

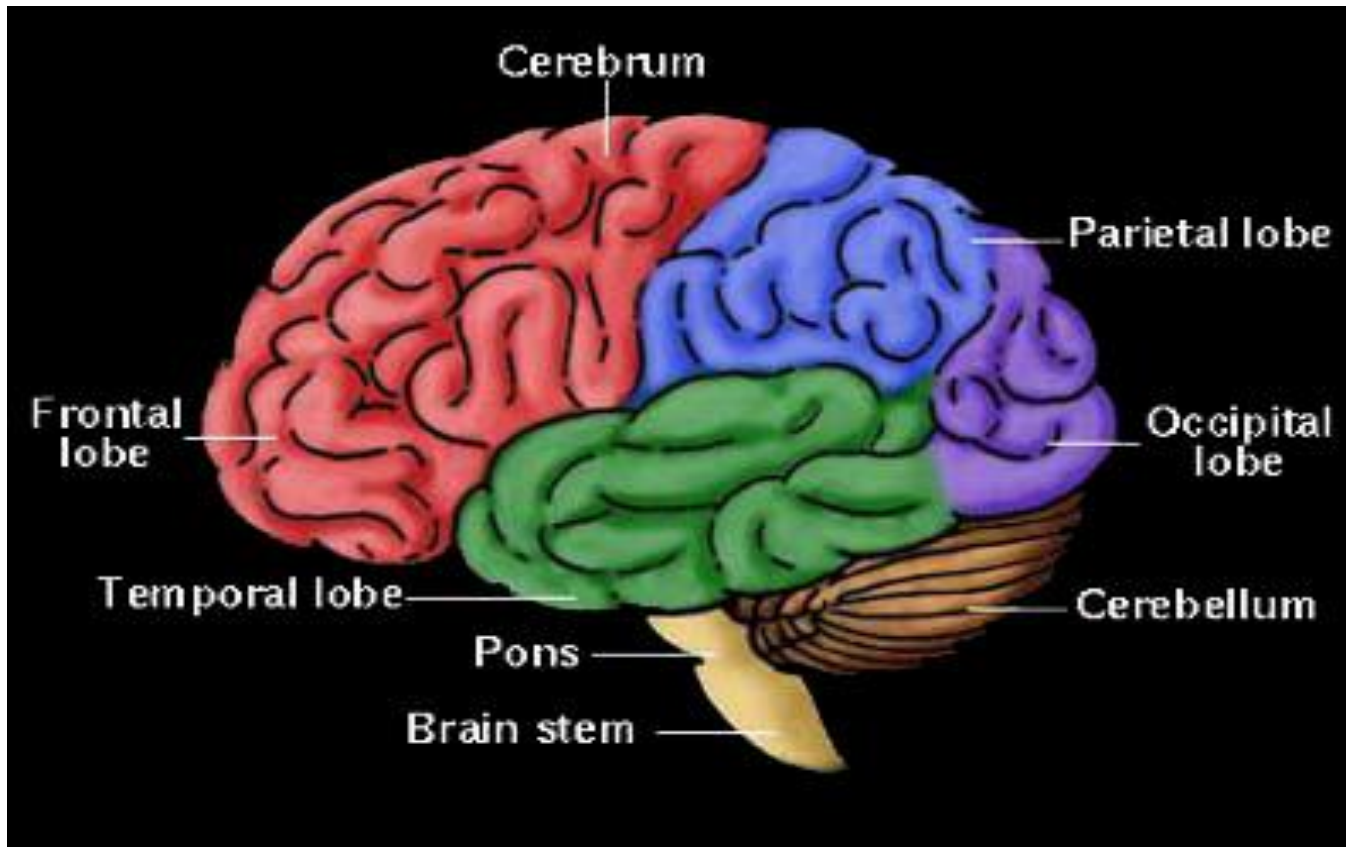
Central nervous system block

Neuropathology practical

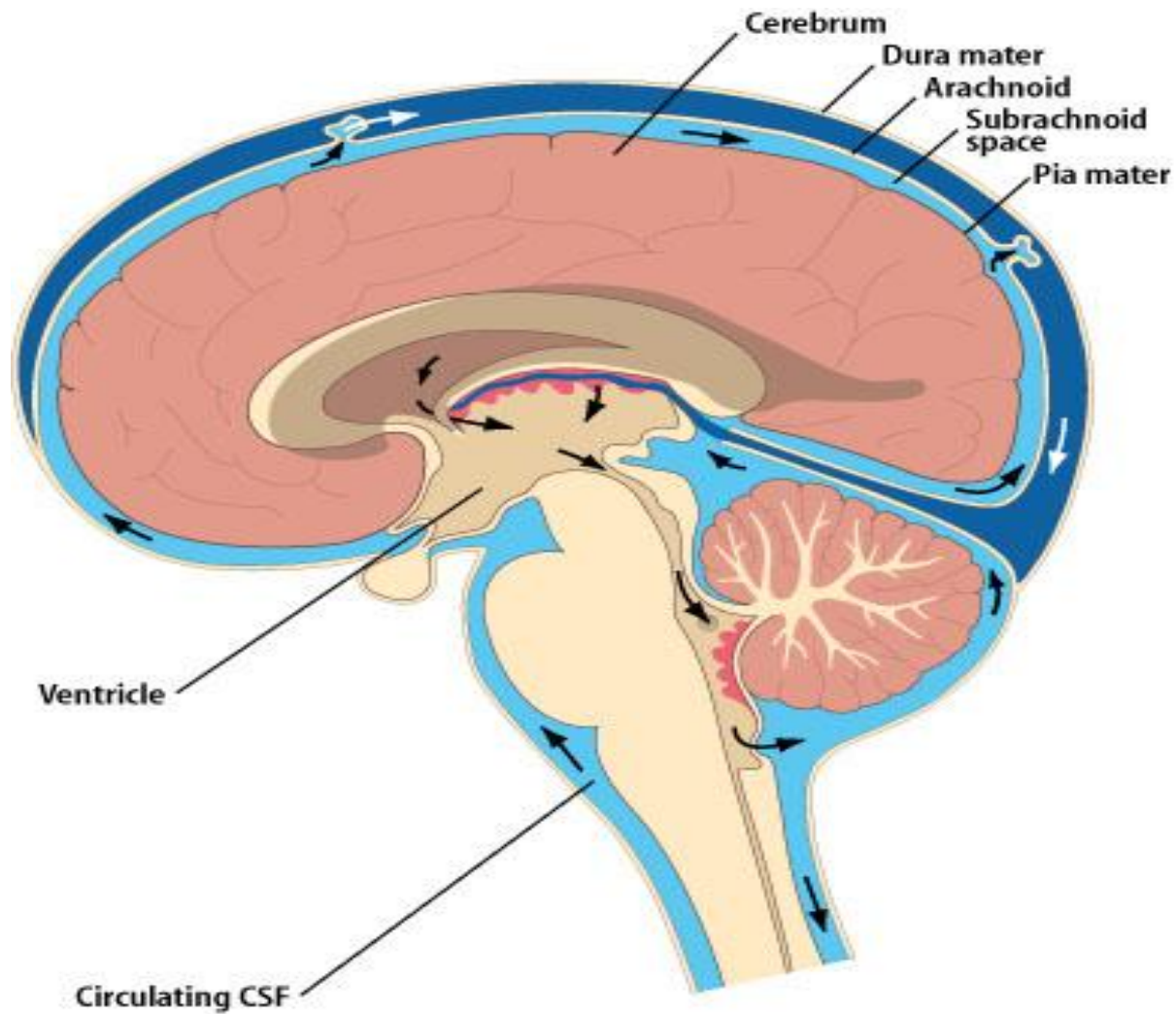
The practical will be 3-4 stations
(scenario based questions followed by
gross or microscopically pictures with
some questions related to the case)

Brief review of Normal anatomy and histology

Cerebrum, Cerebellum and Brain Stem

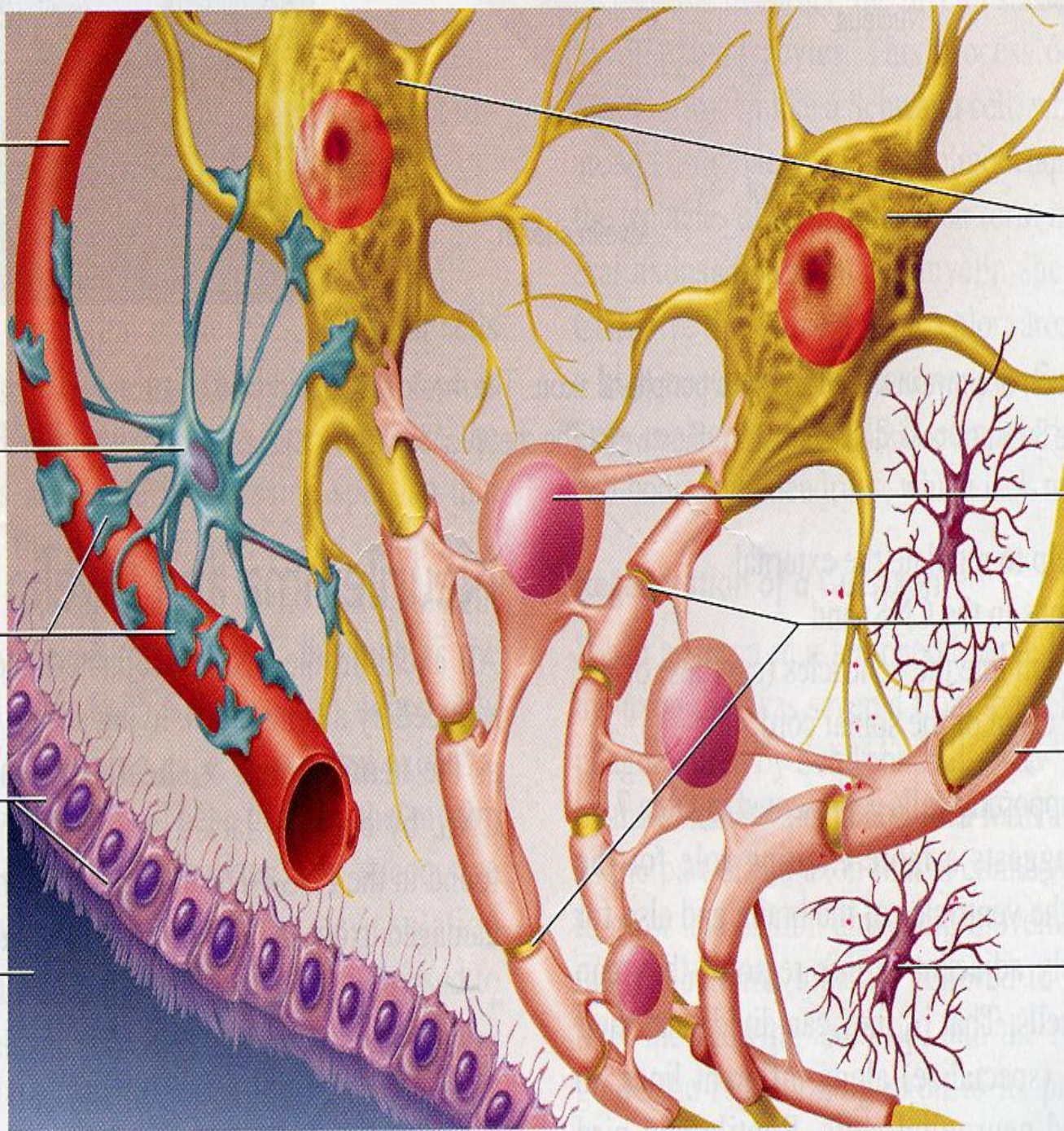


Meninges



CNS Cells

- Two cell types
 - Neuron
 - Conducts nerve impulses
 - Mitosis or cell division cannot take place in neurons so they cannot be replaced if they are destroyed.
 - Neuroglial cells
 - Support, nourish, and protect the neurons
 - Mitosis does take place in neuroglia.
 - Include astrocytes, oligodendrocytes, ependymal cells and microglia
 - A large percentage of brain tumors originate in neuroglial cells.



Capillary

Neurons

Astrocyte

Oligodendrocyte

Perivascular feet

Axons

Myelin sheath

Ependymal cells

Microglia

Cerebrospinal fluid

Gross and microscopic findings of selected CNS diseases

Case No. 1

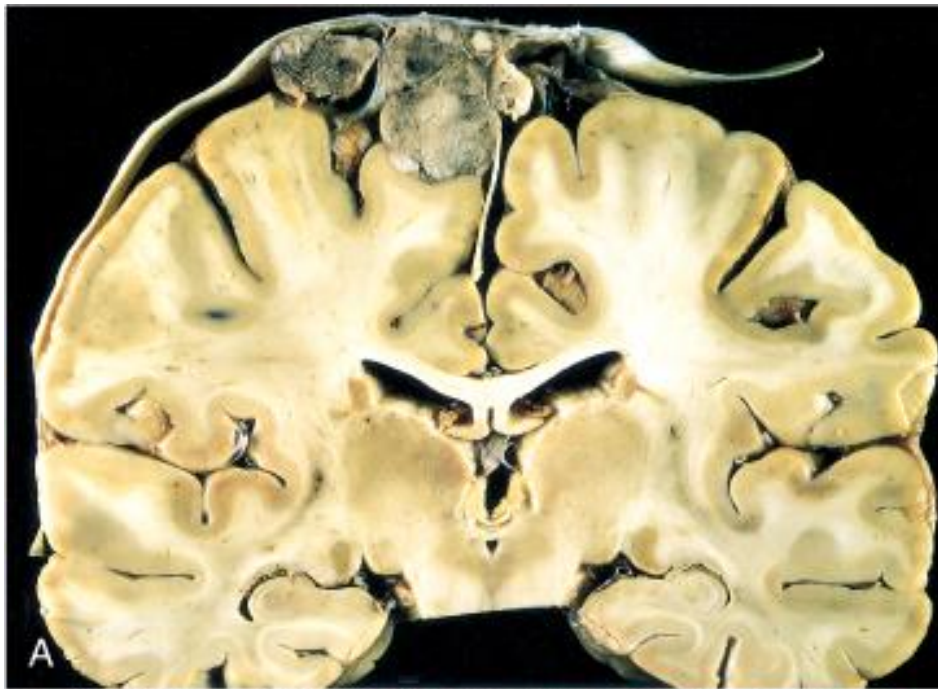
- 43 years old female complained of headache and two attacks of seizures in the past 4 months . Brain MRI revealed a 3 cm. **extra-axial (on meninges) mass in the parietal region**. It was **dural based** with mild edema in surrounding brain tissue.
- What is your provisional diagnosis?

It is meningioma

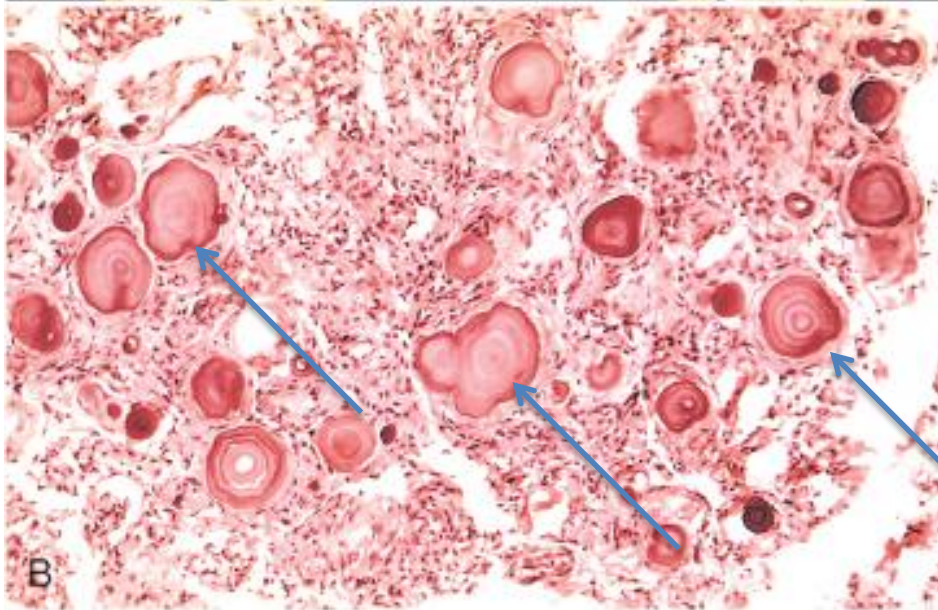
- Differential Diagnosis: schwannoma, brain abscess



Bisection mass from dural based brain tumor most likely to be meningioma. The arrow shows the remnant bone.

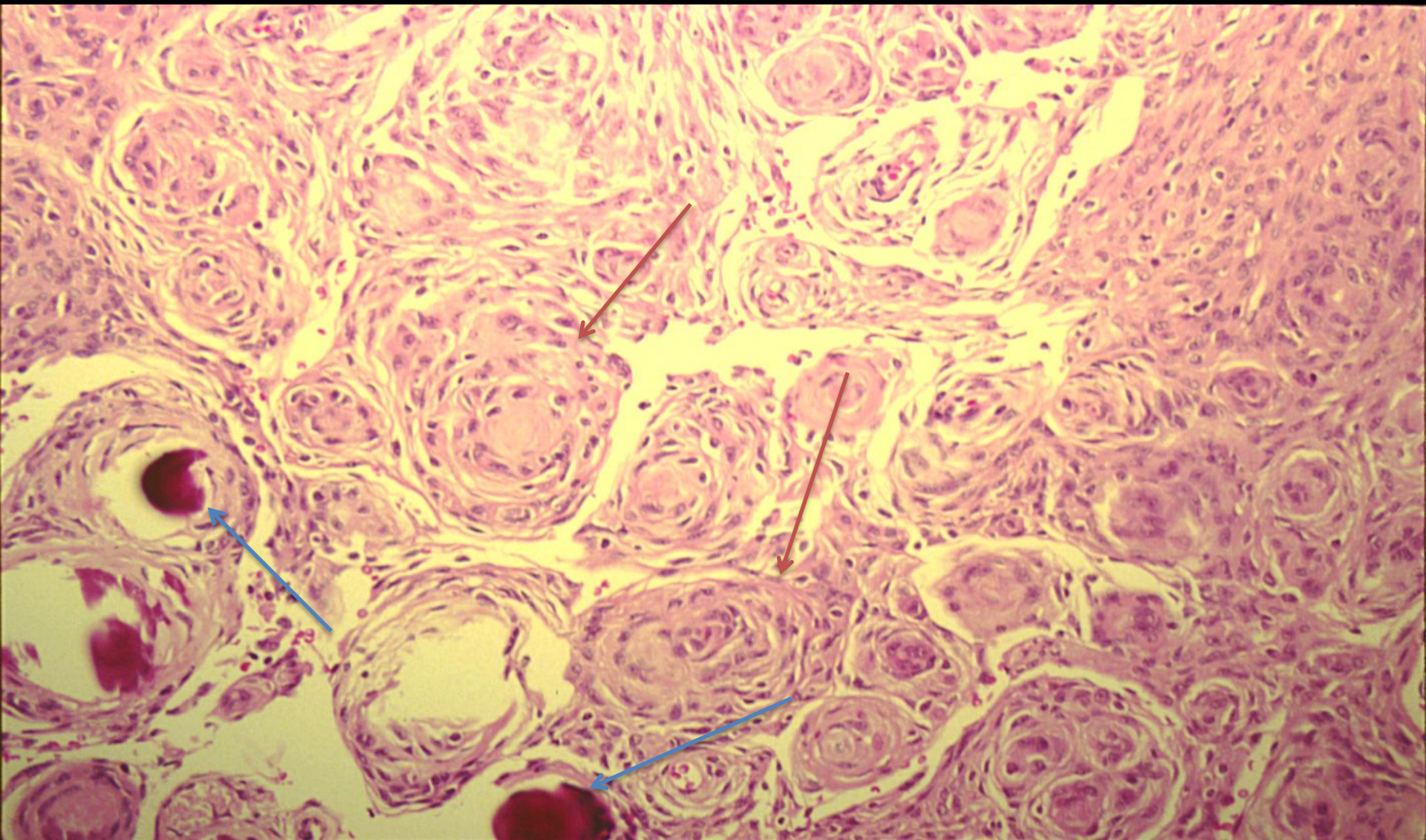


A, parasagittal multilobular meningioma attached to the dura with compression of underlying brain.






B, Meningioma with a whorled pattern of cell growth and psammoma bodies (arrows) (psammomatous meningioma).

MENINGIOMA (Syncytial meningioma)



Meningioma:

Section of tumour shows:

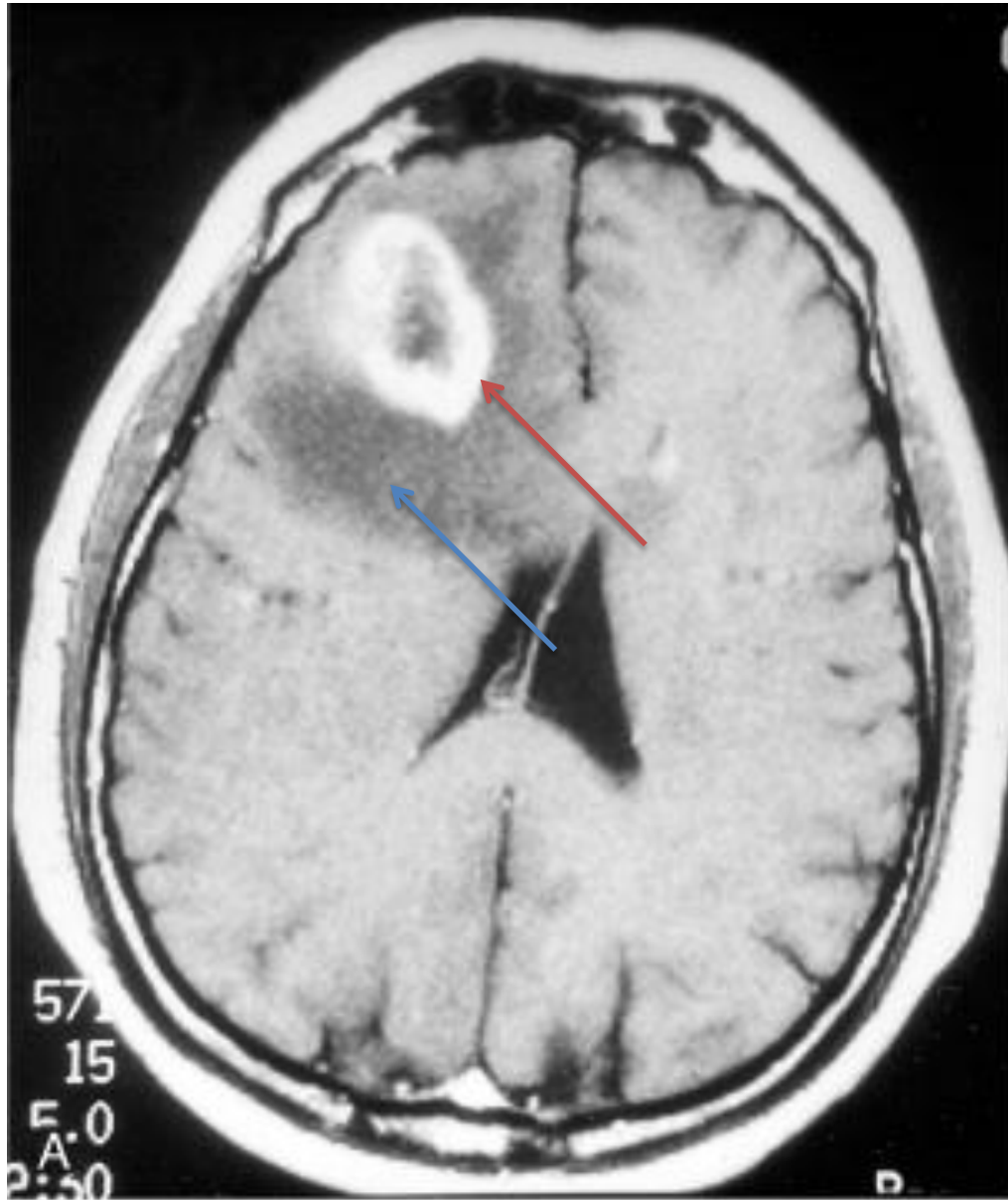
-  **Whorls of fibrocellular tissue (red arrows).**
-  **Cells are oval, spindle shape or elongated and **lack mitosis.****
-  **Psammoma bodies (spherical calcified particles) are also seen within the tumour (blue arrows).**

- Subtypes of meningioma:
- **Non-Malignant (benign, grade I):**
- Syncytial: clusters of cells without visible cell membrane between them.
- Fibroblastic: elongated cells with collagen fibers between them.
- Transitional: a case that shares characteristics of both syncytial and fibroblastic.
- **Atypical meningiomas grade II** (they can be non-malignant or malignant)
- **Anaplastic** (malignant) meningiomas grade III
- Associated with which syndrome ?
Neurofibromatosis type 2

Meningioma

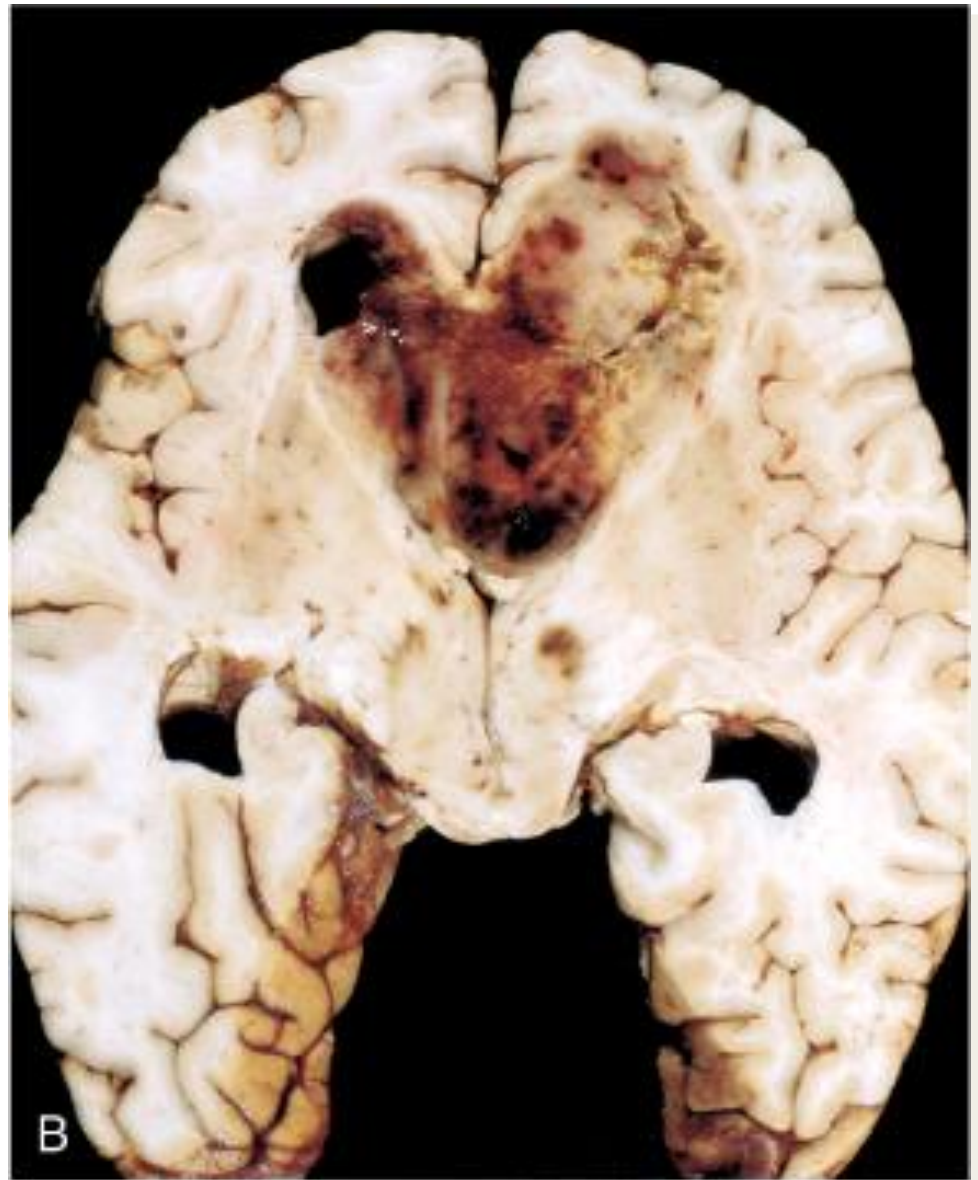
Case No. 2

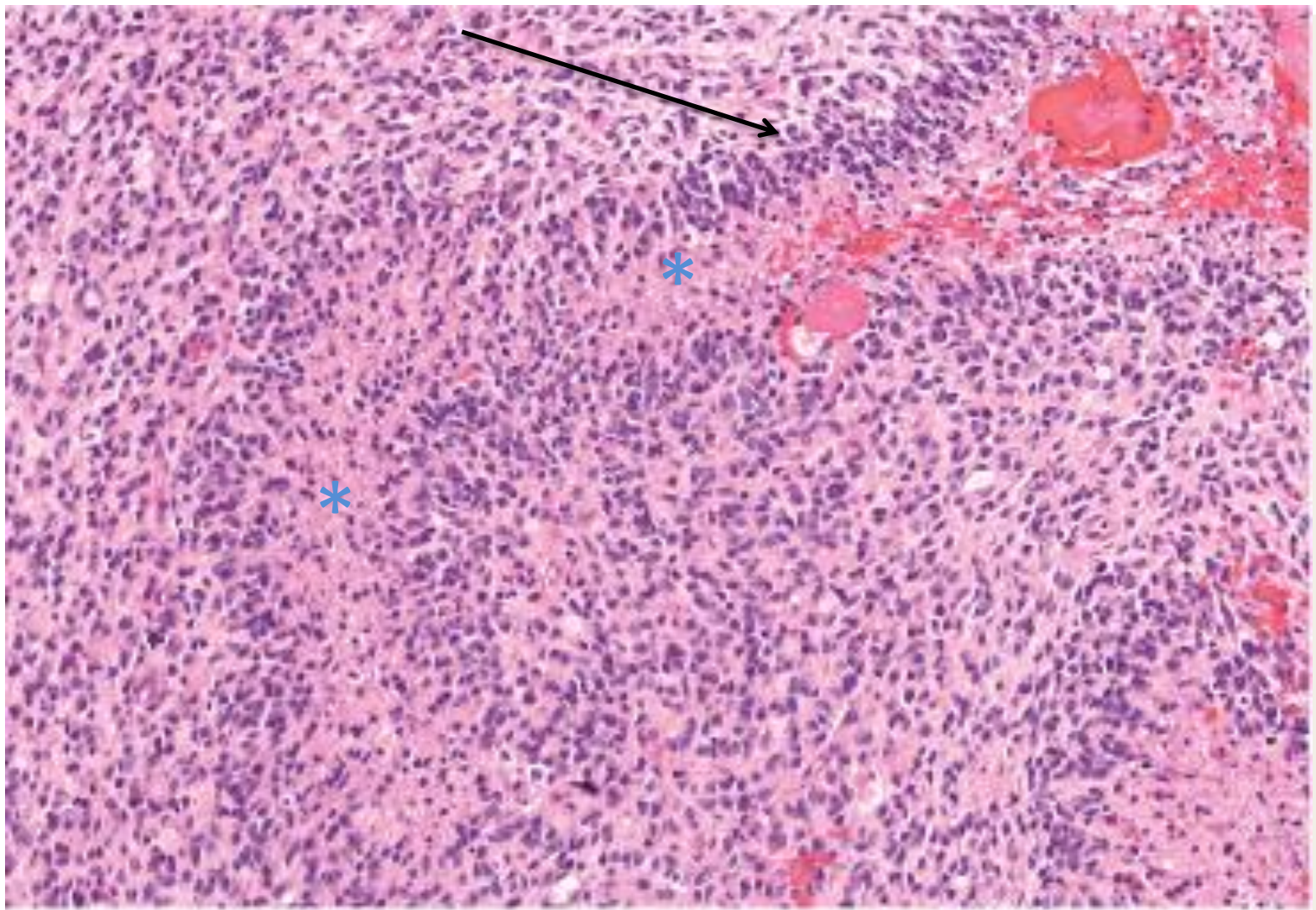
- 55 years old man complained for the last 2 months of headache. Brain MRI reveals a 3 cm. frontal intra-parenchymal space occupying lesion with rim enhancement on contrast studies. What is your provisional diagnosis ?
- DD: brain abscesses, gliomas



Computed tomographic (CT) scan of a large tumor in the cerebral hemisphere showing signal enhancement with contrast material (red arrow) and pronounced peritumoral edema (blue arrow).

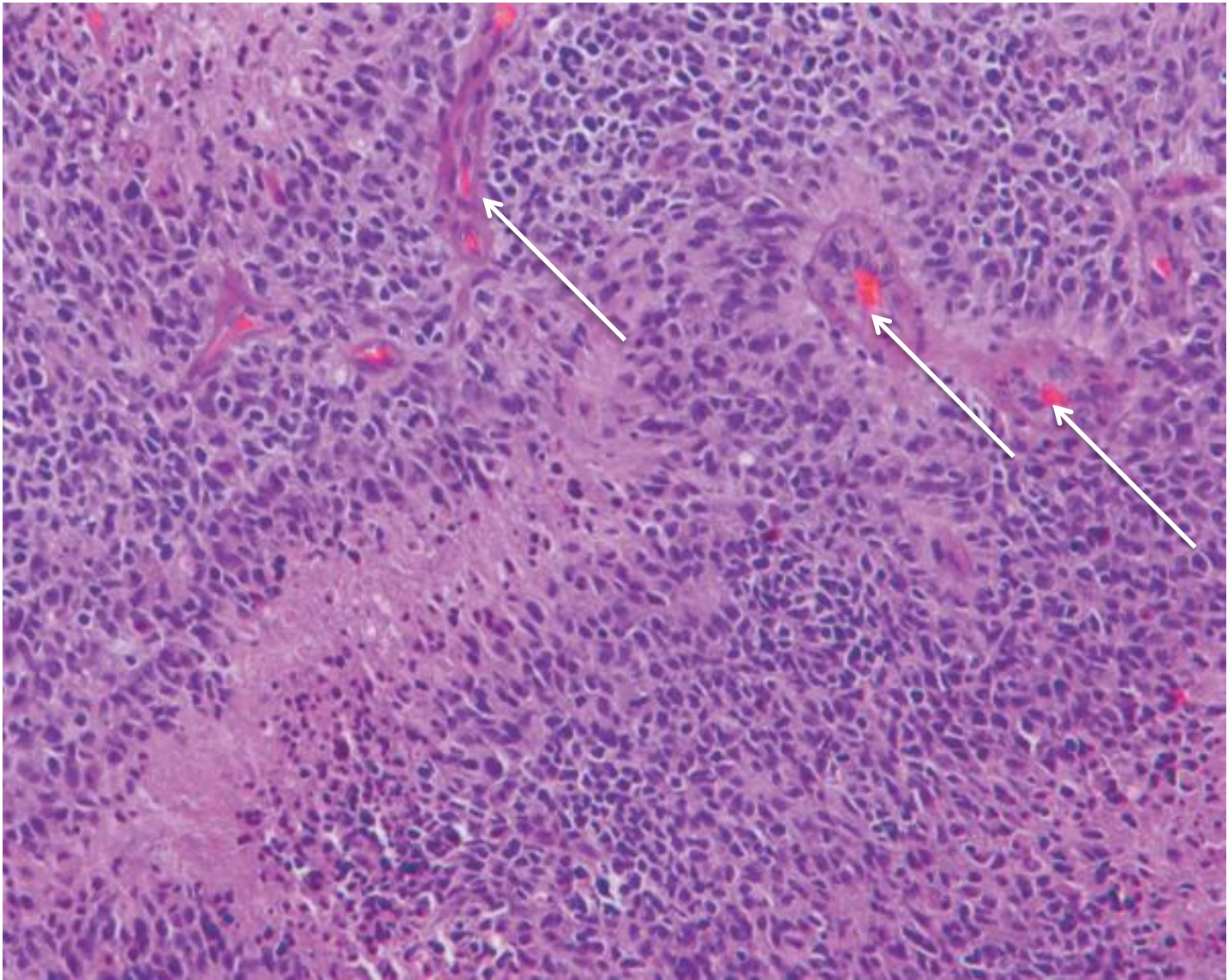
Glioblastoma multiforme
appearing as a necrotic,
hemorrhagic, infiltrating
mass.





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Glioblastoma. Foci of **necrosis** (blue *) with **pseudopalisading of malignant nuclei** (black arrow).



- Glioblastoma. Foci of necrosis with pseudopalisading of malignant nuclei and endothelial cell proliferation (white arrow)

Glioblastoma

Case No. 3

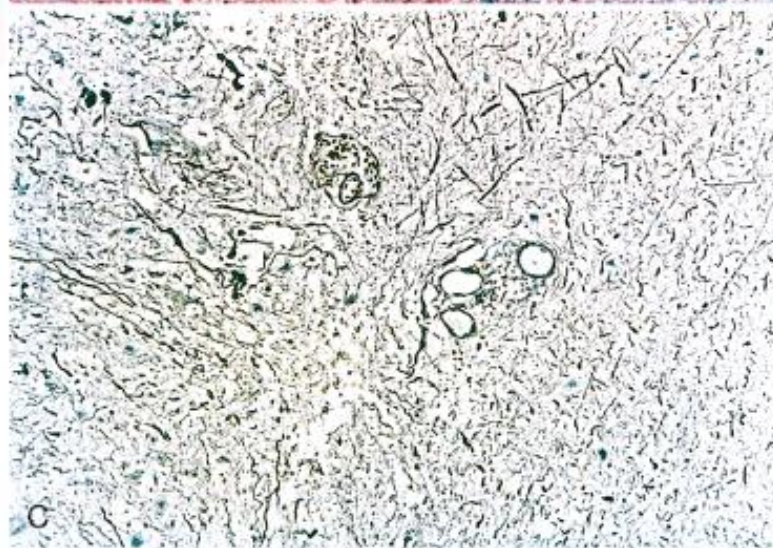
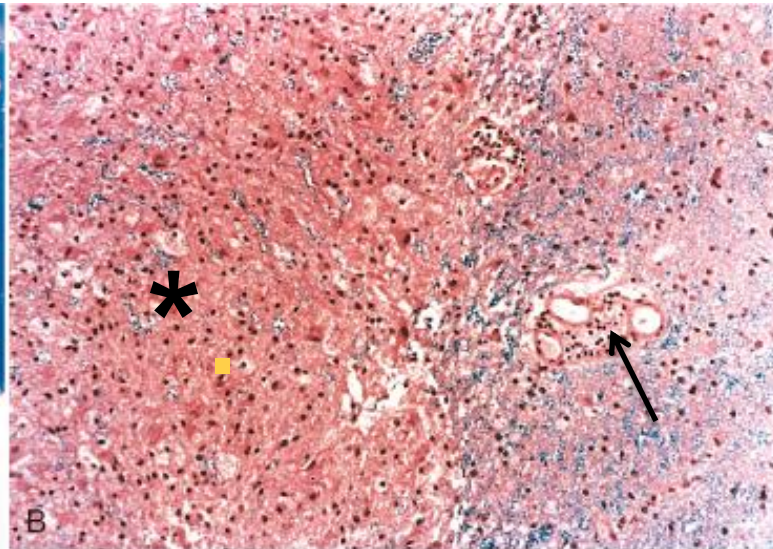
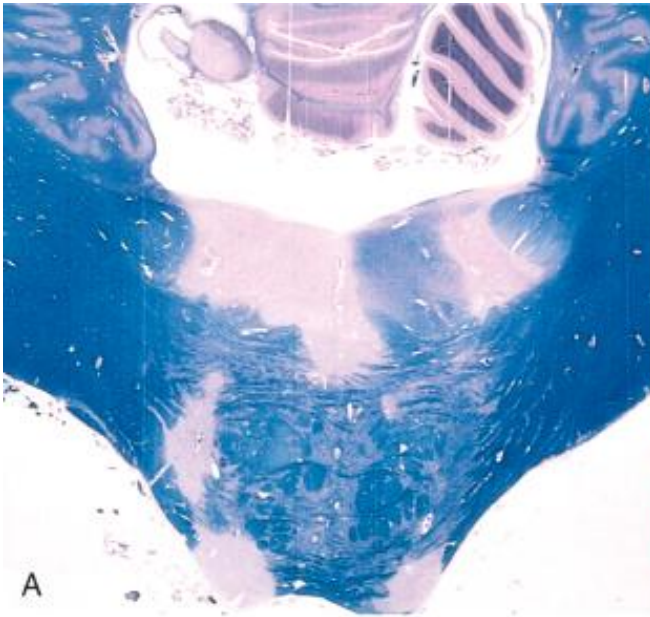
- 27 years old woman presents with a sudden onset of right sided blindness and weakness in her left leg. There is no history of trauma. However, she experienced a similar episode 8 months ago and was diagnosed as aseptic meningitis.

What is your provisional diagnosis?

Multiple sclerosis.

Section of fresh brain showing brown plaque around occipital horn of the lateral ventricle.





Multiple sclerosis.

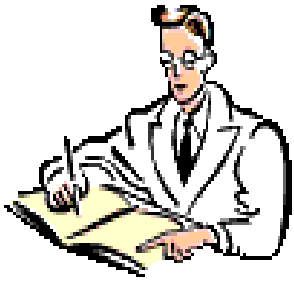
A, Unstained regions of demyelination (MS plaques) around the fourth ventricle (Luxol fast blue PAS stain for myelin). Myelin is blue, and the demyelinated areas are pink.

B, Myelin-stained section shows the sharp edge of a demyelinated plaque (*) and perivascular lymphocytic cuffs (arrow).

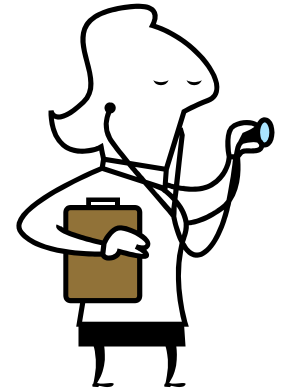
C, The same lesion stained with silver stain for axons to show relative preservation.

MULTIPLE SCLEROSIS

- Multiple sclerosis is the most common disease of CNS myelin; prevalence of 1:1000.
 - Central nervous system myelin is selectively destroyed (axons are relatively preserved)
 - Onset is frequently in 30 and 40 year old age groups.
 - The disease is typically progressive with relapsing and remitting accumulations of focal neurologic deficits.
 - The etiology is thought to be autoimmune in nature



Symptoms of MS

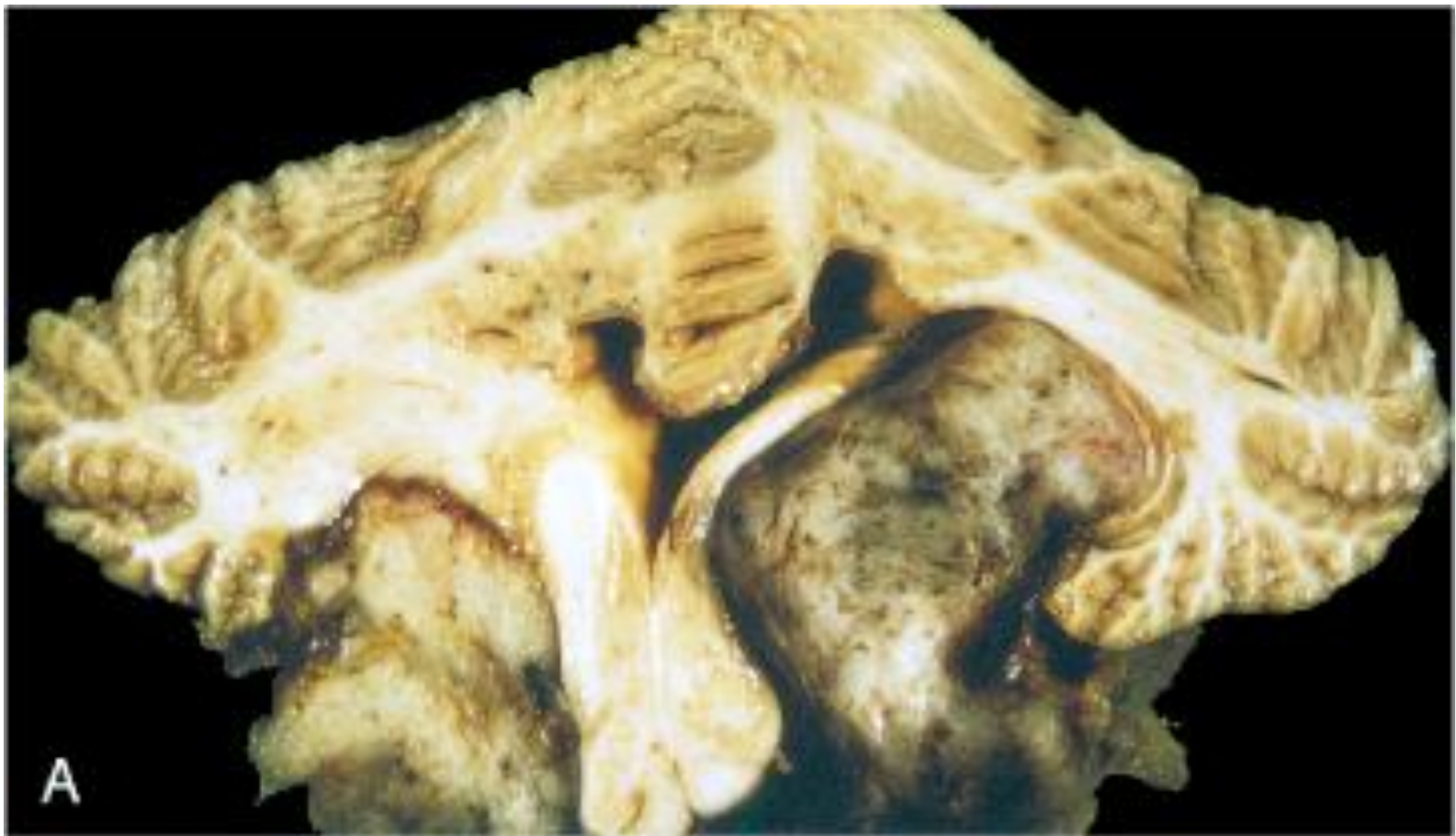


- Fatigue
 - Depression
 - Memory change
 - Pain
 - Spasticity
 - Vertigo
 - Tremor
 - Double Vision/Vision Loss
 - Weakness
 - Dizziness/Unsteadiness
 - Numbness/Tingling
 - Ataxia
 - Euphoria
 - Speech disturbance
 - Bladder/Bowel/Sexual dysfunction
-

Multiple sclerosis

Case No.4

- 39 years old man complains that he had noticed a progressive hearing loss over a 2 years period. Except for occasional headache, he has no other complaints . Evaluation discloses severe sensorineural hearing loss of the left side . MRI shows 1.5 cm. mass at the left cerebellopontine angle . What is your provisional diagnosis ?

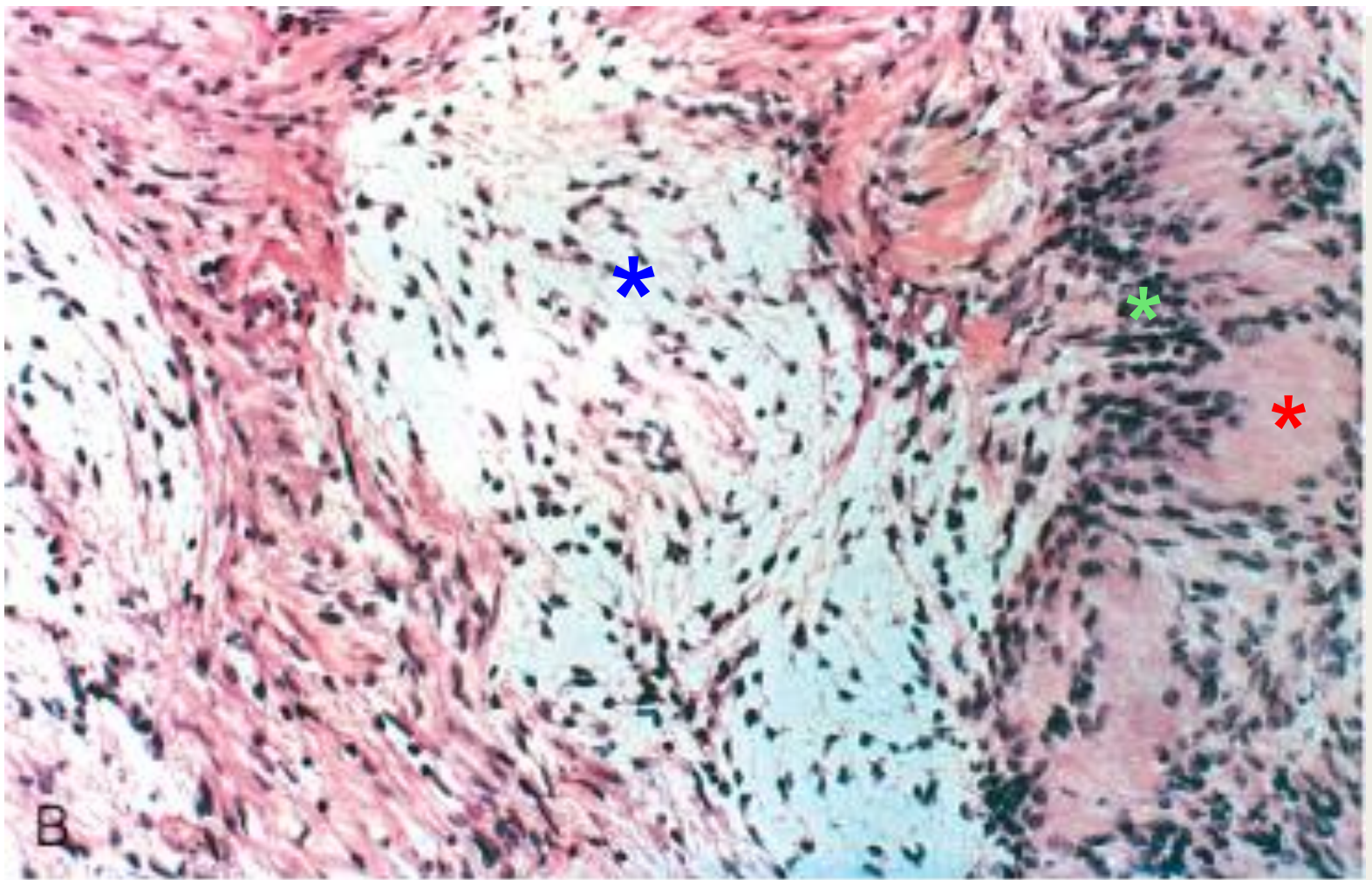


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Schwannoma. A, Bilateral eighth nerve schwannomas.

What syndrome is suggested by such finding?

Neurofibromatosis type 2



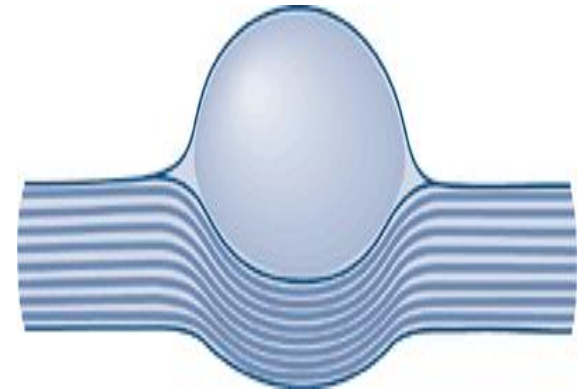
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Schwannoma. B, Tumor showing cellular areas(*) (Antoni A), including Verocay bodies (*), as well as looser, myxoid regions (Antoni B) (*).

Schwannoma

- These benign tumors also known as a neurilemmoma; neoplasm composed of a proliferation of Schwann cell and are associated with neurofibromatosis type 2.
- Pathogenesis is unknown
- Within the cranial vault, the most common location is in the cerebello-pontine angle, where they are attached to the vestibular branch of the eighth nerve.
- Patients often present with tinnitus and hearing loss

Microscopic



- Biphasic Antoni A and B areas

- ❖ Antoni A pattern

- Collagenous background
- Compact elongated spindle cells in bundles
- **Verocay bundles**: palisading arrangement of peripheral aligned nuclei surround central eosinophilic cell processes

- ❖ Antoni B areas: looser, myxoid regions

Schwannoma

Case No. 5

- 9 months infant was suffering from enlarged head size and admitted to hospital with convulsions, went into coma and died. Autopsy was done and the brain was large with dilated ventricles .
What is your provisional diagnosis?

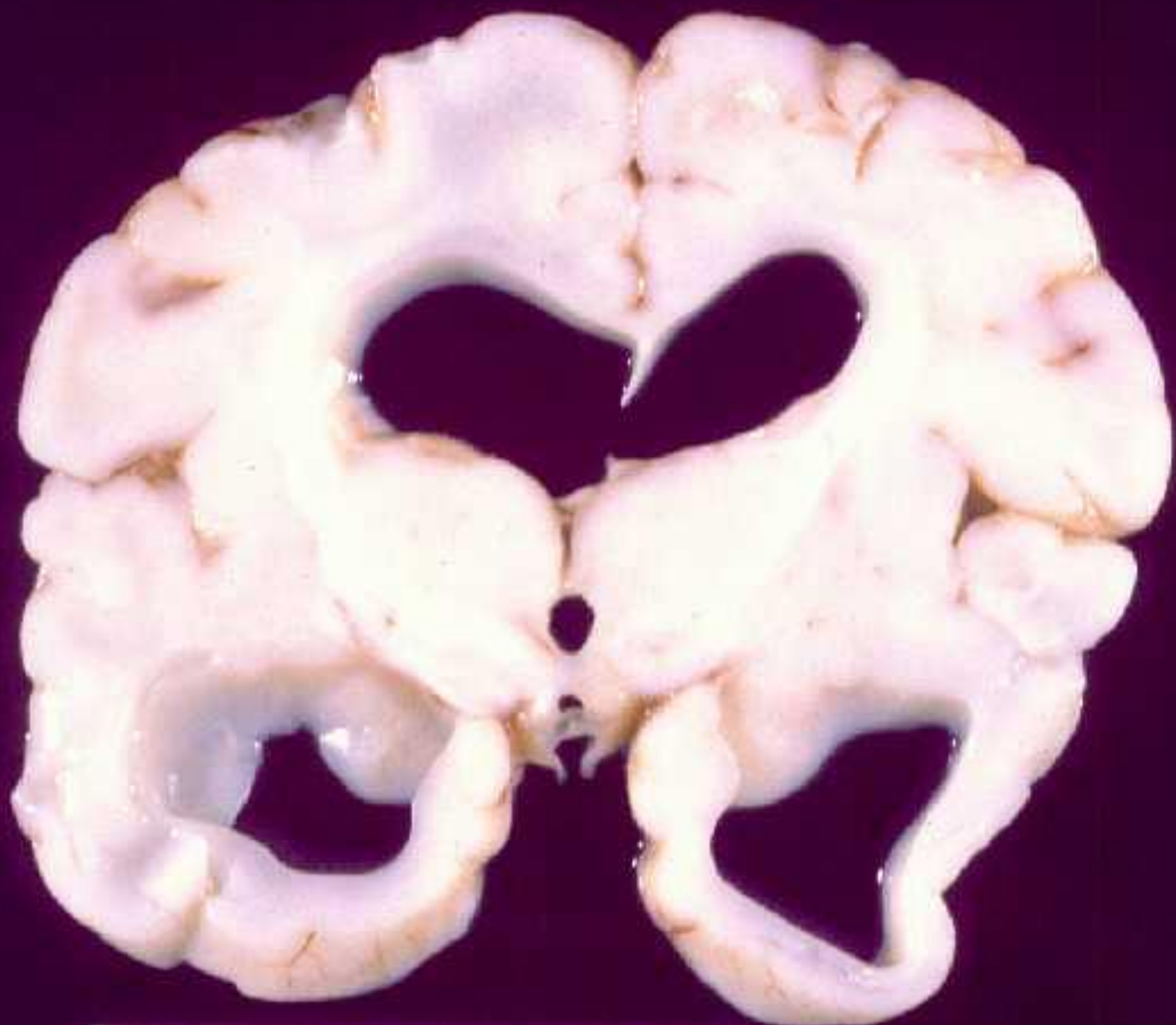
Midsagittal magnetic resonance image of a child with communicating hydrocephalus, involving all ventricles.



Hydrocephalus. Dilated lateral ventricles seen in a coronal section through the midthalamus.



Hydrocephalus is secondary to increased production or decreased reabsorption or obstruction of the CSF, which eventually leads to increased intracranial pressure, herniation, and then death.



CSF Circulation

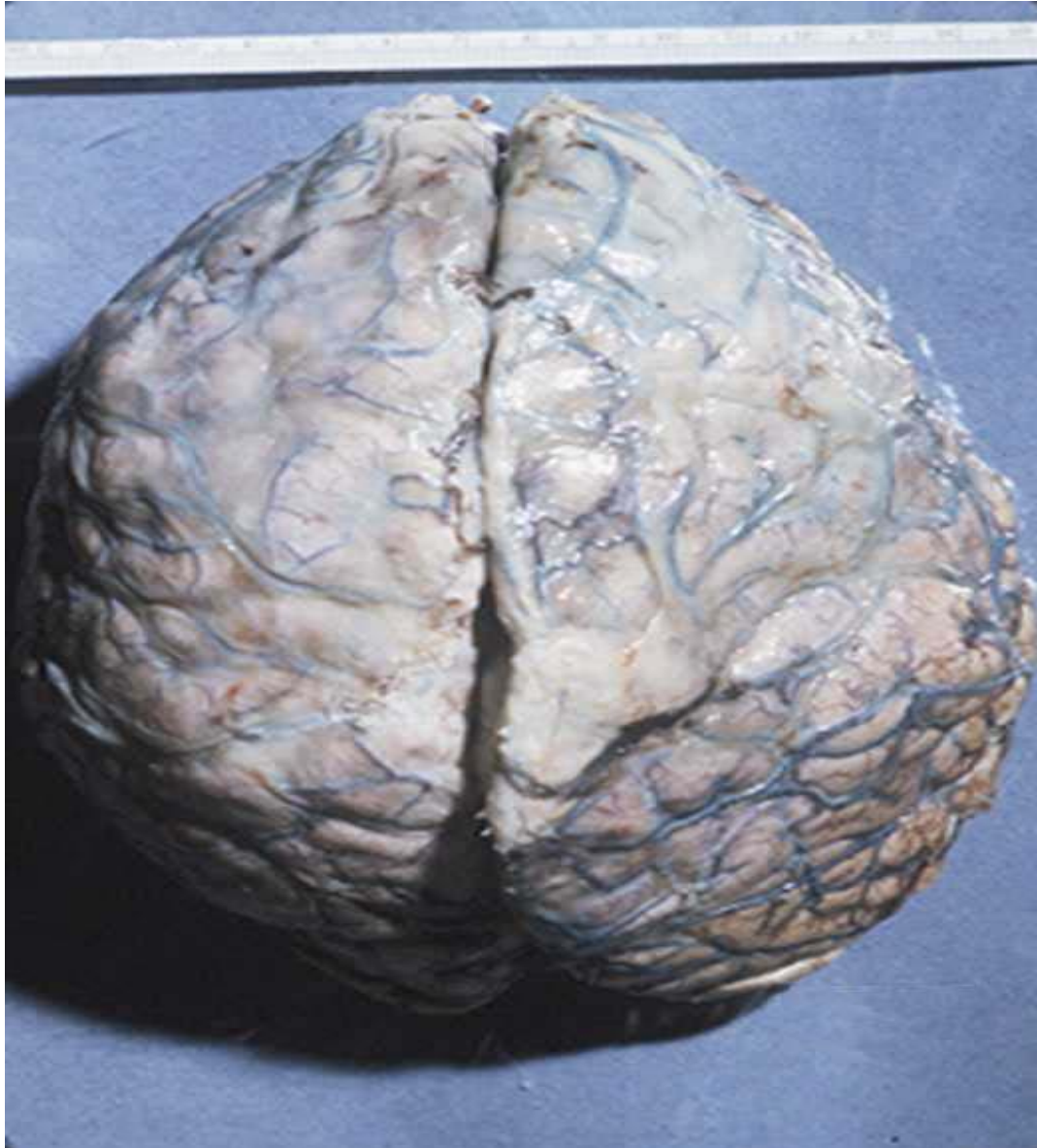
- CSF circulation:
- After being produced by the choroid plexus within the ventricles, cerebrospinal fluid (CSF) circulates through the ventricular system and exits through the foramina of Luschka and Magendie .
- CSF fills the subarachnoid space around the brain and spinal cord, contributing to the cushioning of the nervous system within its bony confines
- The arachnoid granulations are responsible for the resorption of CSF
- The balance between CSF generation and resorption keeps the volume of this fluid stable
- Hydrocephalus is secondary to increased production, or decreased reabsorption or obstruction of the CSF, which leads to increased intracranial pressure and then herniation and death.

Hydrocephalus

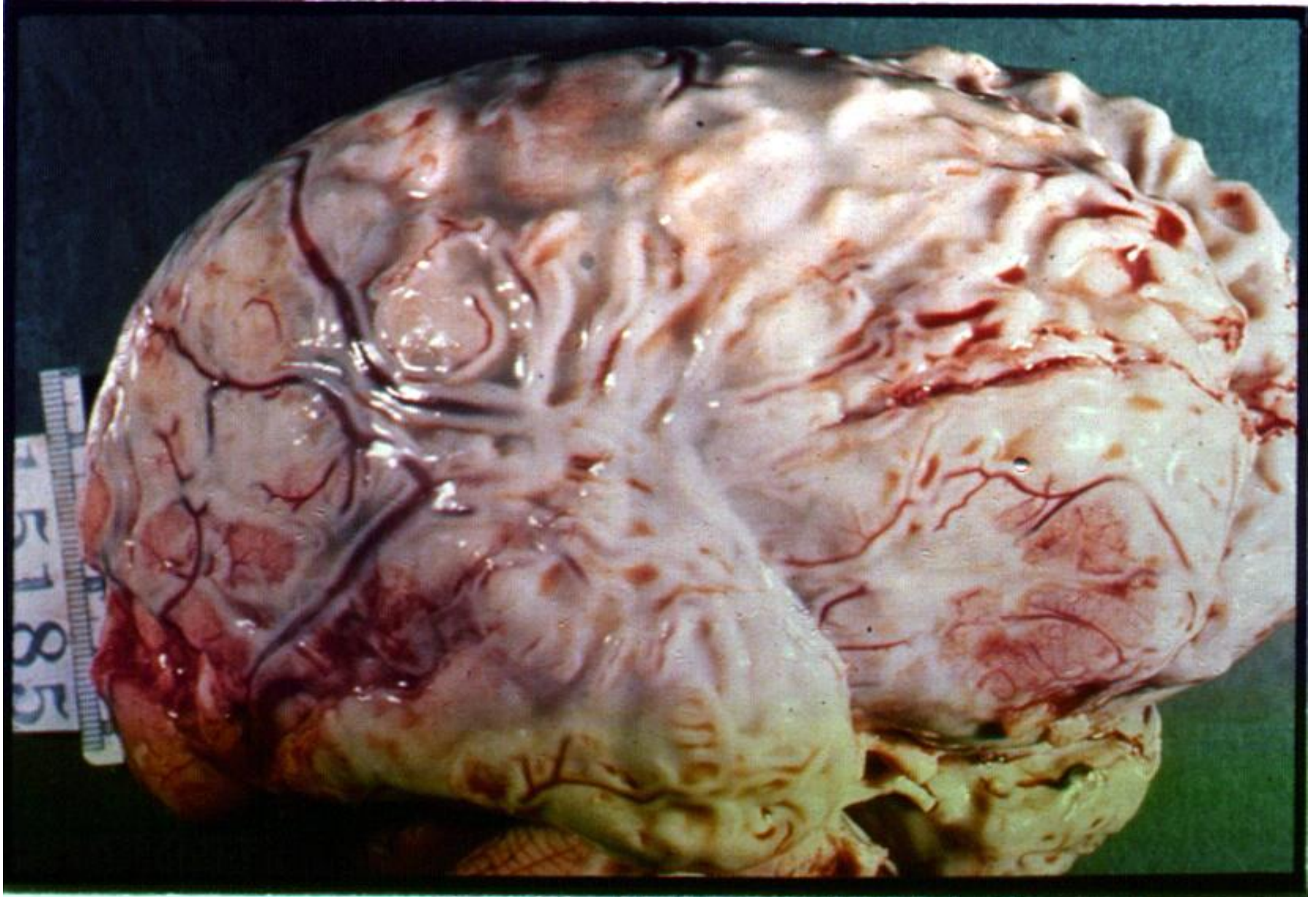
Case No. 6

- 4 years old child who was treated from otitis media and suddenly complained from headache, vomiting, fever and stiff neck. CSF was found to be clouded with abnormal increase of neutrophils, increased protein and absence of sugar. Gram stain of the CSF fluid showed meningiococci .

What is your diagnosis ?



Gross picture of brain covered by inflamed meninges and engorged vessels.



Gross picture of the brain showing purulent exudate covering the meninges.

Absence of Sugar

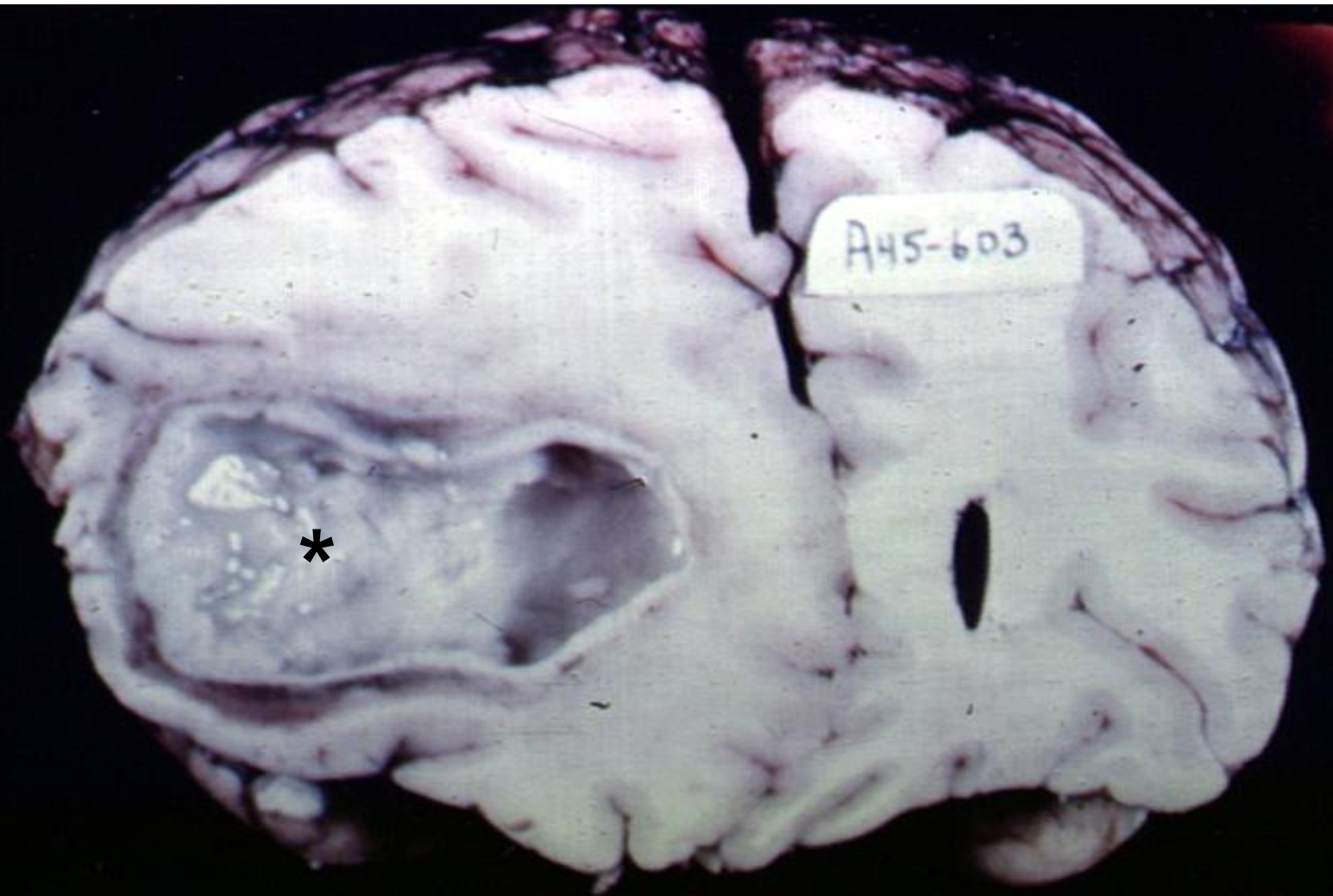
- Absence of sugar is due to:
 1. Disorder in carrier-mediated transport
 - e.g. TB meningitis, sarcoidosis
 2. Active metabolism of glucose by cells or organisms:
 - e.g. acute purulent, amebic, & fungal meningitis
 3. Increased metabolism by the CNS
 - e.g. by CNS neoplasm

Septic Meningitis

Case No. 7

- 35 years old lady complains from otitis media . Suddenly she suffers from headache and convulsions. Brain MRI reveals 5 cm. fluid filled cavity in the temporal lobe. Examination of the CSF shows increased pressure with lymphocytes and increased protein but there is no change of sugar content.

What is your diagnosis ?



Brain abscess (*) surrounded by granulation tissue capsule.



Brain abscess

Case No. 8

- A previously healthy 31-year-old (young) woman experiences a severe headache and loses consciousness within an hour. An emergent head CT scan reveals extensive subarachnoid hemorrhage at the base of the brain. She is afebrile. A lumbar puncture yields cerebrospinal fluid with many red blood cells, but no white blood cells. The CSF protein is slightly increased, but the glucose is normal. Ruptured aneurysm because unruptured won't cause symptoms
- What is your provisional diagnosis ?
- Ruptured aneurysm because unruptured won't cause symptoms

-Sub Arachnoid Hemorrhage

-Causes can be :-

-Vascular malformation

-Aneurysm (our case)

-Trauma

-Rupture of an intracerebral hemorrhage into the ventricular system

-Hematologic disturbances

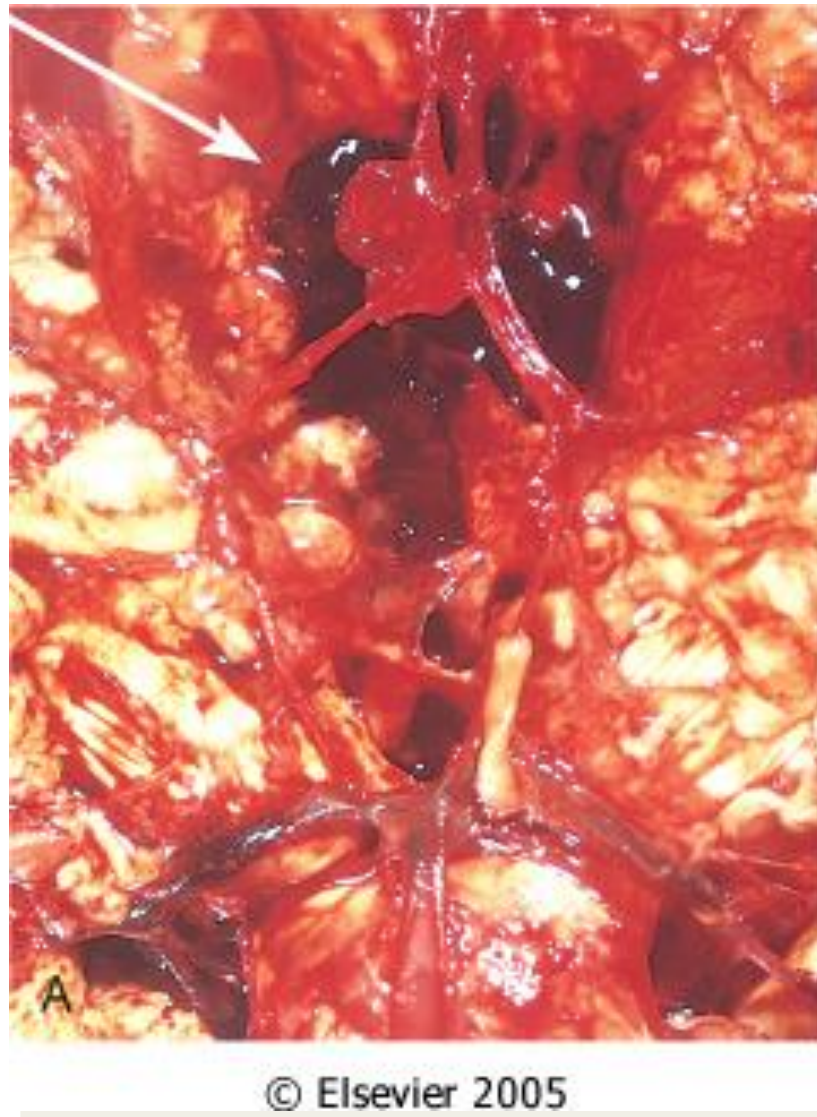
e.g: platelet deficiency

-Tumors

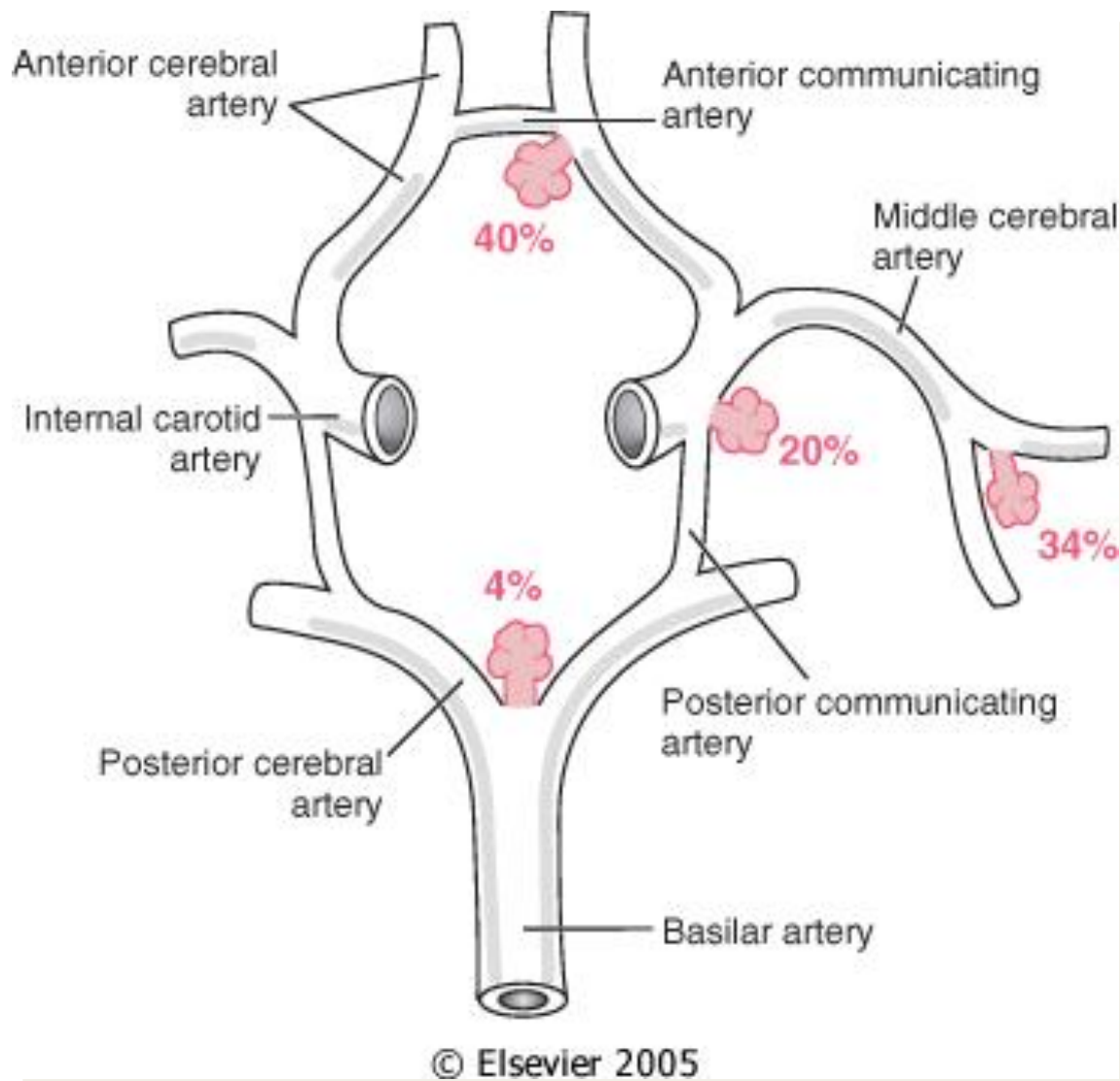
N.B: You have to mention whether the vessel is ruptured or not.

You also have to say that it leads to subarachnoid hemorrhage most likely due to rupture of an aneurysm





View of the base of the brain, dissected to show the circle of Willis with an **unruptured** aneurysm of the anterior cerebral artery (arrow).



Common sites of saccular (berry) aneurysms in the circle of Willis



B, Dissected circle of Willis to show large aneurysm.



C, Section through an Unruptured saccular aneurysm showing the (hyalinized) fibrous vessel wall.

Ruptured berry aneurysm
causing subarachnoid hemorrhage

Case No.9

- An 85 years old man complains of progressive loss of memory, disorientation and alterations in mood and behavior since 20 years. He was admitted to hospital because he was disabled and immobile and he died in hospital after one week of admission. Autopsy was done and the brain cortex was found to be atrophied. What is your diagnosis ?

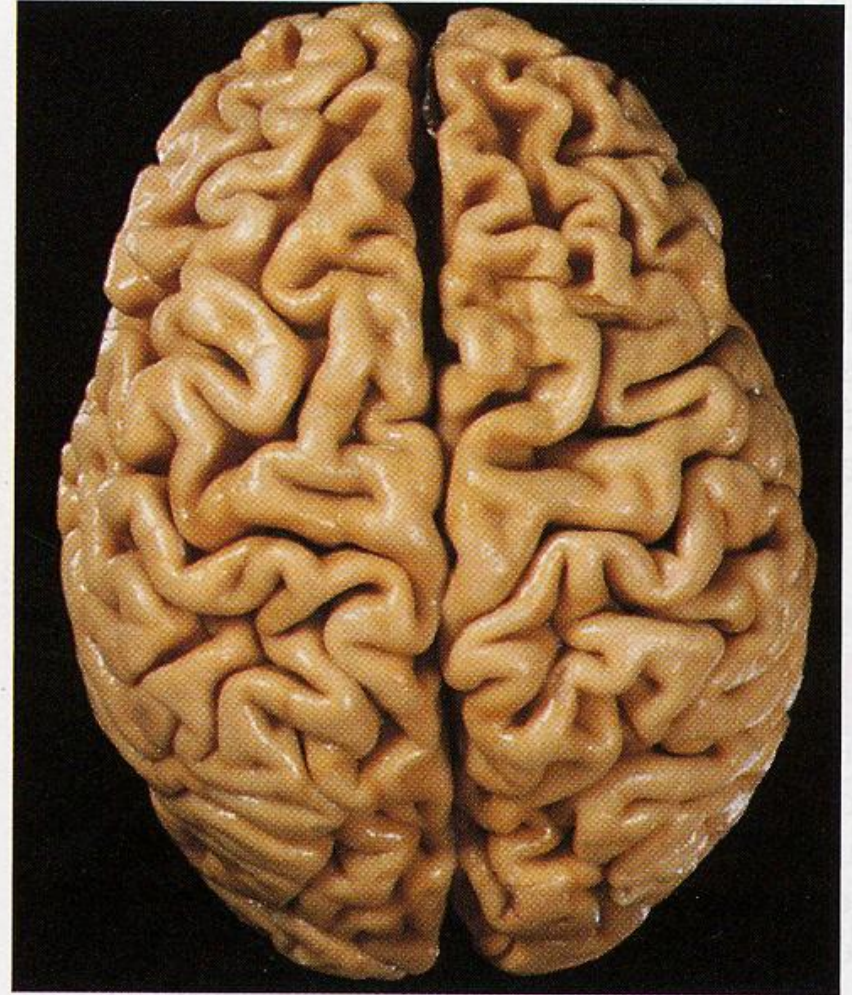
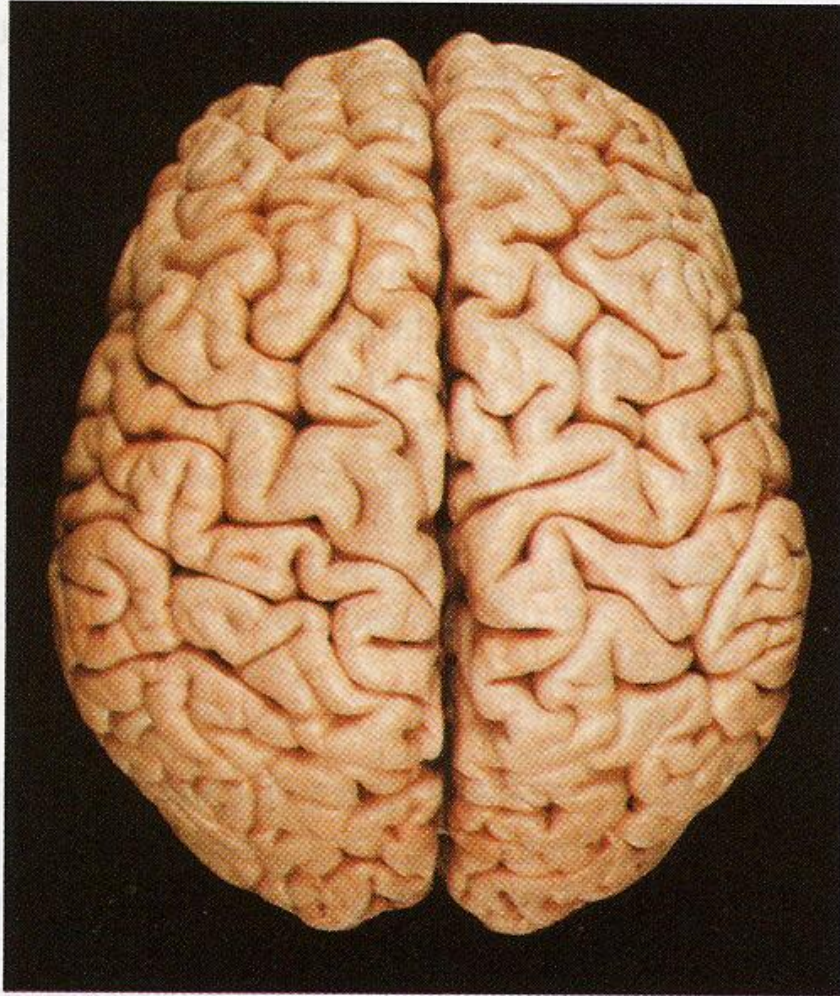


FIGURE 28-123

Alzheimer disease. A. Normal brain. B. The brain of an AD patient shows cortical atrophy with thin gyri and prominent sulci.

Alzheimer disease with cortical atrophy most evident on the right, where meninges have been removed.



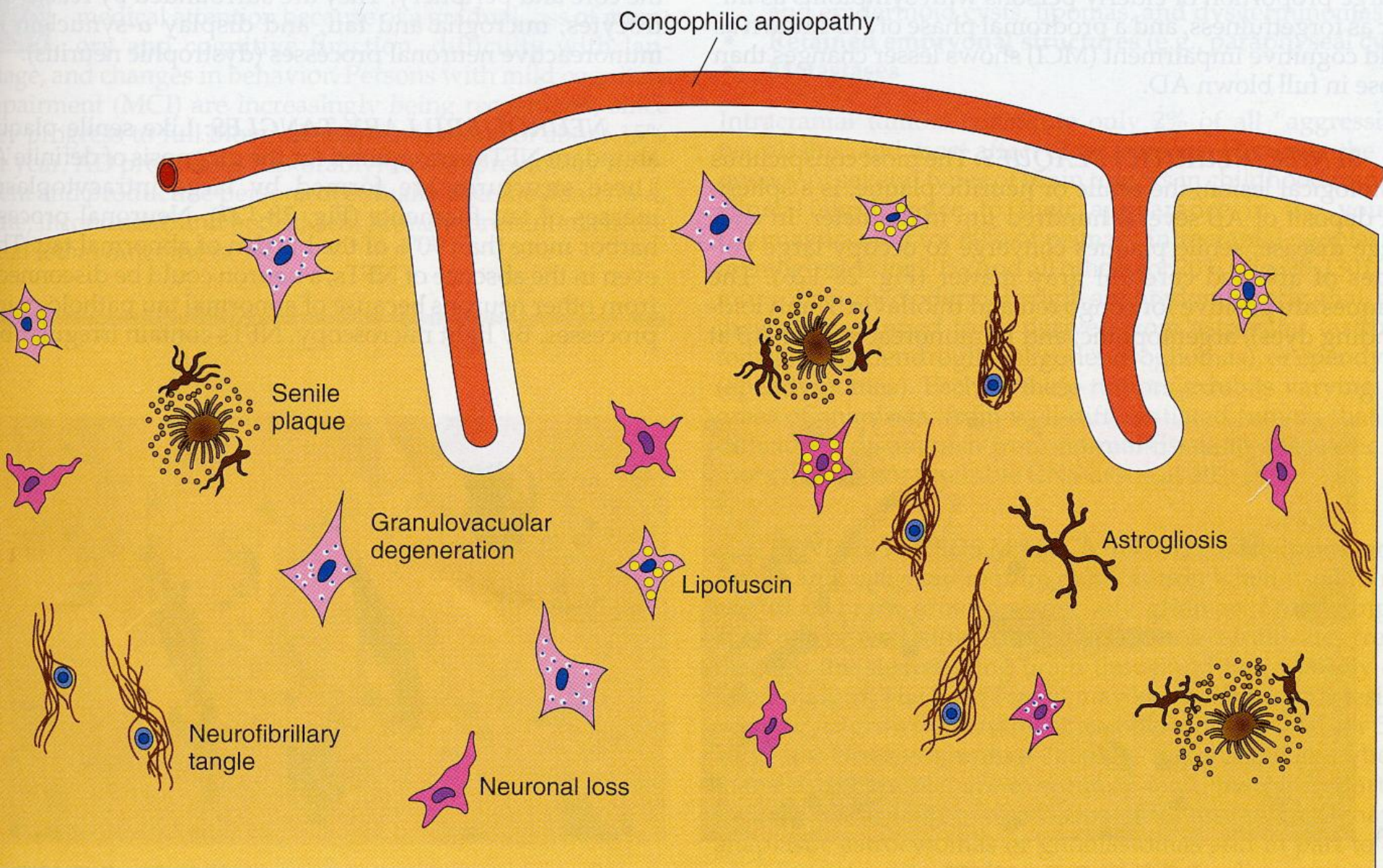
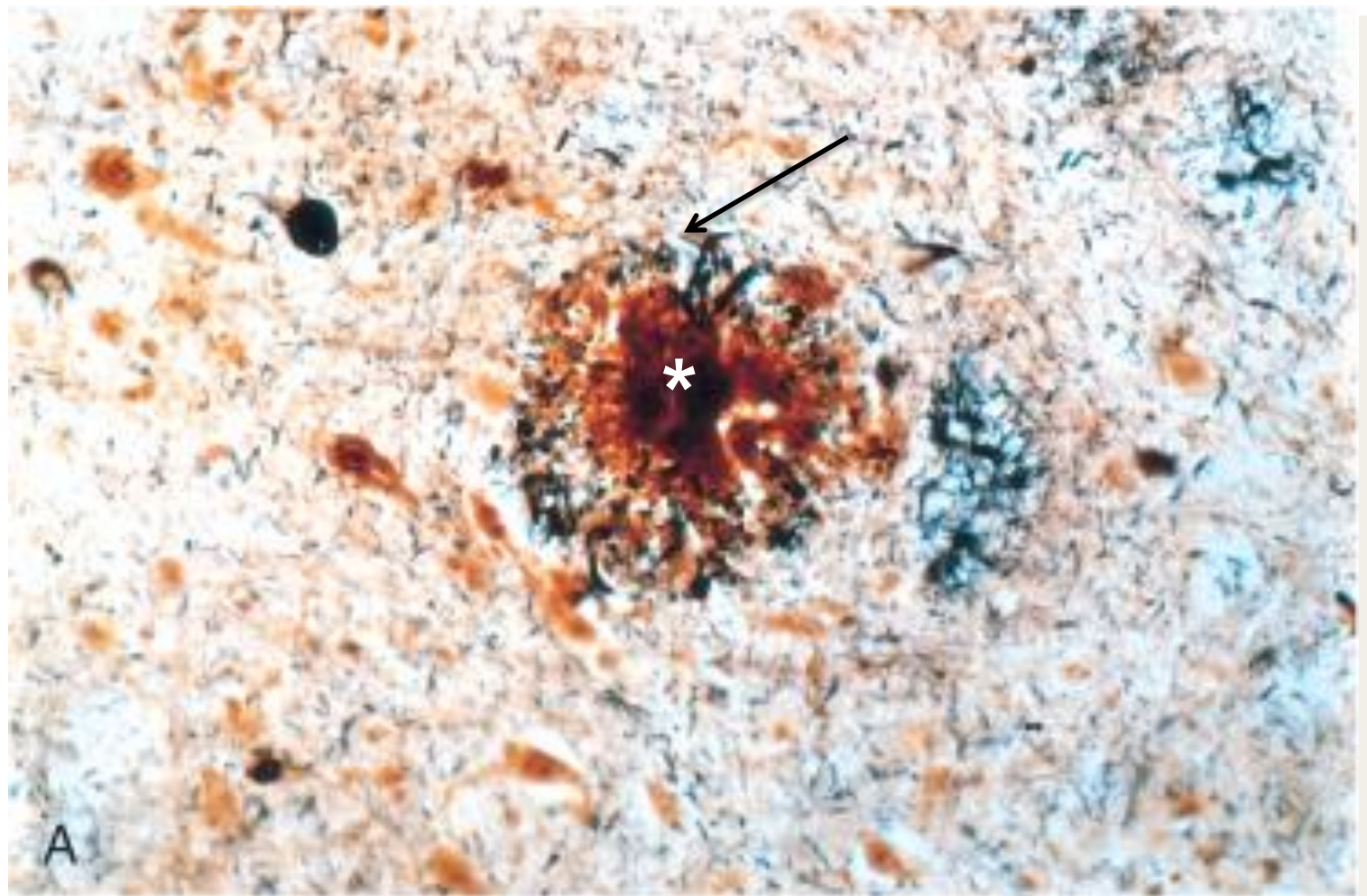
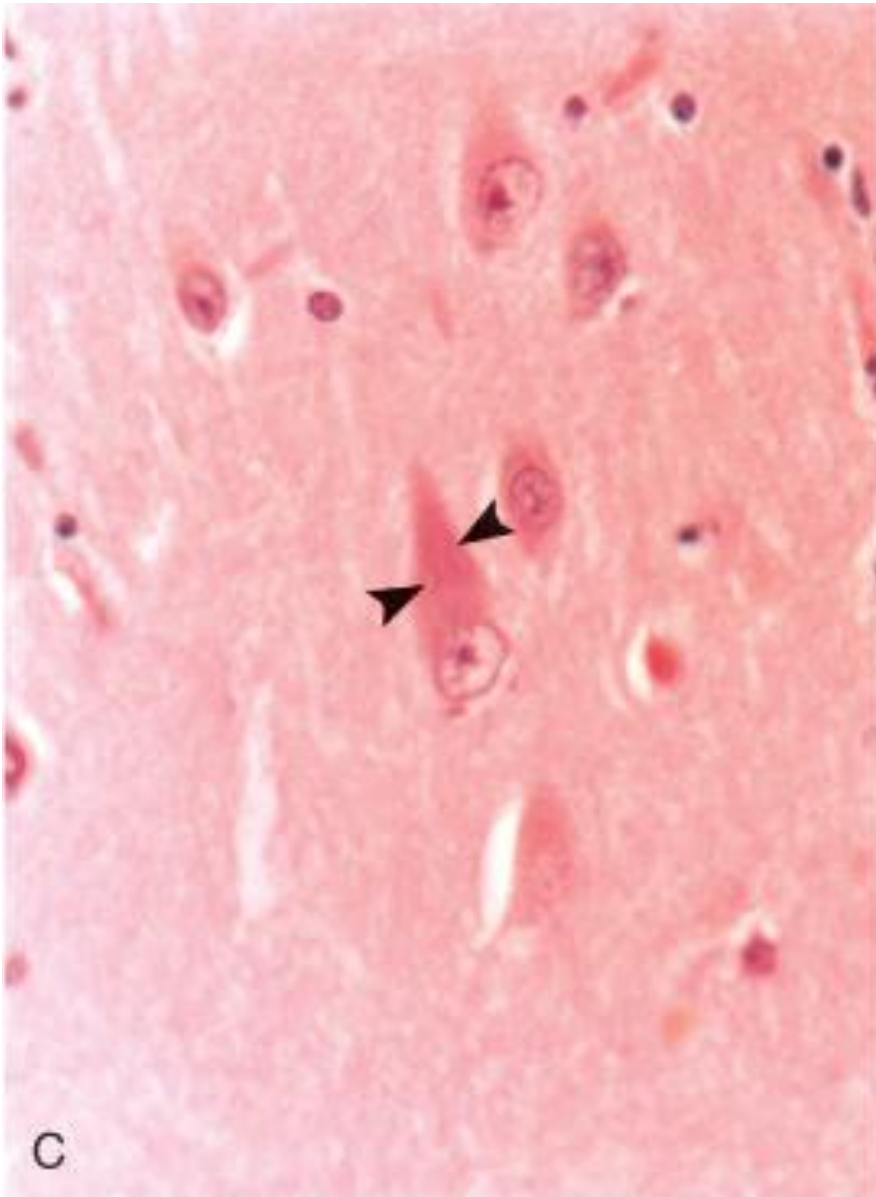


FIGURE 28-125
Microscopic lesions of Alzheimer disease.



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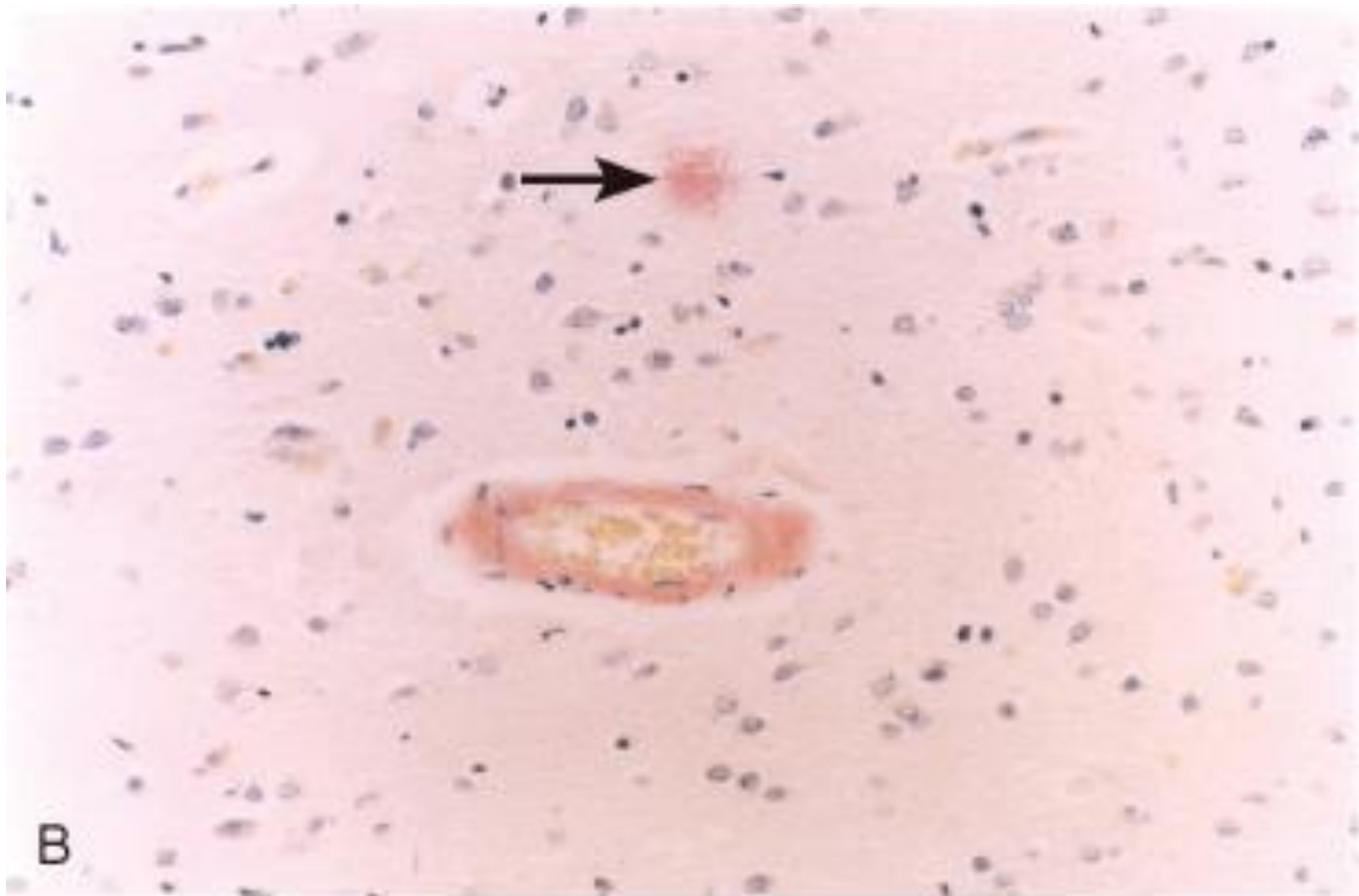
Alzheimer disease. A, Neuritic plaque with a rim of dystrophic neurites (arrow) surrounding an amyloid core (white *)



Alzheimer Disease. C, Neurofibrillary tangles (arrowheads) are present within the neurons.

Alzheimer Disease. D, Silver stain showing a neurofibrillary tangle within the neuronal cytoplasm.





B

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Alzheimer Disease. B, Congo red stain of the cerebral cortex showing amyloid deposition in the blood vessels and the amyloid core of the neuritic plaque (arrow)

Alzheimer Disease

- Macroscopic examination of the brain shows a variable degree of ***cortical atrophy*** with widening of the cerebral sulci that is most pronounced in the frontal, temporal, and parietal lobes
- Microscopic:
- **neuritic (senile) plaques**
- **neurofibrillary tangles**
- **amyloid angiopathy**

Alzheimer disease

- Self Learning Cases 10 & 11
- Parkinson's disease
- Tubercles Meningitis (NOT INCLUDED
ACCORDING TO THE FEMAL DOCTOR)

Self-directed learning

Case 10: Parkinson's disease

Parkinsonism

- Parkinsonism is a **clinical syndrome** characterized by diminished **facial expression**, **stooped posture**, **slowness of voluntary movement**, abnormal gait **rigidity**, and a "**pill-rolling**" tremor.
- Degeneration of neurons of the substantia nigra and locus ceruleus →
a reduction in the striatal dopamine content
→ leading to **motor** disturbance.

Causes of Parkinsonism

- Impaired release of dopamine- **Idiopathic parkinsonism.**
- **Drug Toxin** damaging dopaminergic neuron
- **Viral infection-** Encephalitis ,Japanese encephalitis
- **Trauma**-repeated head injury
- Miscellaneous-wilson disease, huntingtons disease

Usual causes of death in this group of patients are

- Trauma
- infection

Morphology

- The typical macroscopic findings are pallor of the substantia nigra and locus ceruleus.

M/E: there is loss of the pigmented neurons in these regions, associated with gliosis.

- Lewy bodies may be found in some of the remaining neurons.
- These are single or multiple, cytoplasmic inclusions
- Ultrastructurally, Lewy bodies are composed of fine filaments, composed of α -synuclein

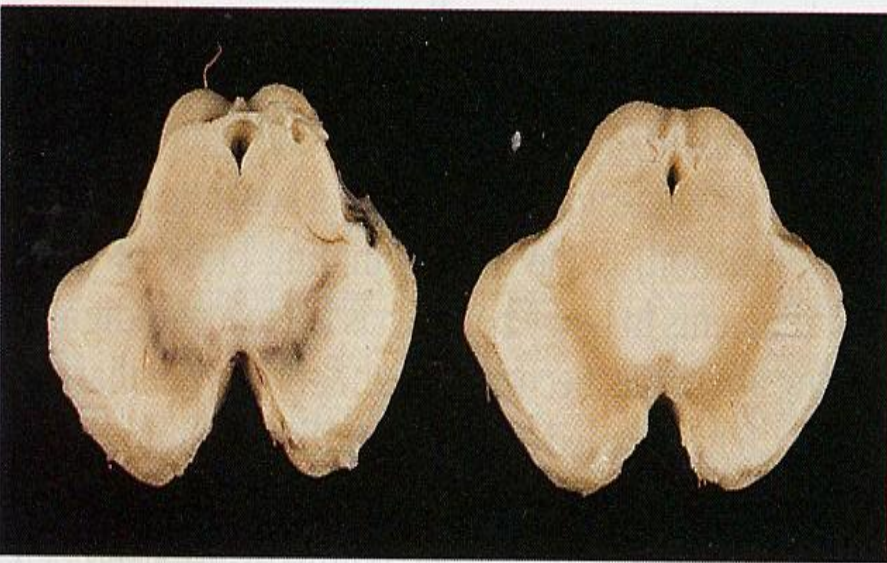
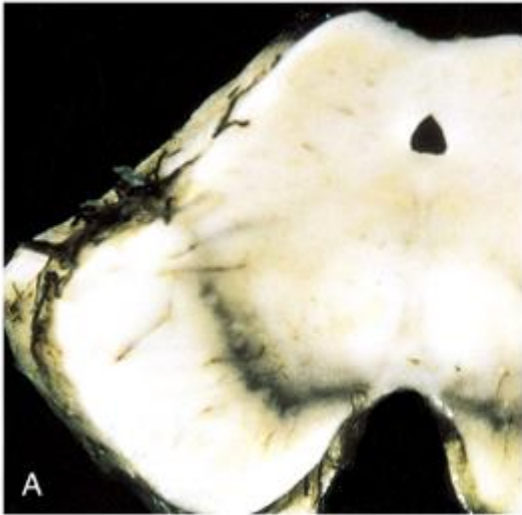


FIGURE 28-118

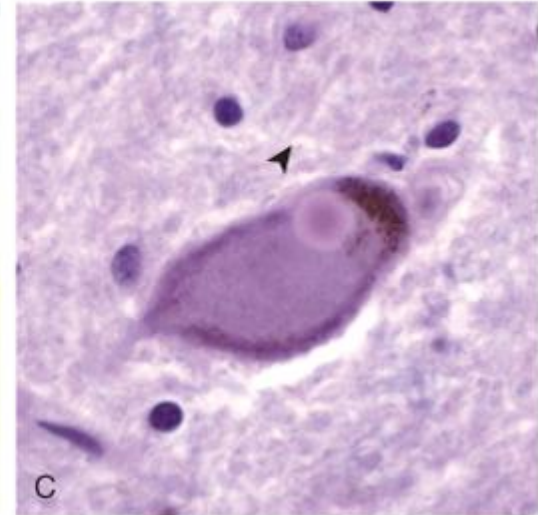
Parkinson Disease. A. The normal substantia nigra of the midbrain (*left*) is heavily pigmented, whereas the same region from a patient with PD (*right*) has lost neurons and neuromelanin. B. A microscopic section of the substantia nigra from a patient with PD shows a Lewy body (a spherical eosinophilic inclusion surrounded by a halo within the cytoplasm of a pigmented dopaminergic neuron.)



A) Normal Mid brain



B) Pallor
(unhealthy pale appearance) of
the substantia
nigra and locus
ceruleus



C) Single or multiple,
intracytoplasmic,
eosinophilic, round to
elongated inclusions
that often have a dense
core surrounded by a
pale halo



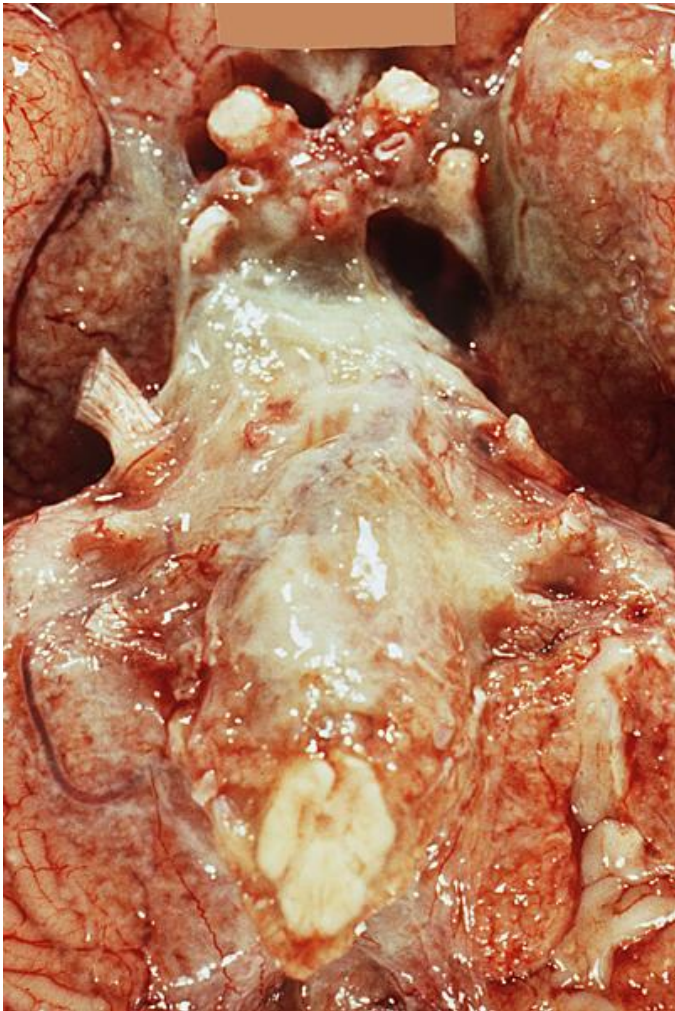
Loss of the dark pigmentation in the substantia nigra of the midbrain on the left with normal one at the right

Case 10: Tubercles Meningitis

CNS Infections

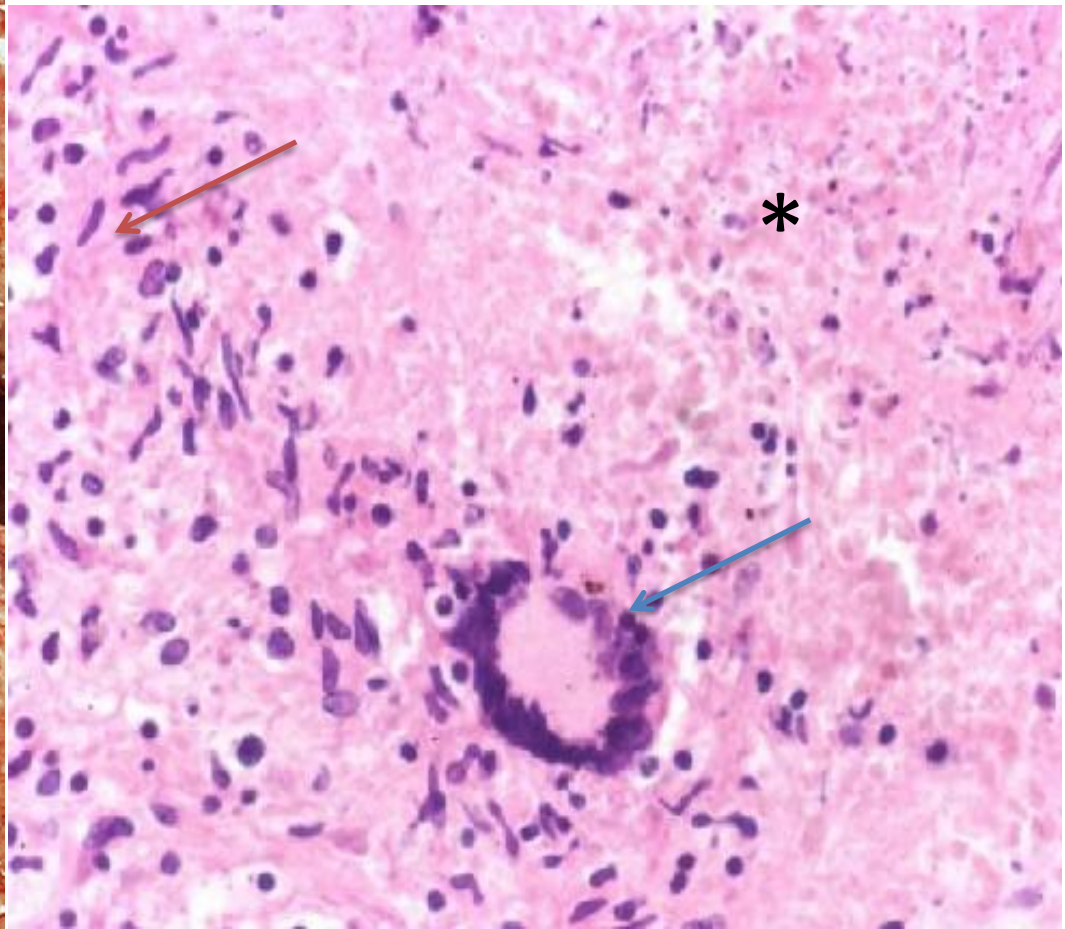
Tuberculosis

- **Tuberculoma** is well-circumscribed intraparenchymal mass
- On microscopic examination, there is usually a central core of **caseous necrosis** surrounded by a typical tuberculous granulomatous reaction

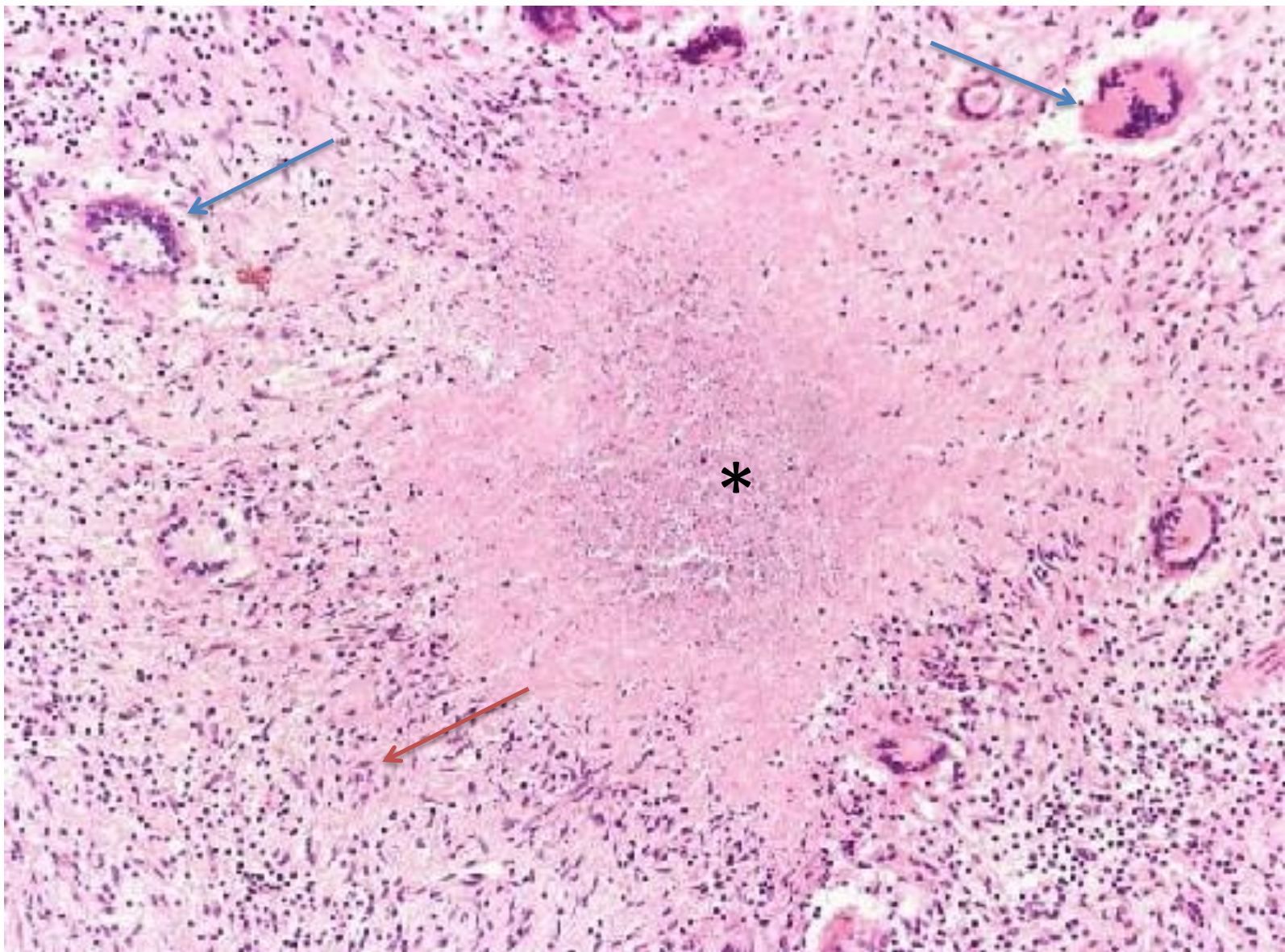


TB meningitis

Exudate at the base of the brain



M/E: Granuloma (tuberculoma) with epithelioid cells (Red arrow), langhan gaint cells (blue arrow), and caseous necrosis (*).



Granuloma with epithelioid cells (Red arrow), langhan gaint cells (blue arrows), and caseous necrosis (*).