Diseases of Nervous System

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Lecture 3

III. Cerebrovascular diseases

- Cerebrovascular diseases denote brain disorders caused by pathologic processes involving the blood vessels.
- The three main pathogenic mechanisms are:

1. Thrombotic occlusion of vessels
2. Embolic occlusion of vessels
3. Vascular rupture.

- Thrombosis and embolism cause ischemic injury or infarction of specific regions of the brain, depending on the vessel involved.
- Hemorrhage accompanies rupture of vessels, leading to direct tissue damage as well as secondary ischemic injury

Clinically

1. Stroke :

- Is the clinical designation applied to

a. Abrupt onset of focal or global neurological symptoms

b. caused by ischemia or hemorrhage

c. The symptoms must continue for more than 24 hours

d. There should be permanent damage to the brain.

2. Transient ischemic attack(TIA):

a. The neurologic symptoms resolve within 24 hours

b. No irreversible tissue damage

c. The cause is small emboli from the carotids or vertebrobasilar circulation that resolve before causing irreversible injury

- From the standpoint of the pathophysiology and pathologic anatomy, cerebrovascular diseases are divided into two main processes

A. Hypoxia, ischemia and infarction

B. Hemorrhage

A. Hypoxia, Ischemia and Infarction

i. Hypoxia

ii. Ischemia can result from:

a. A reduction in the perfusion pressure such as in hypotension

b. Large vessel obstruction

- When blood flow to a portion of the brain is reduced, the survival of the tissue at risk depends on

a. The presence of collateral circulation
b. The duration of ischemia
c. Magnitude and rapidity of of the reduction of the blood flow

- These factors determine

i. The precise anatomic site
ii. Size of the lesion
iii. And consequently the clinical deficit

- Ischemia can be

I. Global cerebral ischemia

II. Focal cerebral ischemia

I. Global cerebral ischemia

- Called diffuse ischemic/hypoxic encephalopathy
- Occurs when there is generalized reduction in the cerebral perfusion

- Causes include;

i. Cardiac arrest

ii. Shock

iii. Severe hypotension

A. Mild global ischemia:

- The patient may have only a transient post-ischemic confusion
- Followed by complete recovery
- No irreversible tissue damage

- Neurons are the most sensitive cells to transient mild global ischemia
- Followed by oligodendrocytes and astrocytes

Note:

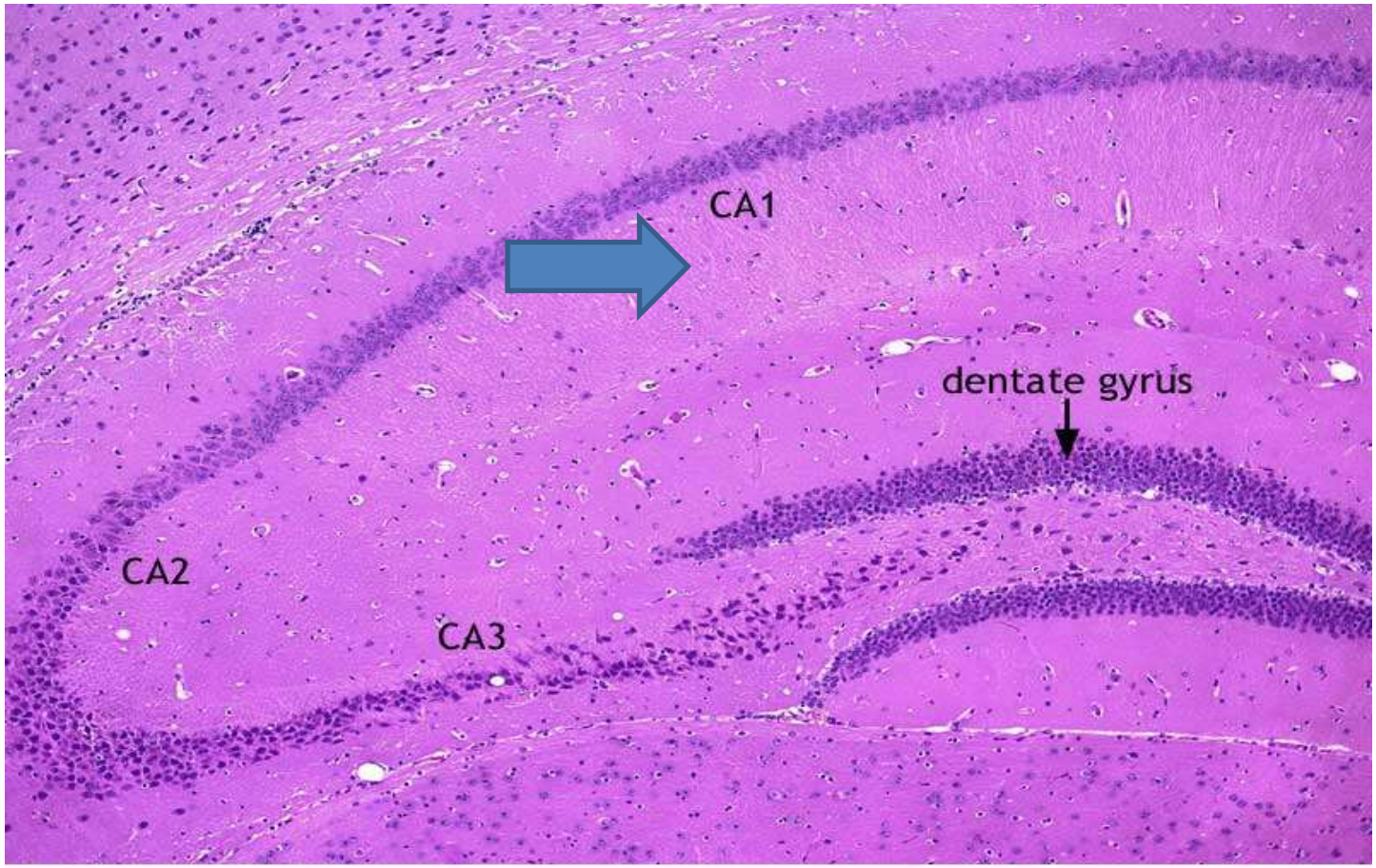
- Neuronal loss in transient global ischemia is due to excitotoxicity
- The susceptible neurons have many receptors to the excitatory neurotransmittor glutamate

- So in transient global ischemia, the astrocytes release glutamate that binds to its neuronal receptors NMDA (N-methyl D-aspartate) leading to increase intracellular calcium and activation of enzymes that leads to death of these neurons

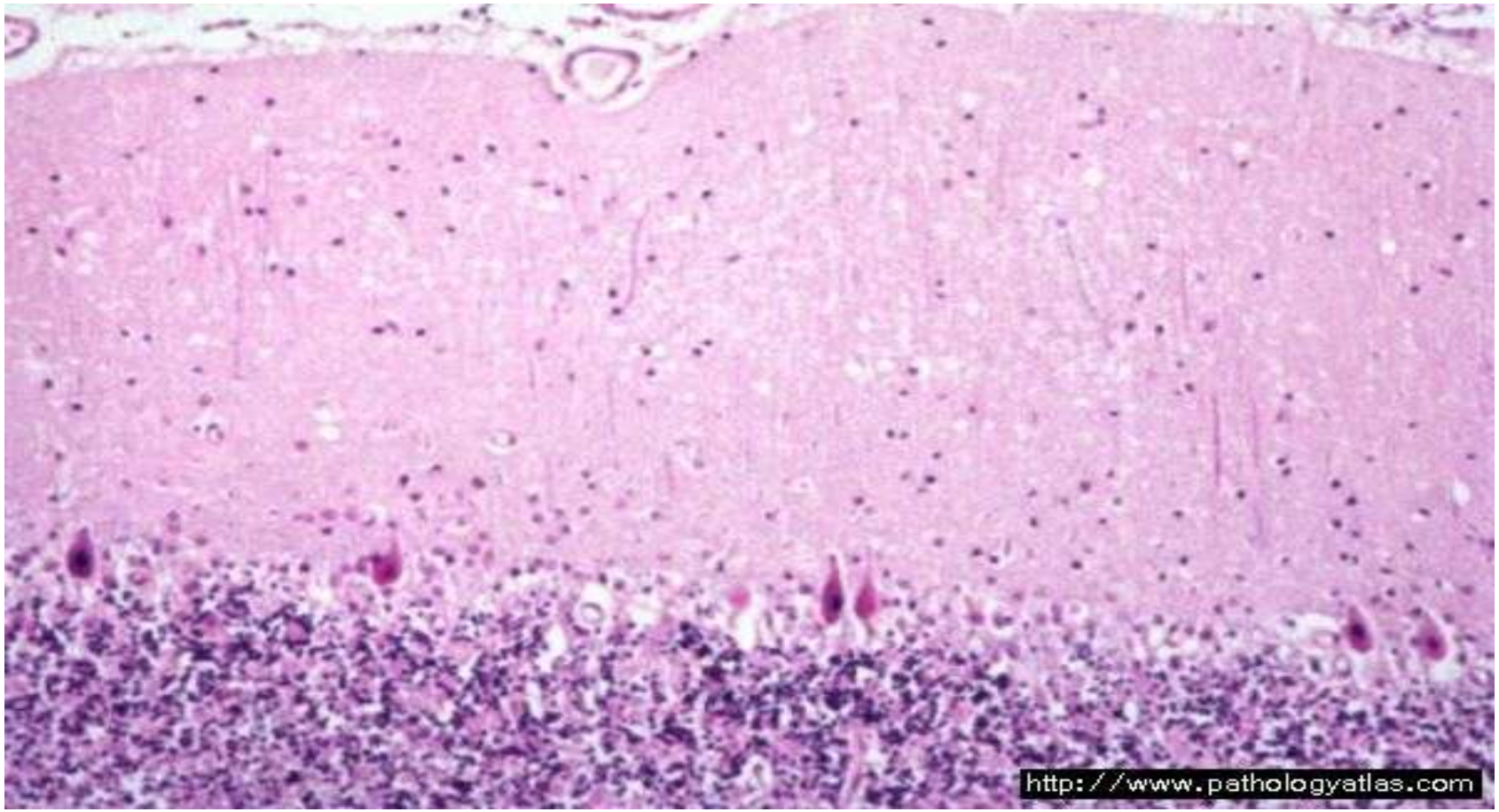
- The most sensitive neurons to transient global ischemia are;

i. The pyramidal cells of the hippocampus (especially) CA1 neurons
ii. Cerebellar purkinji cells
iii. Pyramidal neurons in the cerebral cortex produces a pattern called pseudolaminar necrosis

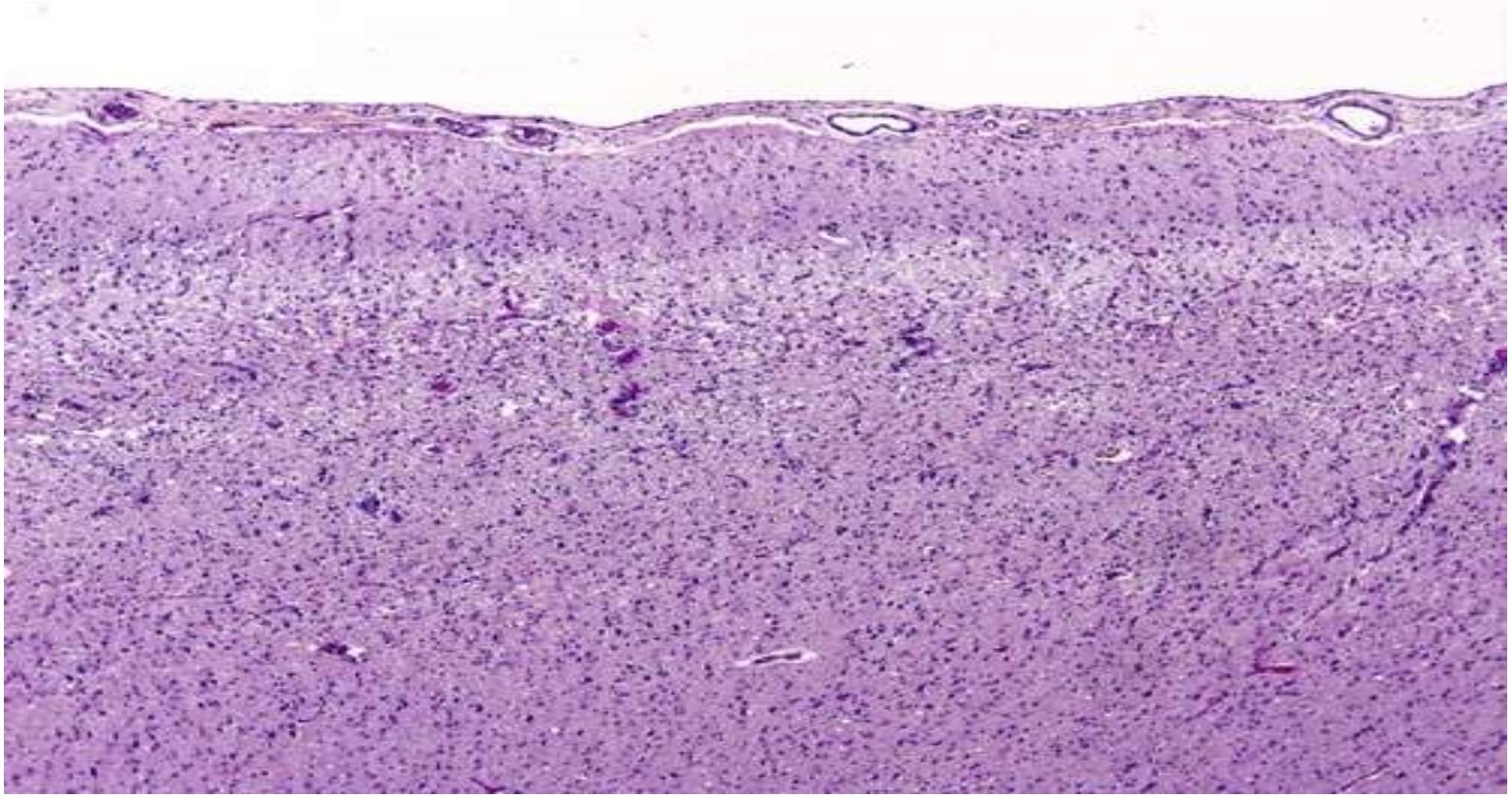
Hippocampus



Death of purkinjii cells



Pseudolaminar necrosis
necrosis of pyramidal cells



B. Severe global ischemia

- Widespread neuronal death occurs irrespective of the regional vulnerabilitya
- Clinical outcomes

i. Patients who survive this injury remains in persistent vegetative state (awake but not aware)

ii. Brain death

- Other patients meet the clinical criteria for "brain death," including:

1. Evidence of diffuse cortical injury (isoelectric, or "flat," electroencephalogram
2. And brain stem damage, including absent reflexes and respiratory drive

Border zone ("watershed") infarcts

- Are wedge-shaped areas of infarction that occur in those regions of the brain and spinal cord that lie at the most distal fields of arterial perfusion.
- Border zone infarcts are usually seen after hypotensive episodes

.- In the cerebral hemispheres

1. **Double watershed area**

- Is the border zone between the anterior and the middle cerebral artery distributions is at greatest risk(double watershed area).
- Damage to this region produces a band of necrosis over the cerebral convexity a few centimeters lateral to the inter-hemispheric fissure.

2. Triple watershed area

- Is the border zone between anterior, middle and posterior cerebral arteries and located posteriorly in the parietal lobe.

Border zone infarcts

II. Focal Cerebral Ischemia

- Caused by reduction or cessation of blood flow to a localized area of the brain due to arterial occlusion or hypoperfusion
- When the ischemia is sufficient , it leads to infarction of region supplied by compromised vessel

- The size , location and the extent of damage are influenced by

i. Duration of the ischemia

ii. Adequacy of the blood supply

- The major sources of collateral flow are

1. Circle of Willis
2. Partial and inconstant reinforcement is available over the surface of the brain for the distal branches of the anterior, middle and posterior cerebra arteries through corticoleptomeningeal anastomosis

- NOTE

- In contrast, there is little if any collateral flow for thalamus, basal ganglia, and deep white matter which are supplied by deep penetrating vesseles.

- Occlusive vascular disease of severity sufficient to lead to cerebral infarction may be due to

1. *Embolization from a distal source*
2. *Insitu throbmosis*
3. *Vasculitidis*

1. Embolism

- Sources of emboli:

a. Cardiac mural thrombi are a frequent source

b. Thromboemboli also arise in arteries, most often from atheromatous plaques within the carotid arteries.

c. Fat emboli

d. Bone marrow emboli

- The territory of distribution of the middle cerebral artery-the direct extension of the internal carotid artery-is most frequently affected by embolic infarction

Note:

- Widespread hemorrhagic lesions involving the white matter are characteristic of embolization of bone marrow after trauma

2. In situ thrombosis;

- Are most commonly associated with atherosclerosis and plaque rupture

The most common sites of primary thrombosis are

a. The carotid bifurcation
b. The origin of the middle cerebral artery
c. And at either end of the basilar artery

3. **Inflammatory processes that involve blood vessels**

a. Infectious vasculitis is common in the setting of immunosuppression and in opportunistic infection such as aspergillosis and CMV encephalitis

2. Primary angiitis of the CNS:

- Is an inflammatory disorder that involves multiple small to medium-sized parenchymal and subarachnoid vessels
- Characterized by chronic inflammation, multinucleated giant cells and destruction of the vessel wall

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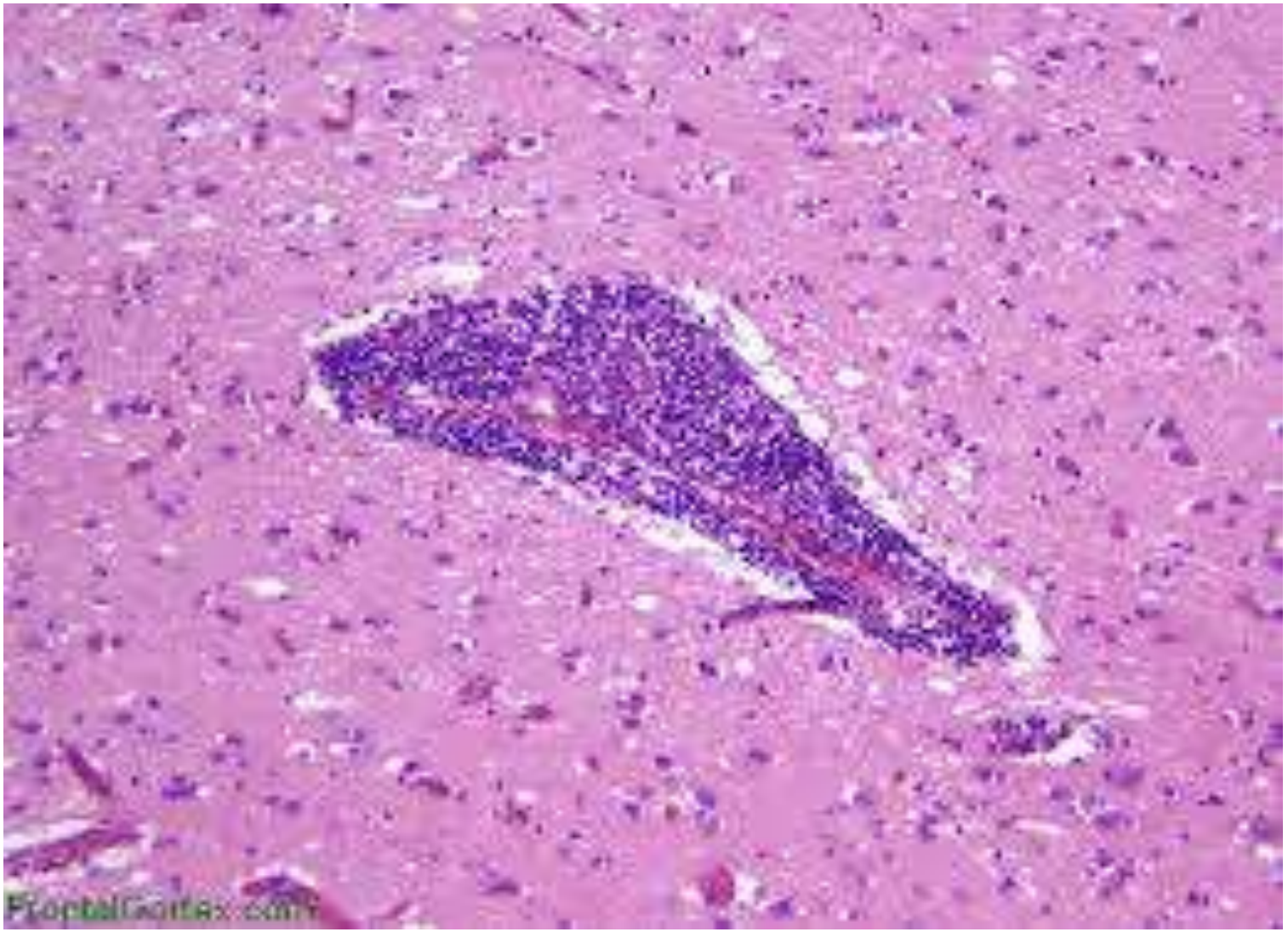
- Granulomas may be present; therefore it might be called granulomatous angiitis of the central nervous system
- Affected individuals may present with diffuse encephalopathy or multifocal clinical picture often with cognitive dysfunction
- Patients improve with steroids or immunosuppressive therapy

Primary angiitis of CNS



- Other causes of infarction

i. Hypercoagulable states

ii. Drug-abuse such as amphetamine, heroin and cocain

Note

- The venous side of the circulation may also undergo thrombosis and cause significant cerebral ischemia
- The striking example is the thrombosis of the superior sagittal sinus which can occur with infections or hypercoagulability state

- Infarcts can be divided into two broad groups hemorrhagic and non-hemorrhagic based on their macroscopic and corresponding radiologic appearance

Morphology

- *The macroscopic appearance changes in time.*

1. During the first 6 hours of iirreversible injury, little is observed
2. By 48 hours

- The tissue becomes pale, soft, and swollen, and the corticomedullary junction becomes indistinct

3. From 2 to 10 days

- The brain becomes gelatinous and friable, with distinct boundary between ormal and abnormal tissue

4. From 10 days to 3 weeks

- The tissue liquefies, leaving a fluid-filled cavity

Microscopically,

1. After the first 12 hours:

a. Red neurons and both cytotoxic and vasogenic edema predominate

b. Disintegration and myelinated fibers .

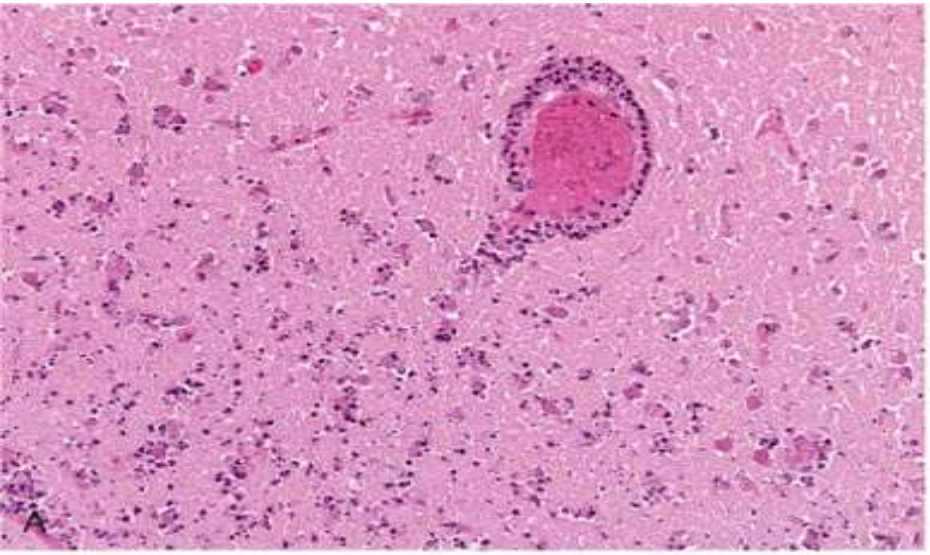
2. Up to 48 hours, there is some neutrophilic emigration

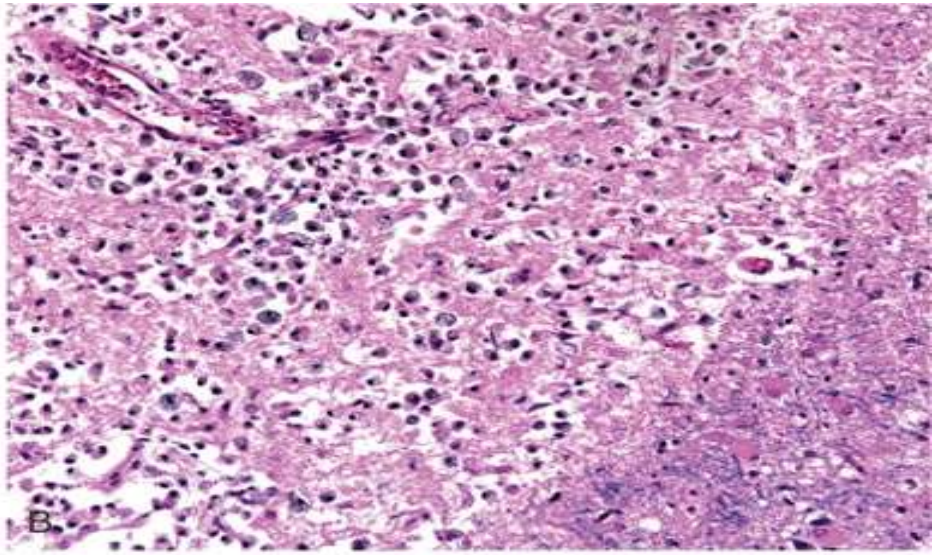
3. 2-3 weeks

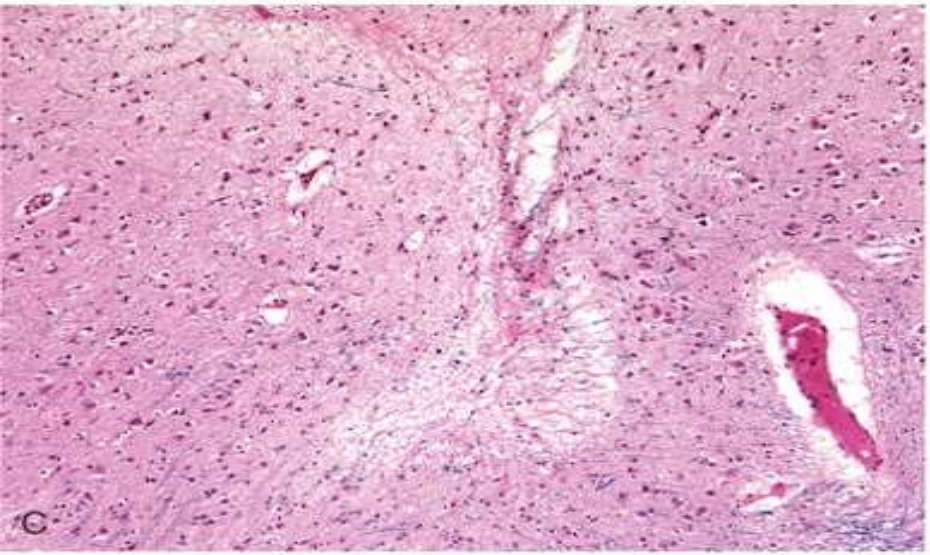
a. Mononuclear phagocytic cells predominate and macrophages containing myelin breakdown products or blood may persist in the lesion for months to years.

b. Gemistocytic gliosis followed by fibrillary astrocytosis after several months

Cerebral infarction







Notes:

a. In the cerebral cortex the cavity is delimited from the meninges and subarachnoid space by a gliotic layer of tissue, derived from the molecular layer of cortex.

b- The pia and arachnoid are not affected and do not contribute to the healing process.