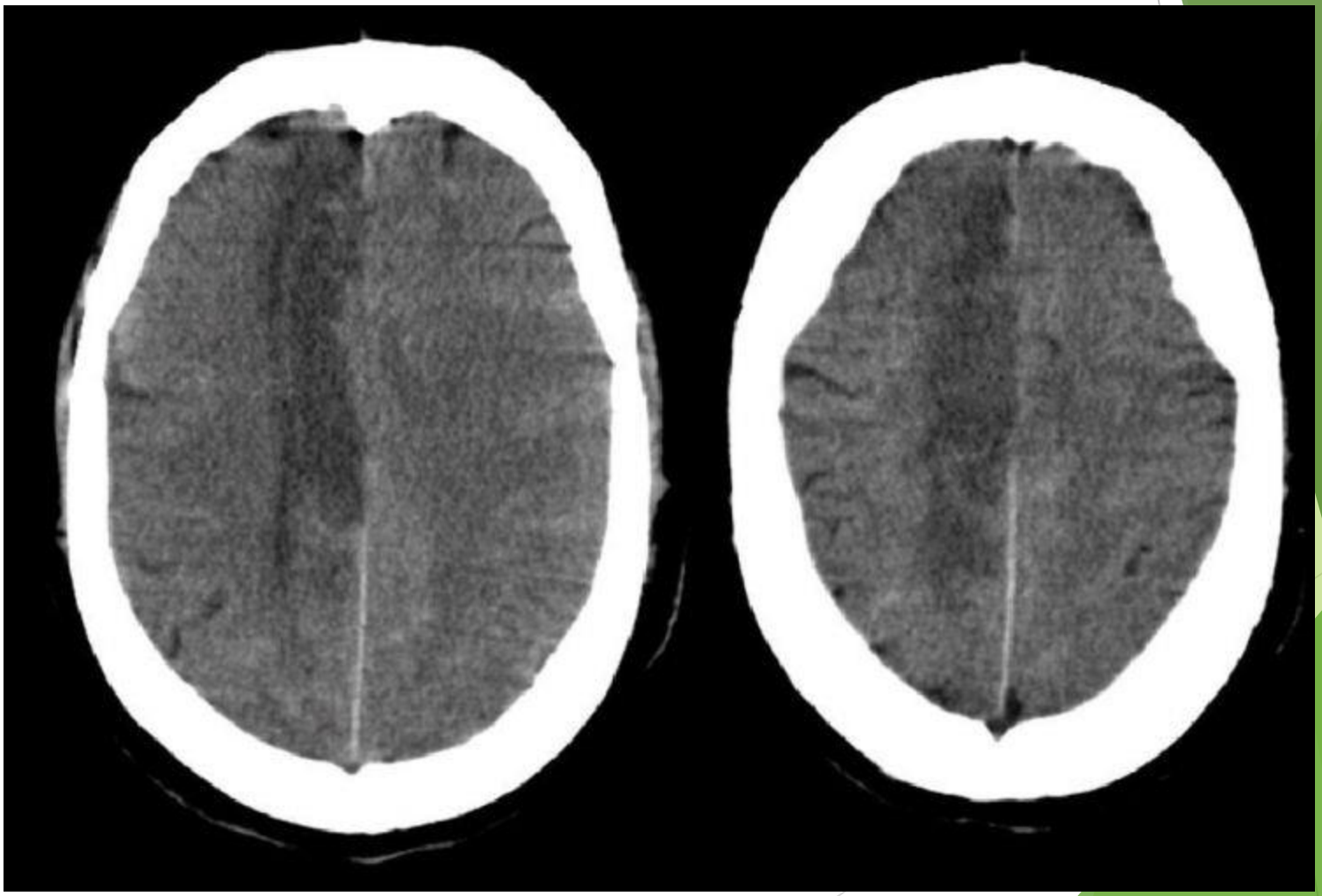
- Focal neurological deficit > 24 hours
- Headache in 40 % of patients which is usually due to involvement of the meninges
- seizures

Diagnosis

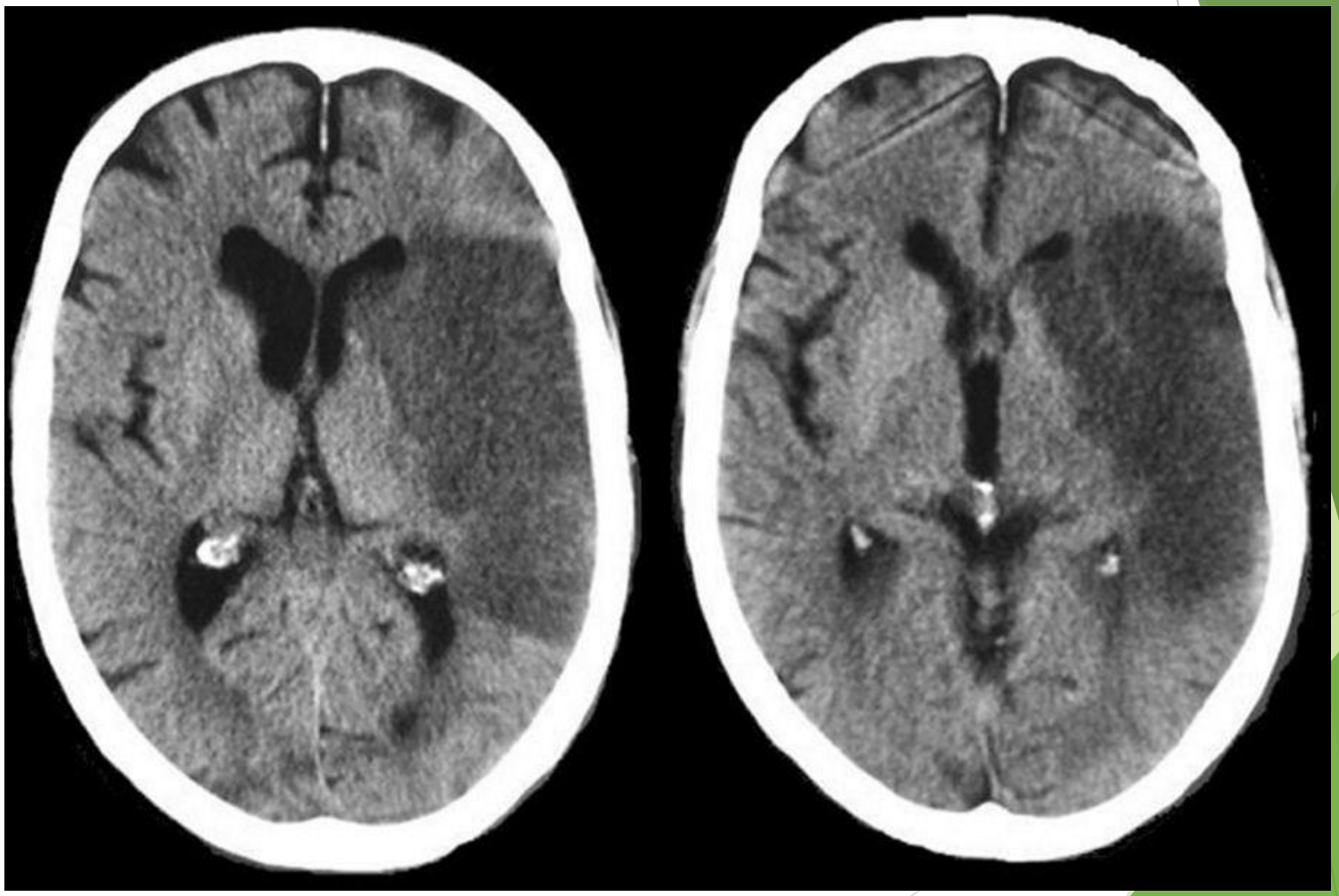
- CT (computed tomography): acute infarction may be identified by hypodensities at the interface of the gray and white matter (e.g., the insula and external capsule, the basal ganglia and internal capsule) or by sulcal effacement. however, CT within the first 3 hours is often normal



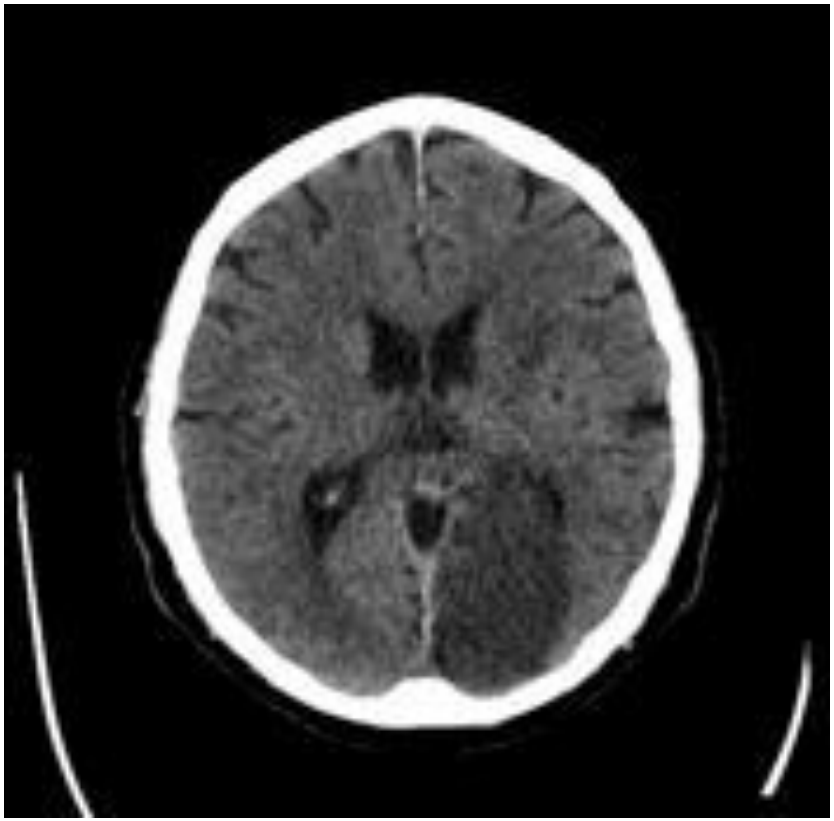
ACA stroke



MCS stroke



PCA stroke



Diagnosis

- MRI (magnetic resonance imaging): 90% of acute infarctions are identified with diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping.

diagnosis

- TIA: 40% exhibit neuroanatomically relevant DWI and ADC changes despite symptomatic resolution
- Carotid artery stenosis: For the purpose of identifying endarterectomy and stent candidates, cerebral angiography should be used
- Cardiac abnormalities: echocardiography may identify an enlarged left atrium, intracardiac thrombi, and coagulated material

diagnosis

- For patients > 45 years of age: evaluation of risk factors; sedimentation rate and C-reactive protein when suspecting temporal arteritis in patients > 50 years of age
- For patients < 45 years of age: evaluation of risk factors, as per older patients; consider evaluation for antiphospholipid antibodies , coagulation cascade disorders, and genetic-based stroke disorders

Acute treatment

- IV tissue plasminogen activator (tPA)/ alteplase: time window for treatment up to 4.5 hours from the time the patient was last known normal

Acute treatment

- Acute endovascular interventional procedures: used in select patients, typically with National Institutes of Health Stroke Scale (NIHSS) ≥ 10 and evidence of MCA occlusion or basilar occlusion on vascular imaging; time window for use may extend beyond 4.5 hours

Acute treatment

- Carotid endarterectomy: may be performed on an urgent basis in patients with TIAs that are referable to a severe stenosis
- Aspirin: given acutely, relative risk reduction of recurrent stroke within 14 days = 30%; also has small benefit in terms of mortality (a) Do not give aspirin (or other antiplatelet or anticoagulant agents) within 24 hours of thrombolytic administration

Acute treatment

- Blood pressure management: elevated blood pressures following a stroke are associated with better outcomes, thus hypertension is often left untreated 2– 3 days post-stroke unless systolic blood pressure (SBP) > 220 mmHg, diastolic blood pressure (DBP) > 130 mmHg, mean arterial pressure (MAP) > 130 mmHg, or if the patient is treated with tPA
- Avoid using clonidine or diazoxide because they reduce cerebral blood flow

Acute treatment

- Hyperglycemia management: elevated blood glucose is associated with worsened outcomes in stroke patients irrespective of the patient's diabetic status
- Seizure prophylaxis: no indication in the absence of a seizure. With a single seizure occurring < 2 weeks from the time of stroke, treat with antiepileptics for 3– 6 months before considering discontinuation (low risk of epilepsy). For a single seizure > 2 weeks from the time of stroke or for multiple seizures, treat for 2– 3 years before considering discontinuation (high risk of epilepsy)

Subarachnoid haemorrhage

It accounts for 10% of all strokes

Causes

- Aneurysms: account for 80% of all nontraumatic SAH
- Other vascular malformations: arteriovenous malformations (AVMs), moyamoya disease
- Head trauma: the most common cause of SAH
- Perimesencephalic hemorrhage: caused by venous or capillary bleeding into the prepontine and/ or ambient cisterns; not associated with aneurysms
- Venous thrombosis

Risk factors for SAH

- Hypertension
- Coagulopathy or anticoagulant use
- Smoking
- Drug use, particularly cocaine and amphetamines: suspecting drug abuse as the cause of SAH does not eliminate the need to search for a vascular malformation
- Estrogen use: high-dose preparations (e.g., birth control pills) may increase SAH risk; no effect of hormone replacement therapy

Symptoms of SAH

- pronounced headache
- Nausea ± focal neurological deficits; severity of nonfocal symptoms in SAH is generally greater than in intracranial hemorrhage
- Seizure at the time of SAH (5%)
- Vision loss may be due to intracranial focal injury or to simultaneous retinal haemorhage (terson haemorrhage)
- Mild nonfocal symptoms often occur with small SAH {sentinel hemorrhage}

Diagnosis

- CT scan to determine the Fisher scale for SAH
- Fisher scale:

1- no haemorrhage

2- thin and diffuse

3- local and thick

4- intraparnchymal or intraventricular

Diagnosis of SAH

- CT identifies only 95% of SAH cases within the first 24 hours; therefore, must evaluate for nonclearing hemorrhagic cerebrospinal fluid and xanthochromia if CT scan is negative but suspicion of SAH is high
- Cerebrospinal fluid xanthochromia is present in 70% within 6 hours and in 90% within 12 hours of SAH, but is rarely present within 2 hours of SAH

Diagnosis

- Angiography, either conventional or CTA
- MRA detects only 70% of aneurysms and has high false-positive rate in the MCA and ACA territories.
- Angiography is negative for aneurysms in 20% of SAH cases, probably because the aneurysm is hidden by the blood clot; therefore, if the first angiogram is negative, repeat it after 2– 3 weeks
- 50% of angiography-negative SAH is perimesencephalic hemorrhage

Treatment

- Blood pressure management: with an untreated aneurysm, reduce blood pressure to premorbid levels or to a mean arterial pressure 130 mmHg while keeping cerebral perfusion pressure > 70 mmHg
- Controlled (clipped aneurysm) allows for more aggressive therapy

Treatment

- Surgery:

Early clipping or coiling of the aneurysm reduced risk of rebleeding but increases the risk of iatrogenic brain injury; generally reserved for patients exhibiting focal neurological deficits and lethargy

Treatment of SAH

Vasospasm: a focal arterial constriction related to a loss of vasodilatory substances vascular reaction

- Period of highest risk is 4– 7 days post-SAH, but may occur up to 3 weeks post-SAH ii. Symptomatic effects of vasospasm may be focal or diffuse
- Diagnostic testing: screen patients for vasospasm with daily transcranial Doppler ultrasonography to detect increased flow velocities in major arteries

Treatment of vasospasm SAH

Nimodipine 60 mg PO q 4 hours for 21 days beginning immediately after SAH

- May have direct protective effect on the brain since it does not have much effect on vascular caliber
- Hypervolemic-hypertensive-hemodilution (“ triple H”) therapy has no proven benefit, but is commonly employed
- Intravascular papavarine or angioplasty of the vasospastic artery segments has no established benefit

Intracranial haemorrhage

- hemorrhage within the brain parenchyma that separates tissue planes, forming a well-demarcated hematoma; ICHs are commonly located in the putamen, cortex, thalamus, cerebellum, and pons

Intracranial haemorrhage

- ICH from large-vessel disease is rare, occurs after rupture of an AVM or extension of SAH into the brain parenchyma
- ICH from small vessels disease is caused by hypertensive angiopathy, amyloid angiopathy,

Risk factors

- Coagulopathy/ anticoagulant use: risk of ICH is greatly increased with INR > 3
- Drug use (amphetamines, cocaine): tend to cause ICH in cortex; IV route of administration is more prone to cause ICH than other routes
- Alcohol use, which is linearly related to the risk of ICH d. Hyperperfusion states (e.g., after carotid endarterectomy)
- Brain tumor, either primary (e.g., high-grade astrocytomas, pituitary adenoma) or meta-static (e.g., lymphoma, choriocarcinoma, melanoma)
- Previous ICH g. Cerebral venous sinus thrombosis
- Thrombocytopenia

Symptoms of ICH

- focal neurological deficits, often resembling ischemic infarction; symptoms are always persistent
- Headache (30%)
- Seizures: occur in 30% with cortical hemorrhage, but only in 5% with subcortical hemorrhage

Diagnosis

- Diagnostic testing: neuroimaging may demonstrate some enlargement of the ICH within the first 12 hours, but generally the hemorrhage is a monophasic event a. MRI signal characteristics of ICH.
- Small spots (< 2 mm) of decreased T2 signal are suggestive of microhemorrhages, which are typically observed in amyloid angiopathy.

Treatment

Acute treatment

- Medical: reduce blood pressure to pre-morbid levels or keep the MAP < 130 mmHg with cerebral perfusion pressure > 70 mmHg if premorbid blood pressure is unknown;
- reverse anticoagulation.
- Surgery: first-line treatment for cerebellar ICH > 3 cm or in patients exhibiting clinical deterioration; otherwise, surgery is only reasonable in cases of expanding ICH with simultaneous worsening of the patient's clinical condition
- More favorable locations for surgery are in the putamen, frontal cortex, and temporal cortex

Chronic and preventative treatment:

- control of hypertension; avoidance of anticoagulants

Special stroke conditions

- Marantic endocarditis: caused by the hypercoaguable state associated with chronic disseminated intravascular coagulation, AIDS, mucin-secreting tumors, or lupus (i.e., Libman-Sacks endocarditis
- Infectious endocarditis: mycotic aneurysms and microabcesses
- Watershed infarction

Watershed infarction