



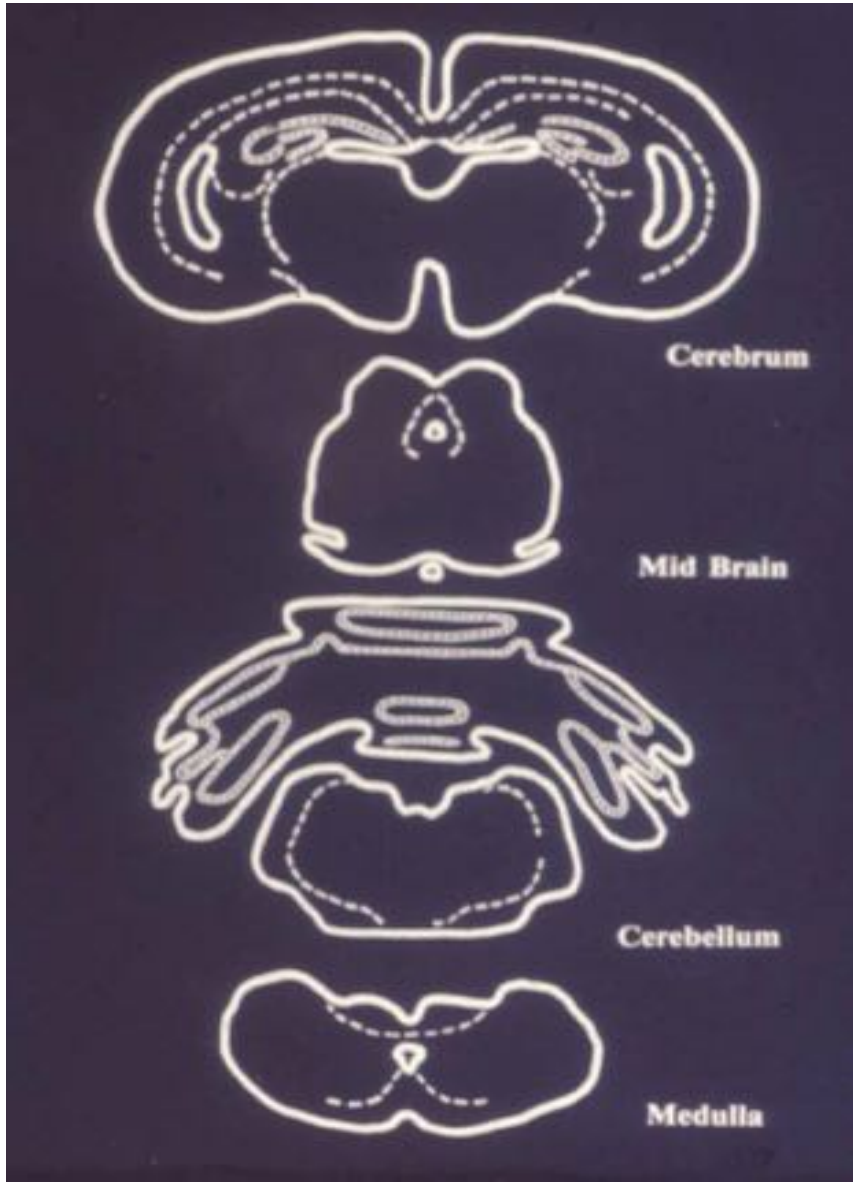
# Brain tumours in rodents

By Dr. C Gopinath  
STPI- 2016



# Astrocytoma





## Incidence of Brain Tumours Among Untreated Controls

Glial tumours	Males	Females
Astrocytoma	40	23
Oligodendrocytoma	1	1
Ependymoma	1	0
Meningeal tumours		
Meningioma*	24	11
Malignant Meningioma	4	0
Meningeal Fibrosarcoma	2	0
Others		
Polymorphic Sarcoma	0	1
Haemangioma	2	0
Choroid Plexus Lipoma	1	0
Total Brain Tumours	75	36
Total Brains Examined	3356	3490

\* Includes 8 males and 6 female granulocytic tumours

## Incidence of Spontaneous Murine Brain Tumors \*

Authors	% incidence
Swenberg	0.01-0.07
Ward and Rice	0.05-0.15
Morgan et al	0.061

\* excluding BRVR and VM strains

# Brain tumours- rat Classification

## 1. Neuroepithelial- Glial

- Astrocytoma
- Oligodendroglioma
- Mixed glioma
- Anaplastic glioma

## 2. Ependymal & Choroid plexus

- Ependymoma
- Choroid plexus papilloma
- Choroid plexus carcinoma
- Lipoma

## Classification continued

- Neuronal & primitive
  - Ganglioneuroma
  - Medulloblastoma
- Meninges
  - Meningioma
  - Meningeal sarcoma
  - Granular cell tumour
  - Meningeal melanoma
  - meningeal Haemangioma

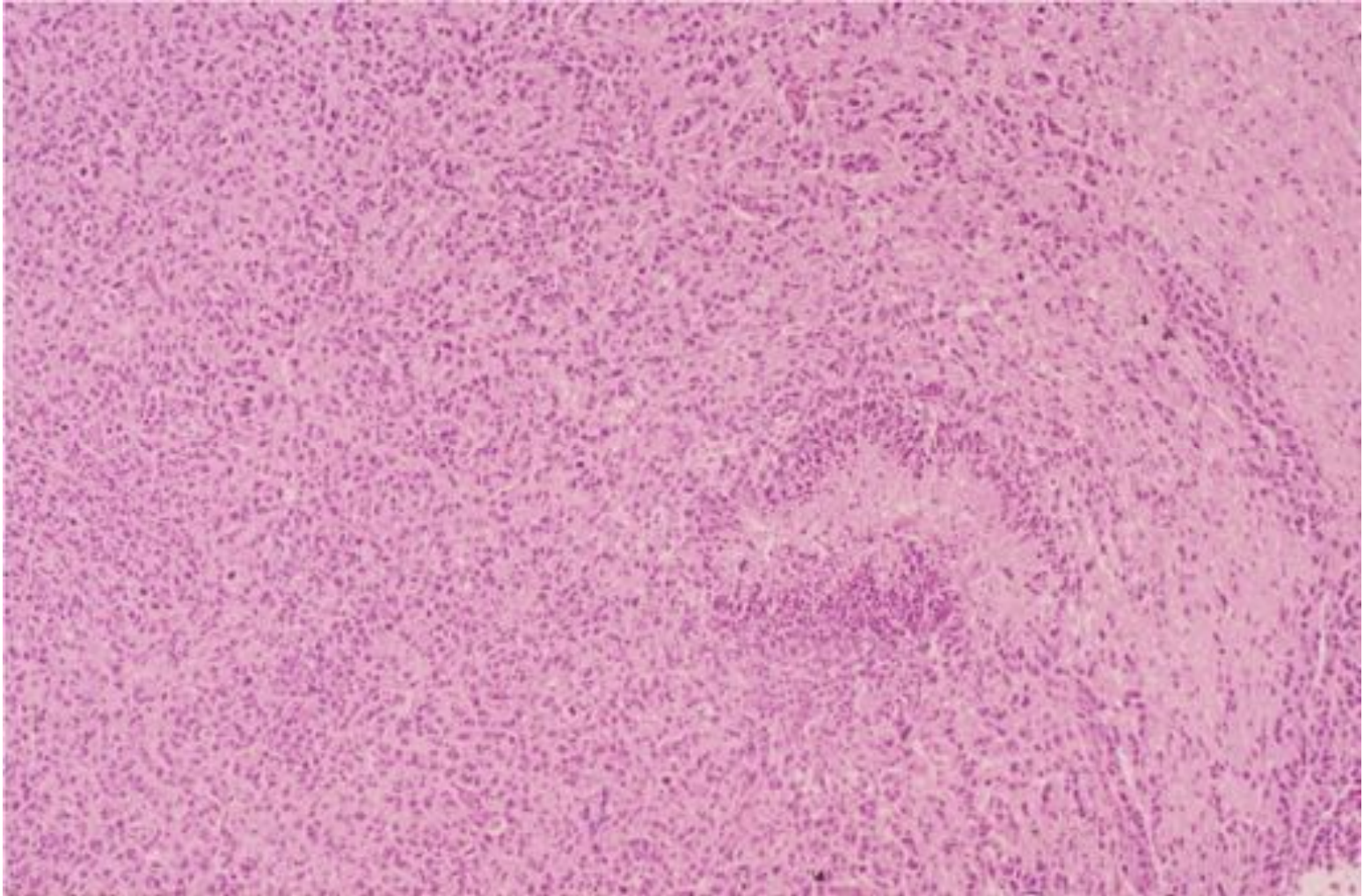
## Classification continued

- Others
  - Malignant reticulosis
  - Primary lymphoma
  - Lipoma
- Nerve sheath
  - Benign and malignant Schwannoma
- Pineal gland
  - Pinealoma
  - Pineal gland carcinoma
  - Secondary neoplasms

# Astrocytoma

- Densely cellular, poorly circumscribed
- Uniform cells with eosinophilic cytoplasm indistinct cell borders, round/oval dark nuclei
- Merging tumour edge with perivascular cuffing & satellitosis
- Necrosis with palisading pattern
- GFAP negative

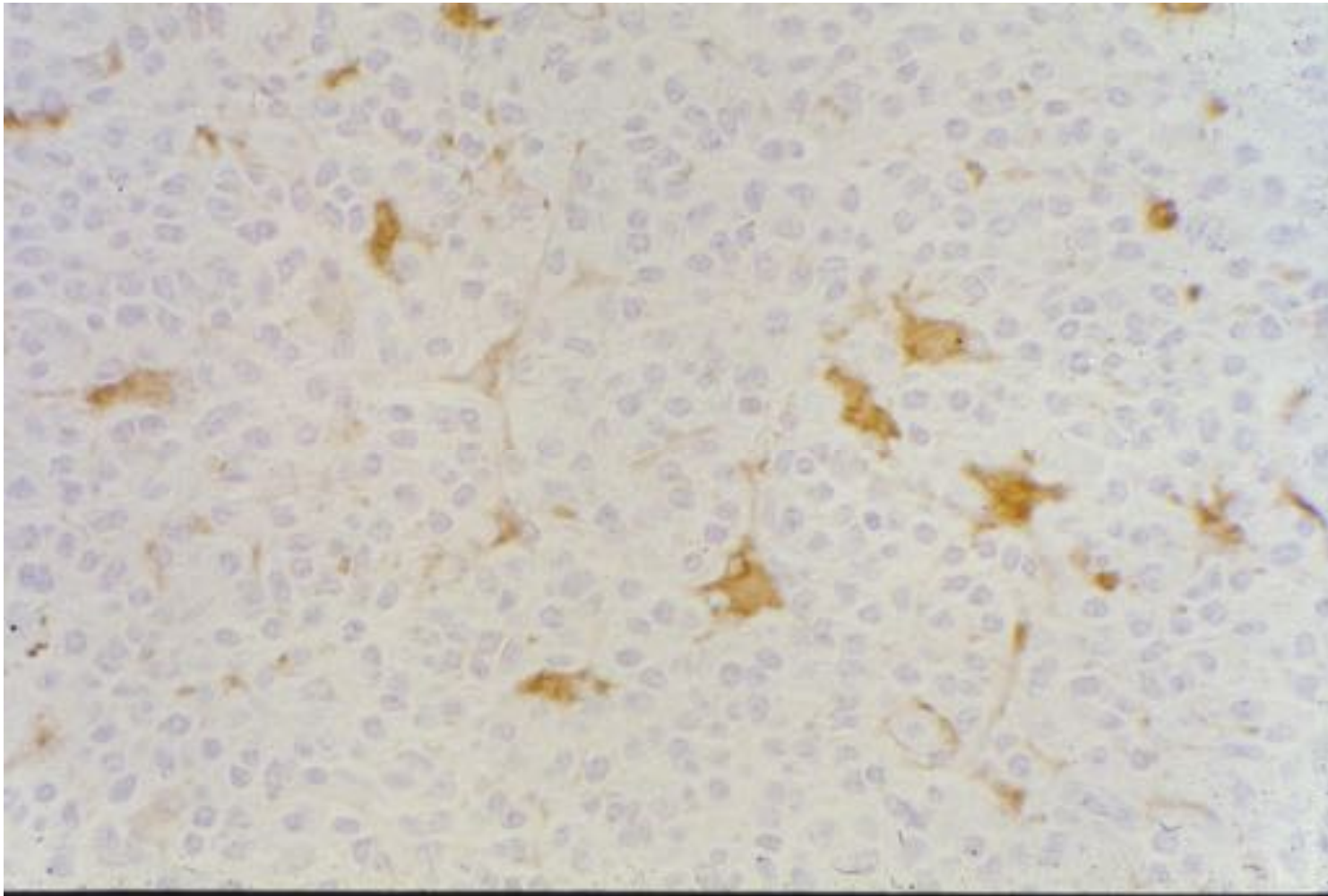
# Astrocytoma



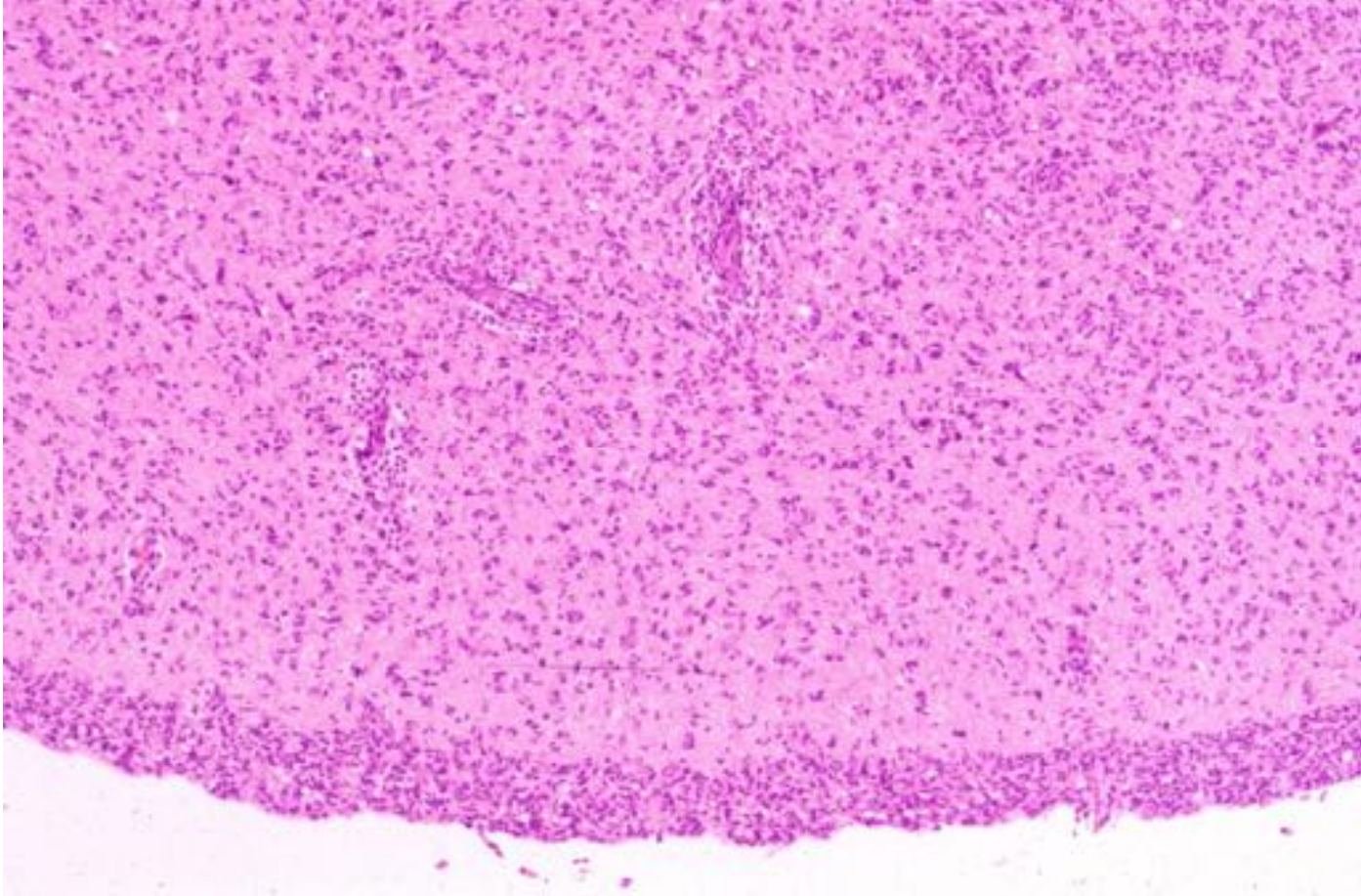
# Astrocytoma



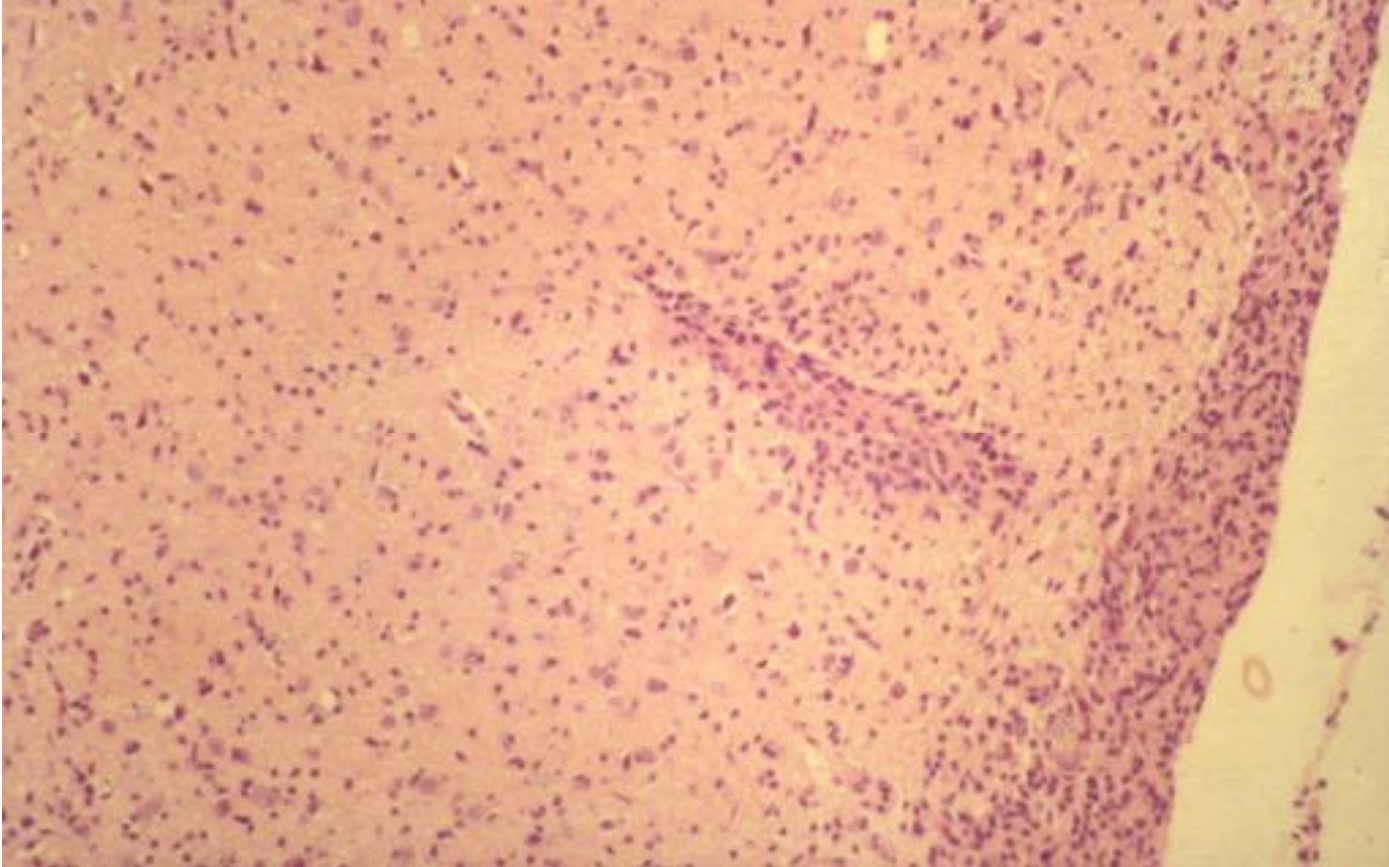
# Astrocytoma, GFAP



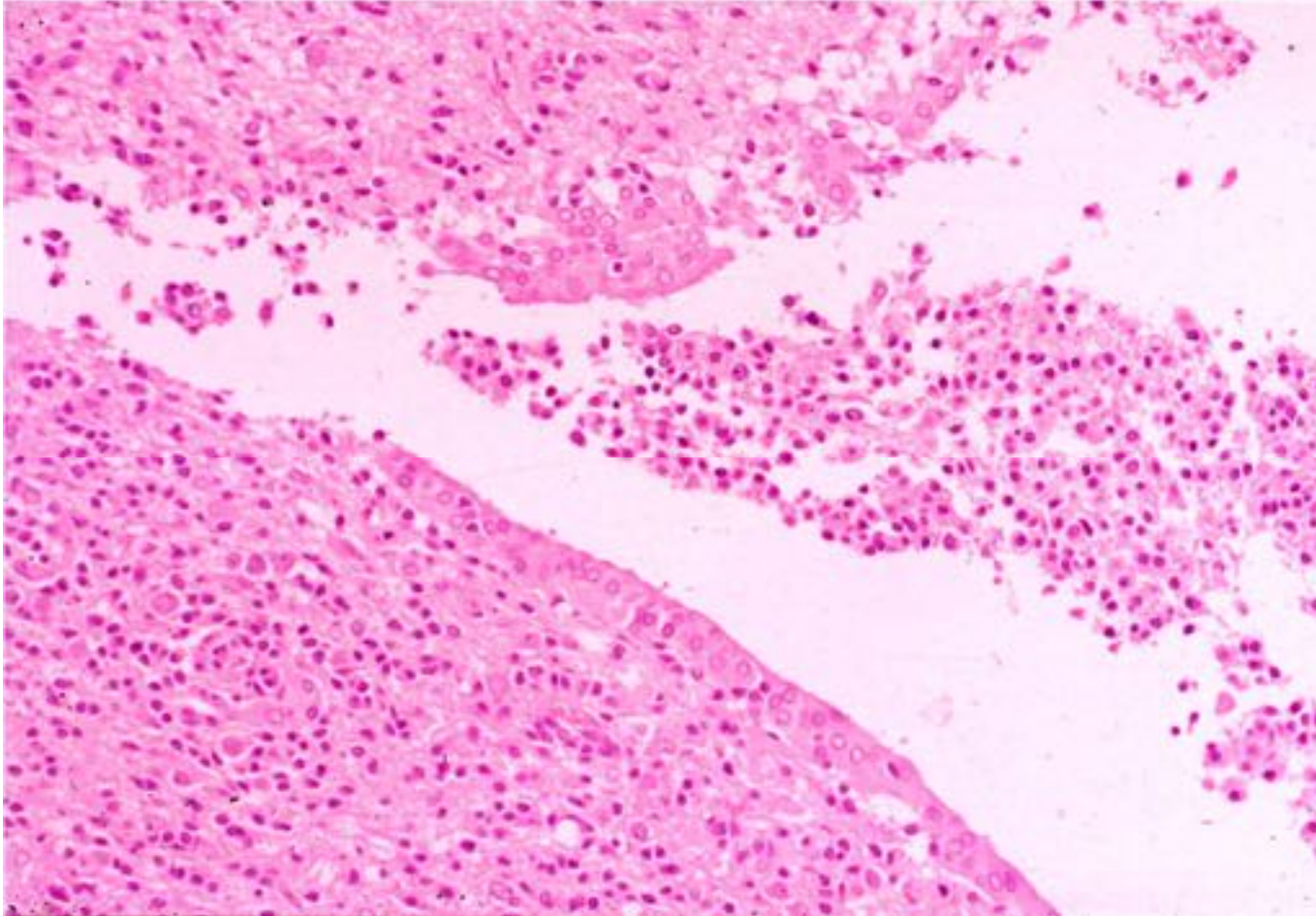
# Astrocytoma



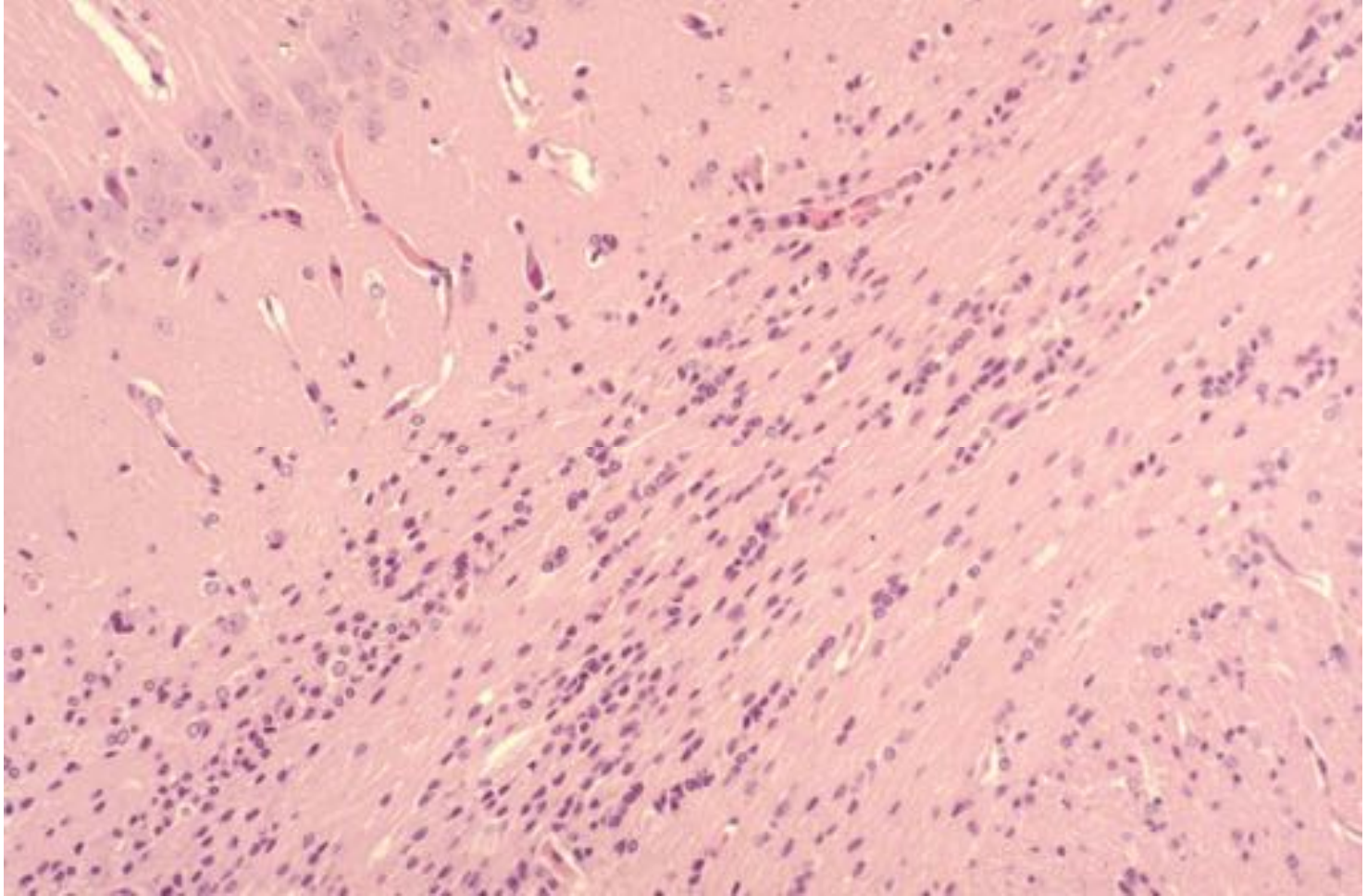
# Astrocytoma



# Astrocytoma



# Gliosis



# Astrocytoma

- Males
  - Range 0/100 to 3/50
  - Incidence 40/3356 (1.19%)
  - (out of 2.2% brain tumours)
- Females
  - 0/100 to 2/50
  - 40/3490 (0.66%)
  - (out of 1.03% brain tumours)

## Astrocytoma- clinical signs

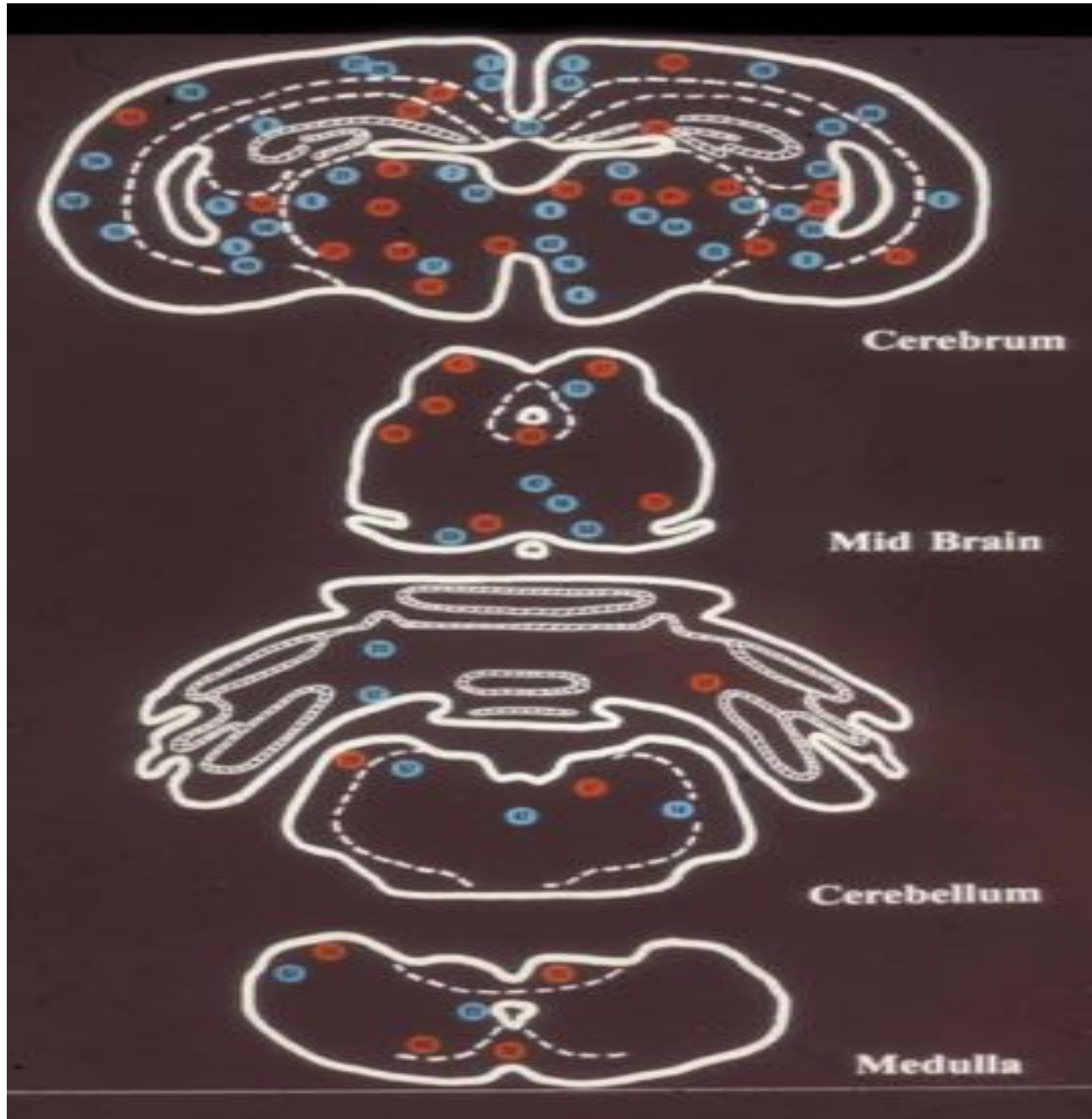
- 8/40 males and 4/23 females showed CNS signs including:
- Loss of balance, loss of grip reflex, posterior paralysis, unsteady gait, leaning to one side, hunched posture, torticollis, muscular seizures and or rigidity.

## Astrocytomas- macroscopic

- Only 35% of males and 26% of female rats with astrocytomas were detected at autopsy
- Appeared as: swollen areas, greyish mass, discoloured areas, surface depression, haemorrhage

# Astrocytoma, haemorrhage & necrosis

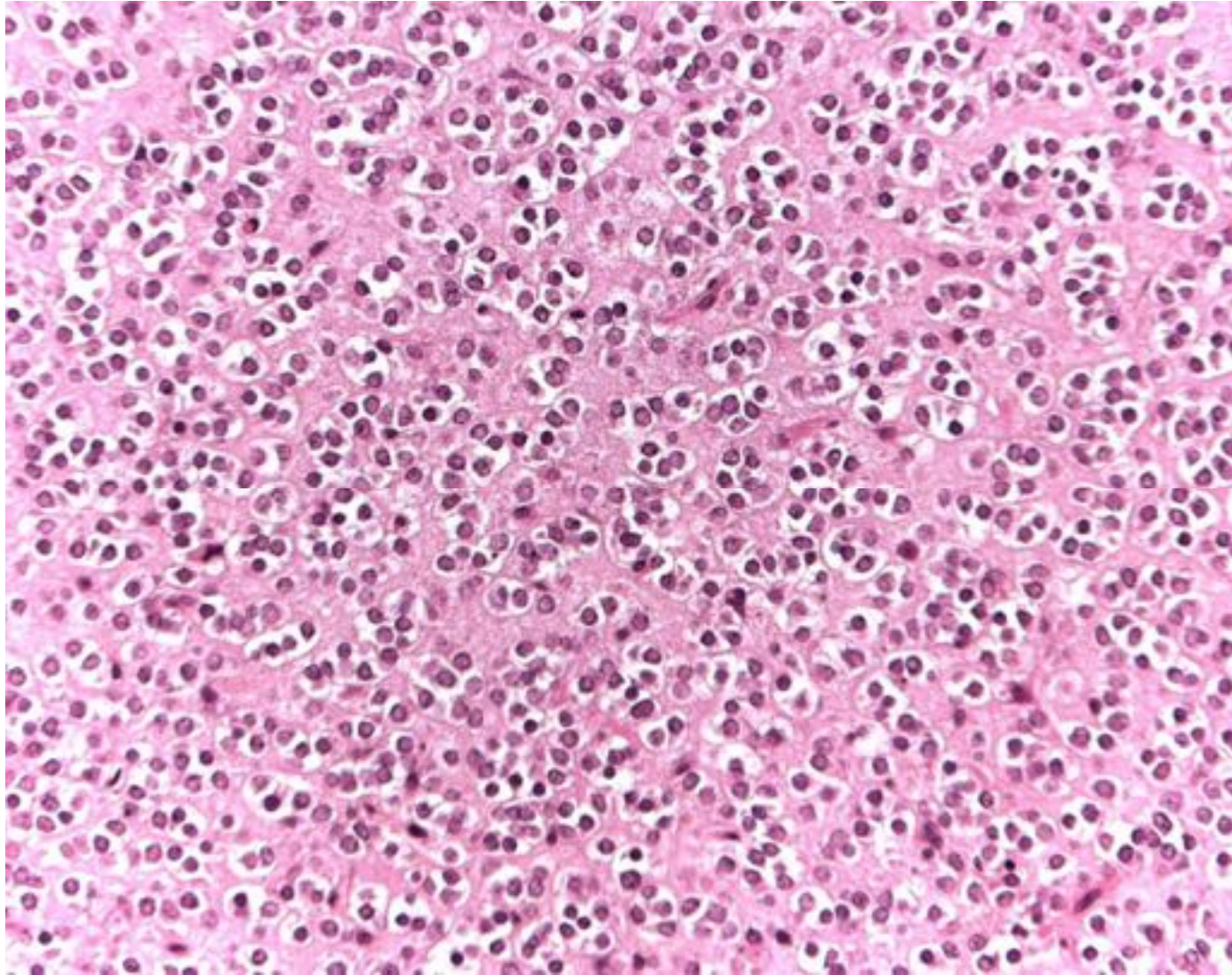




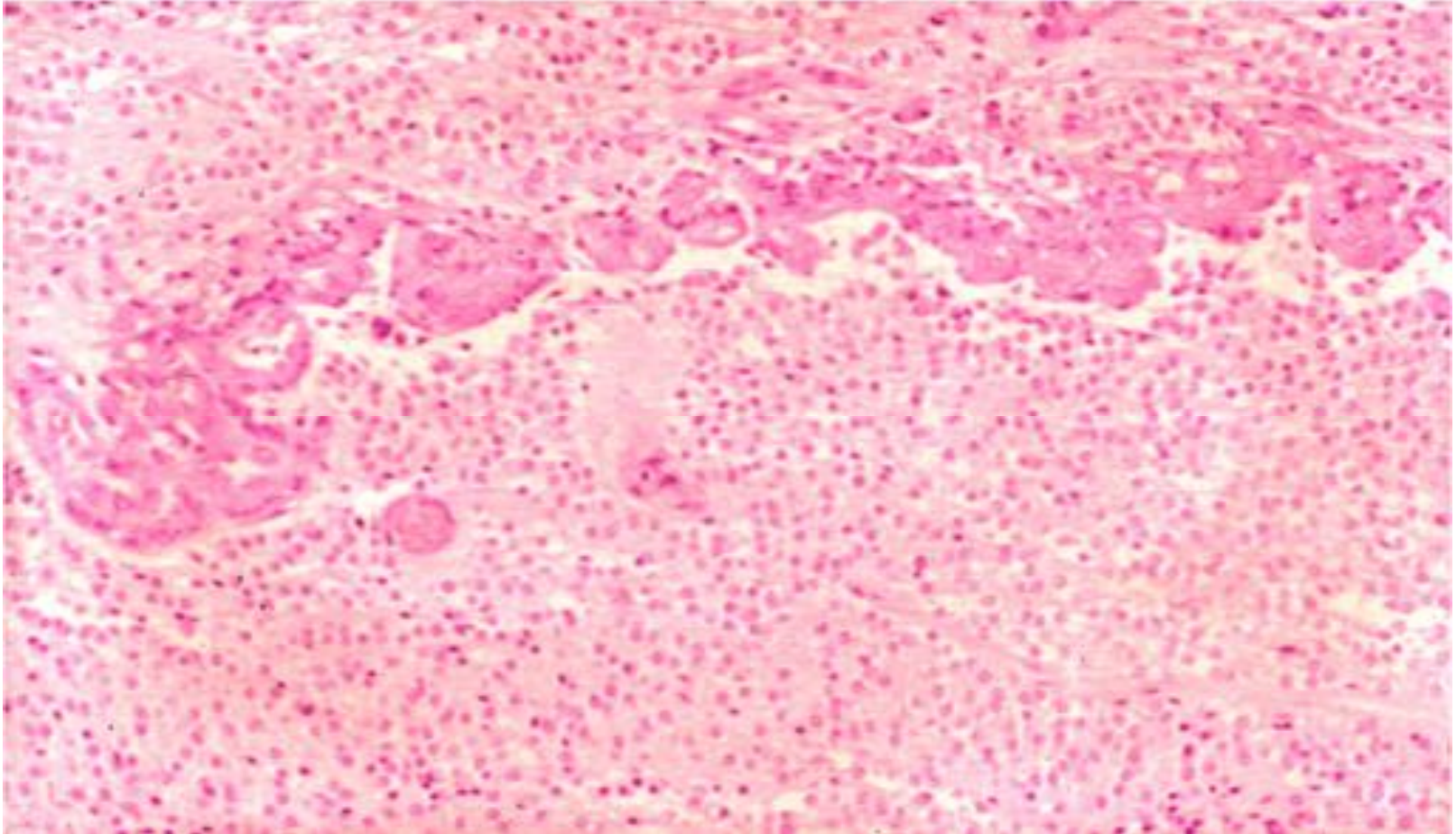
# Oligodendroglioma

- Somewhat circumscribed
- Round/polygonal cells with distinct cell walls and round nuclei, clear cytoplasm honey-comb pattern
- Sometime darker/larger cells arranged in rows with a canal like pattern, both patterns can co-exist, vascular endothelial hypertrophy noted

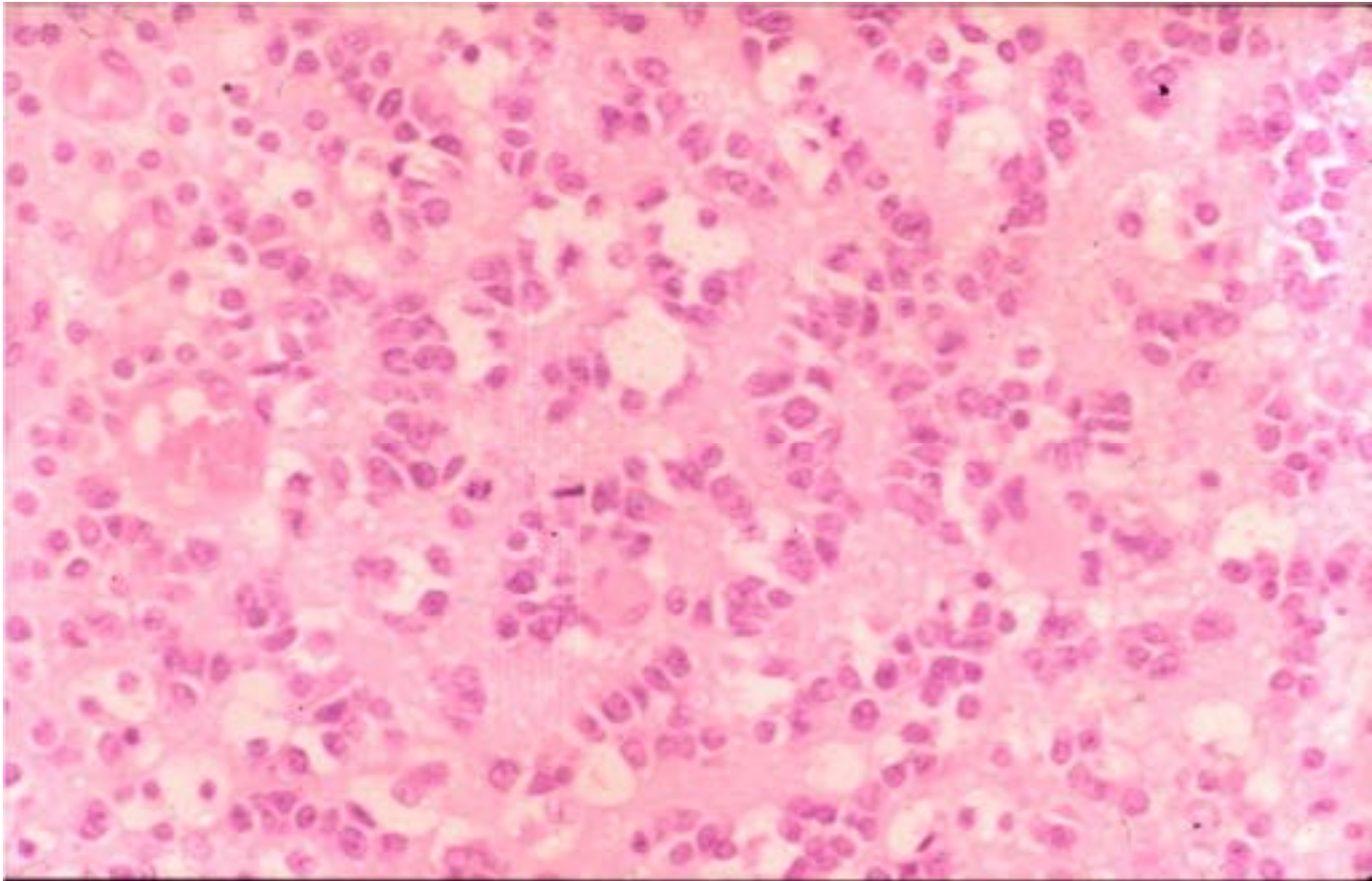
# Oligodendroglioma



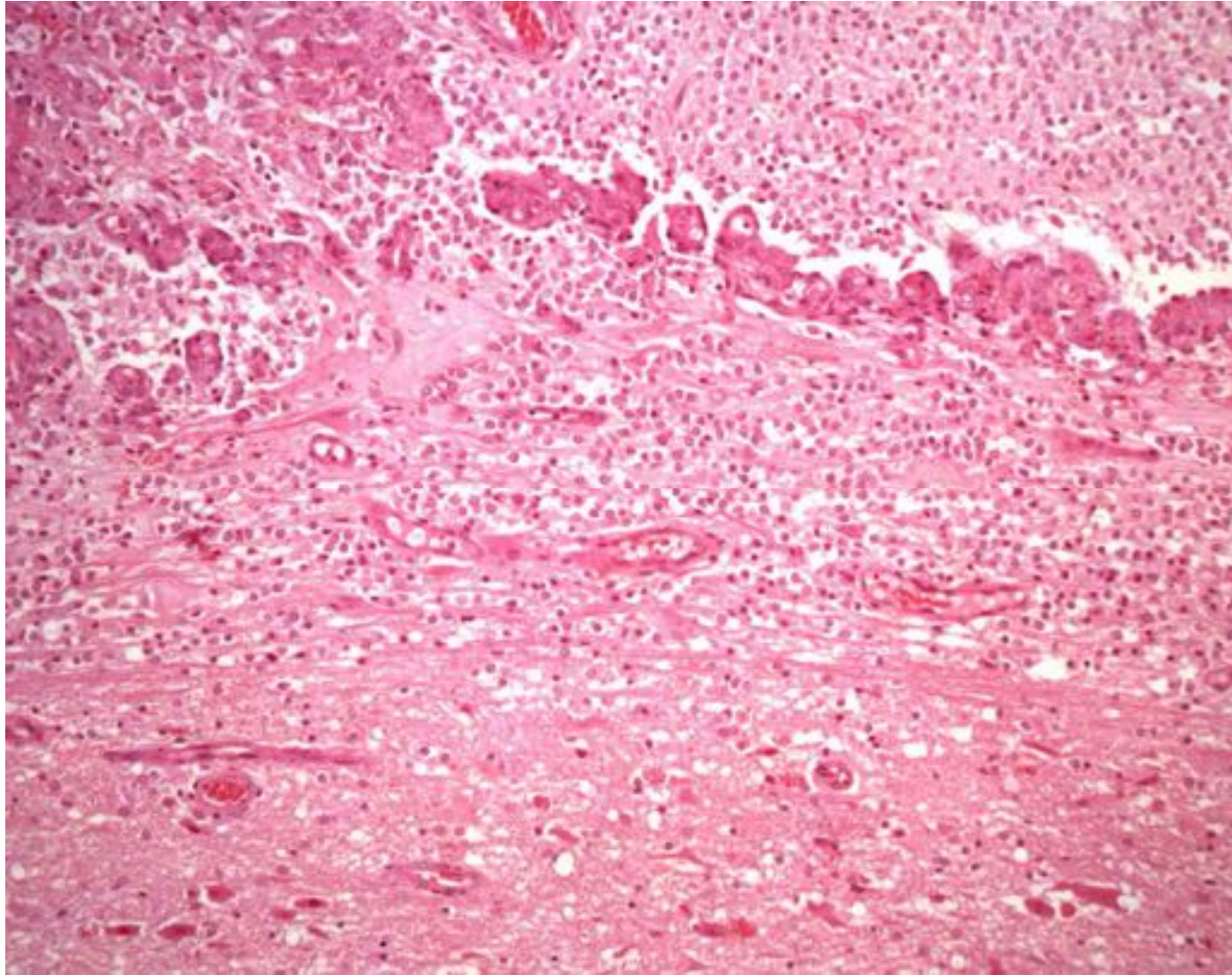
# Oligodendroglioma



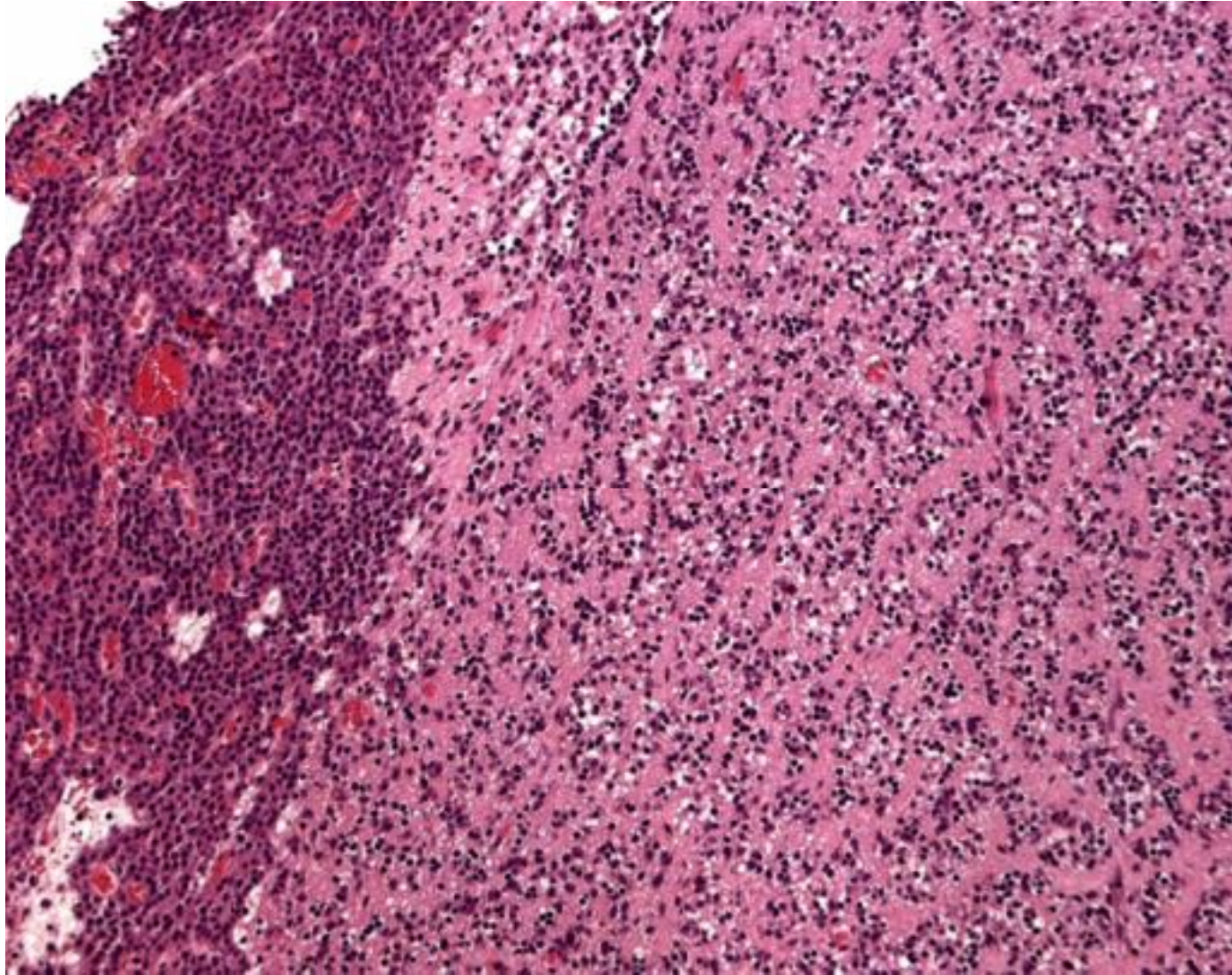
# Oligodendroglioma



# Oligo- sp c



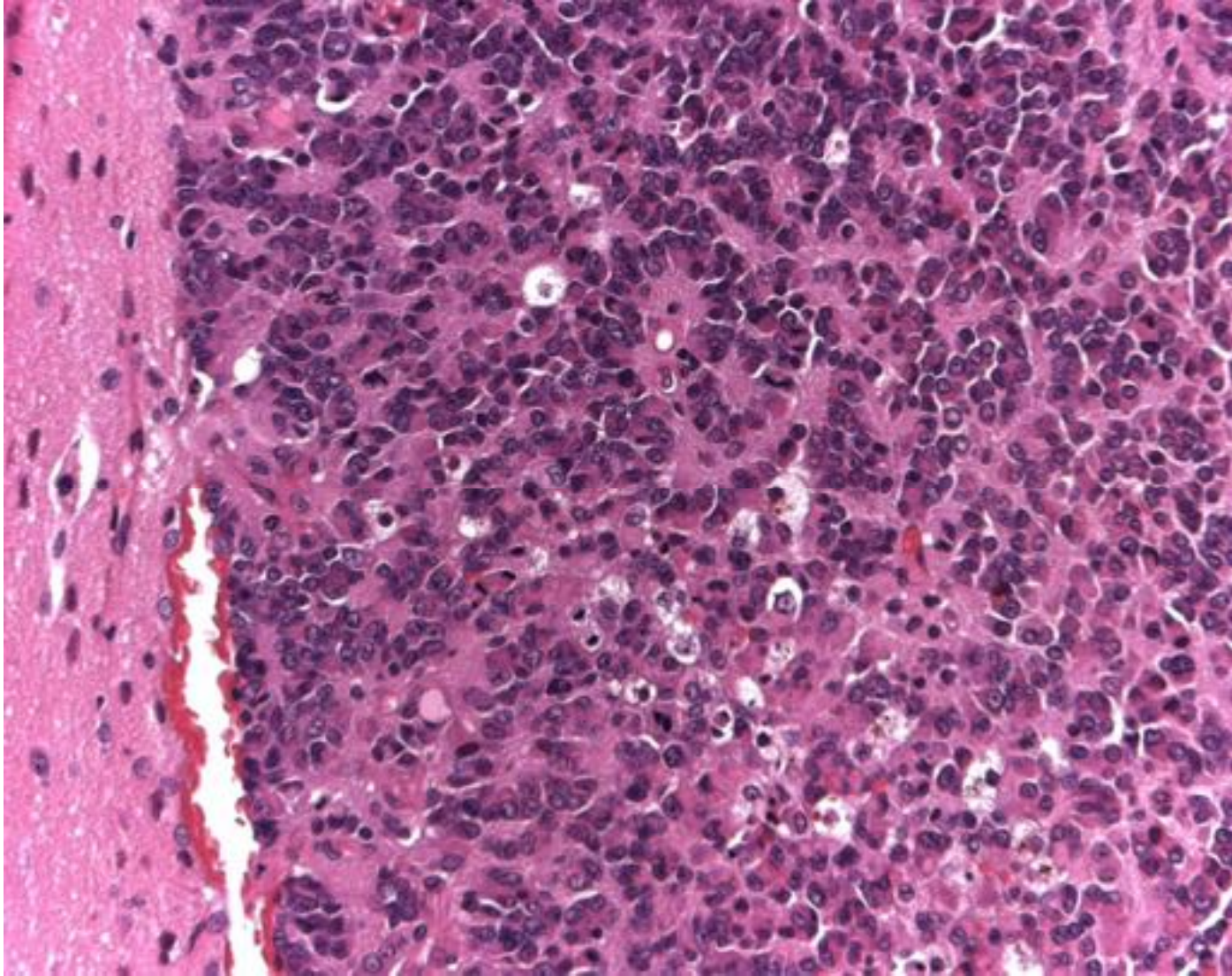
# Oligo pituitary



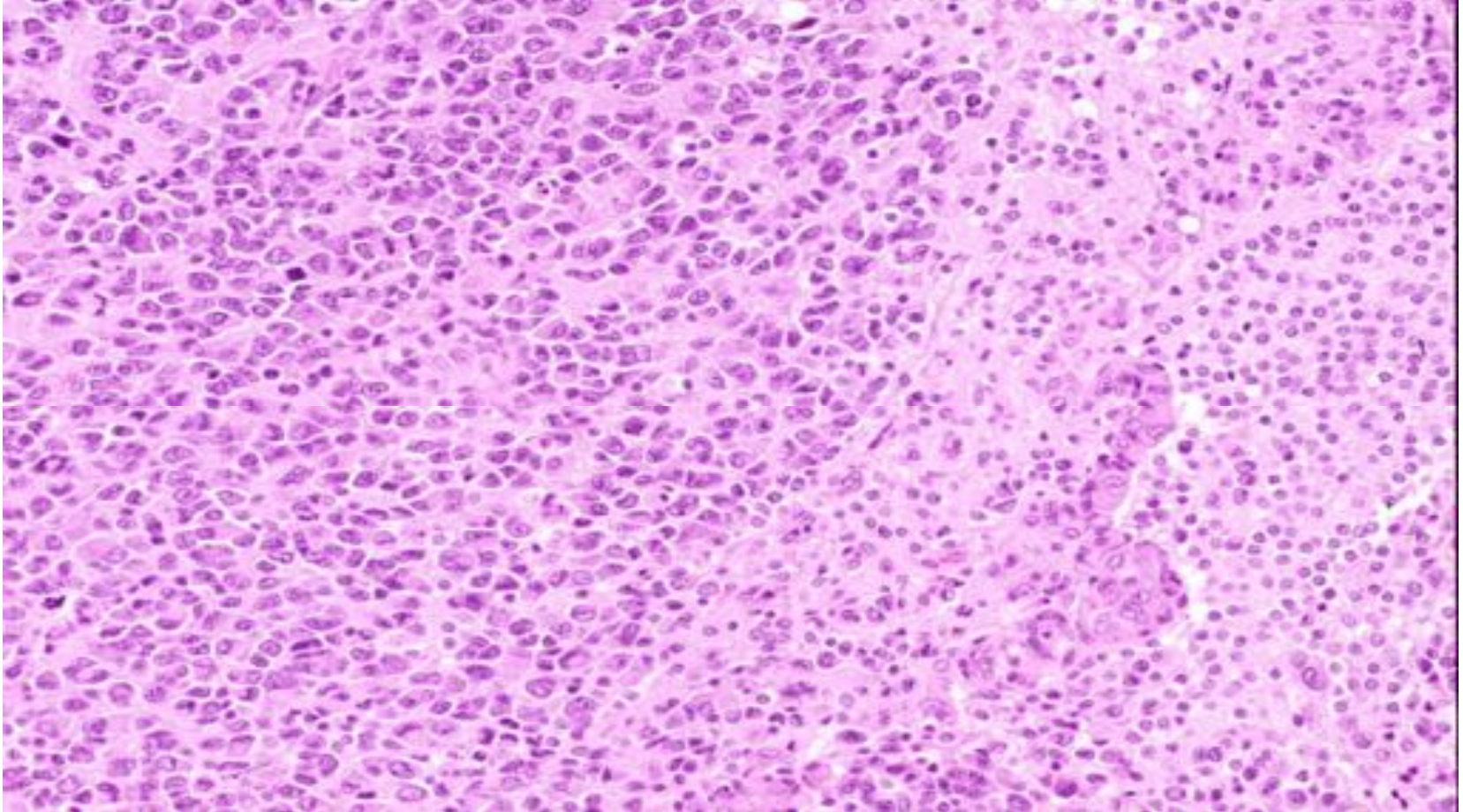
## Mixed glioma

- Reveal area of oligodendrocytic and astrocytic cells, also frank admixture of glial cells
- Show vascular endothelial hypertrophy and merging tumour edge

## Mixed gl



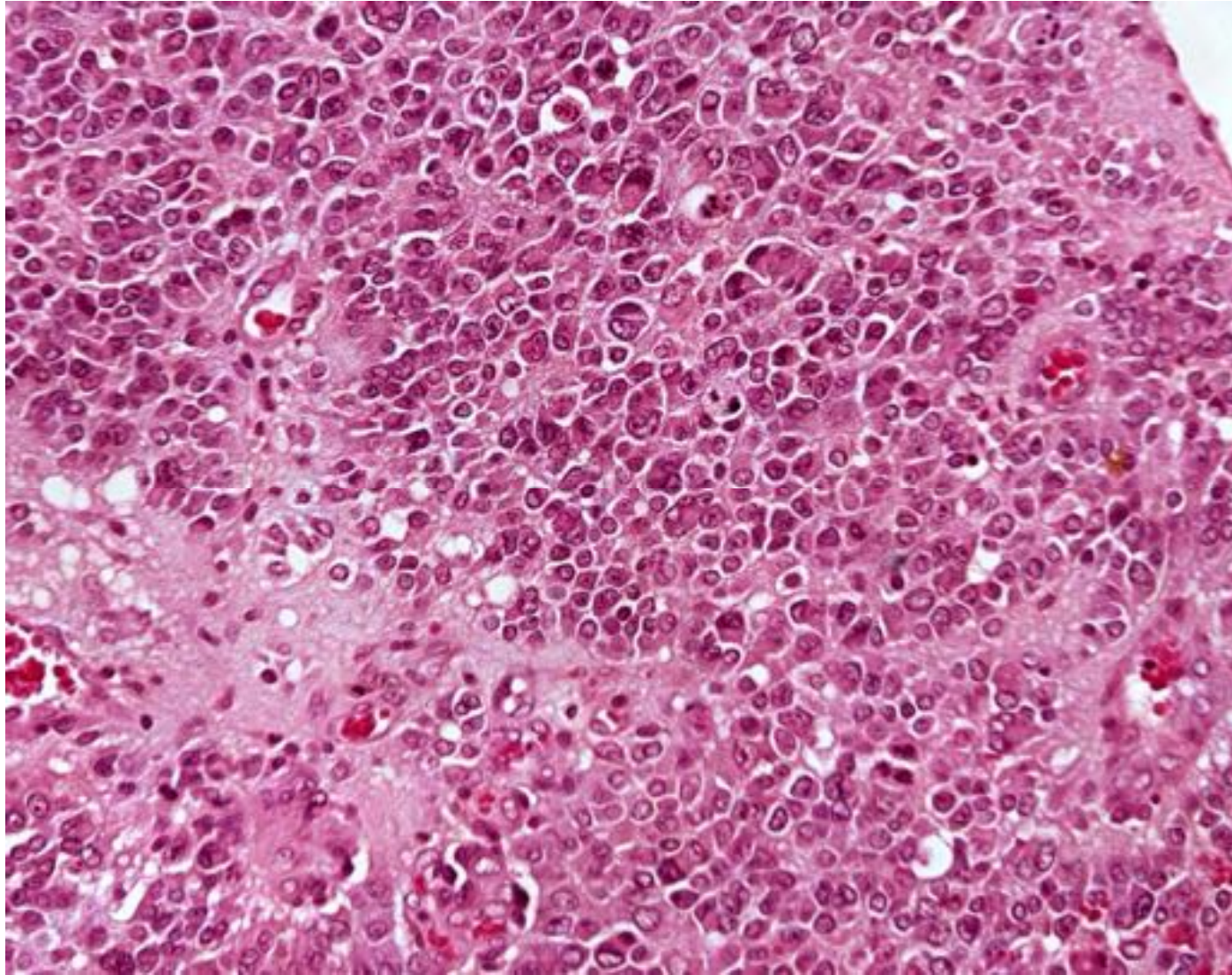
# Mixed glioma



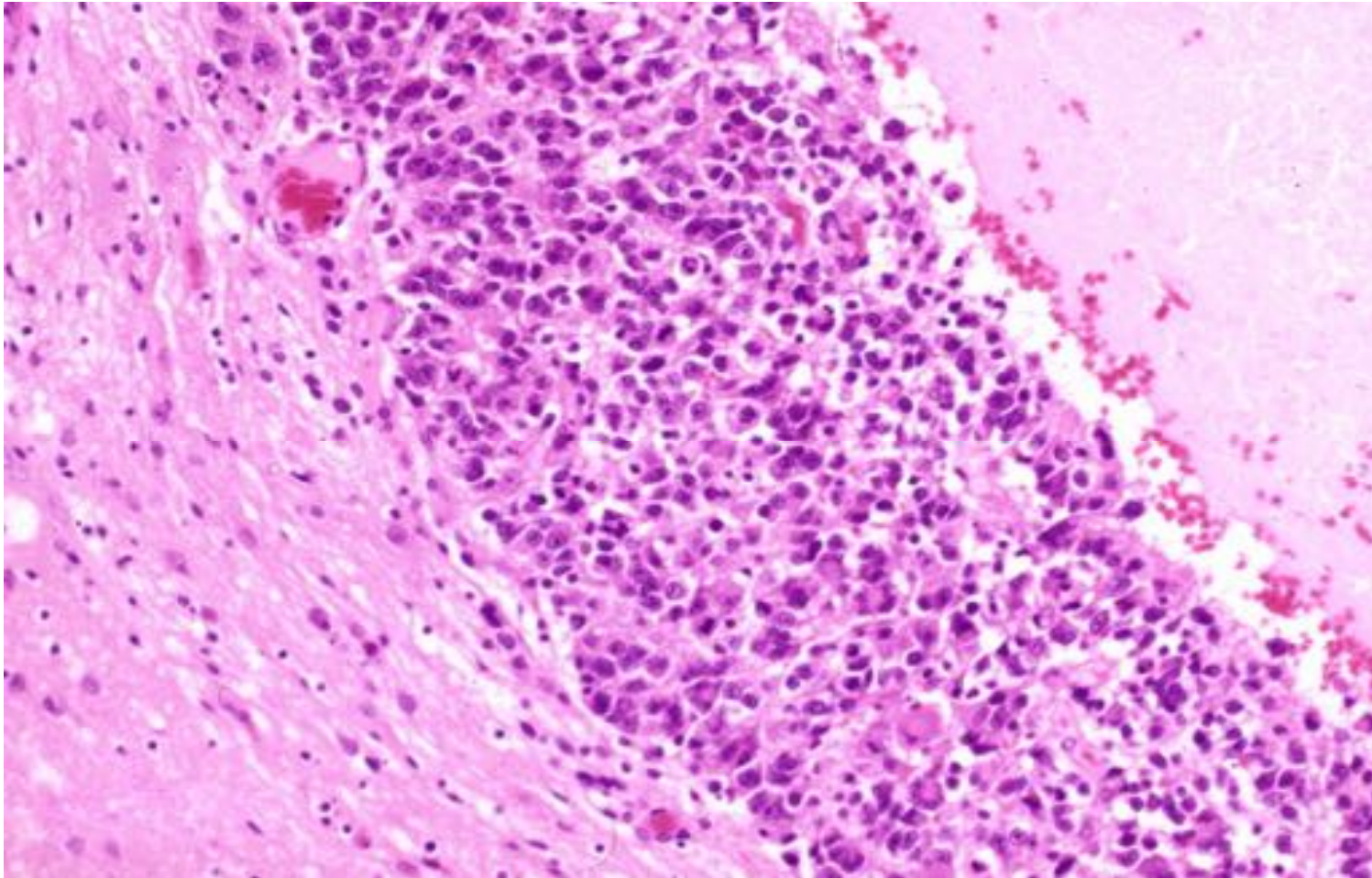
# Anaplastic glioma

- Undifferentiated glial cells
- Pleomorphic cell population
- Cellular atypia and occasional giant cells
- Cyst formations noted

# Anaplastic glioma



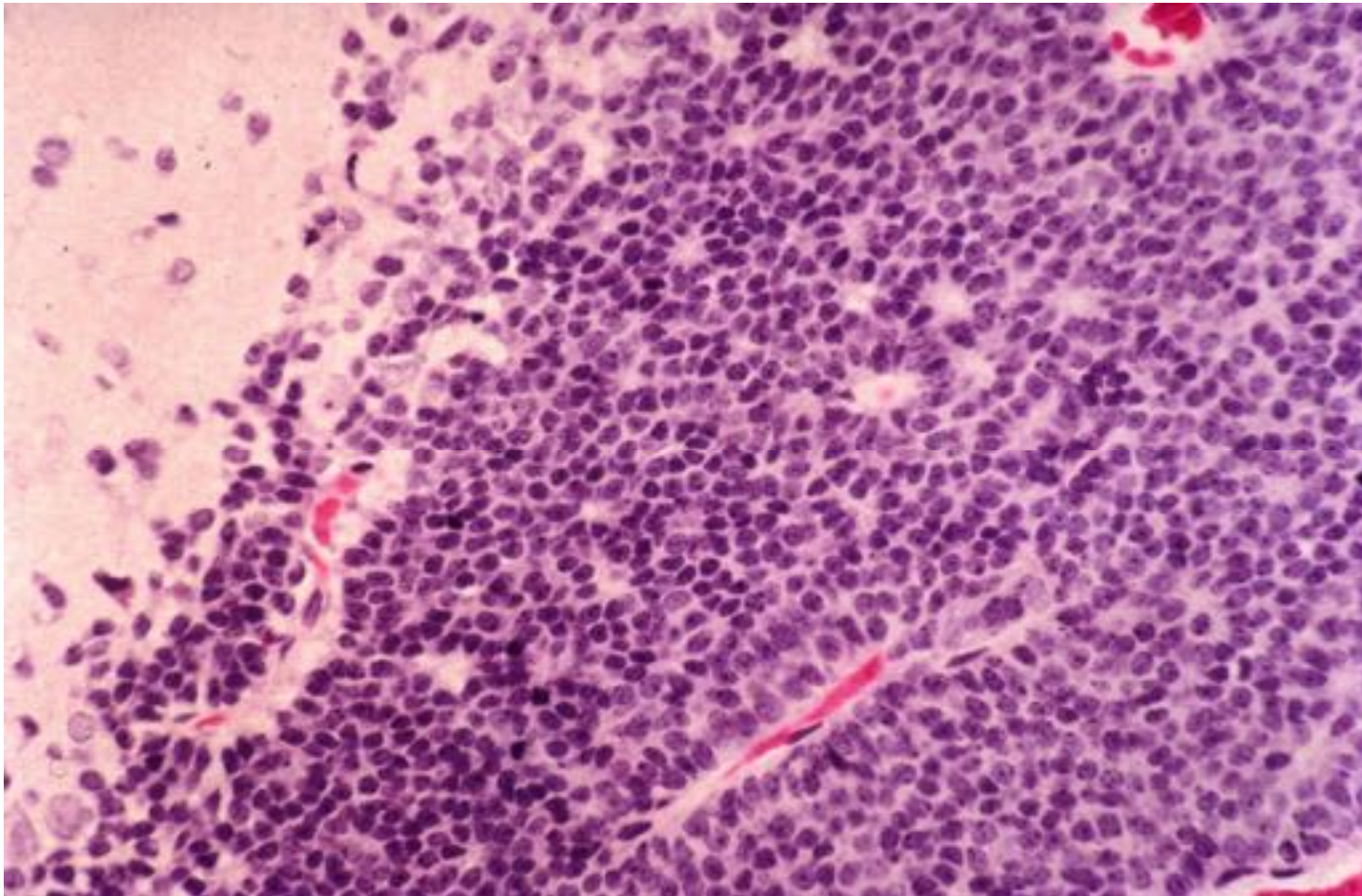
# Anaplastic glioma



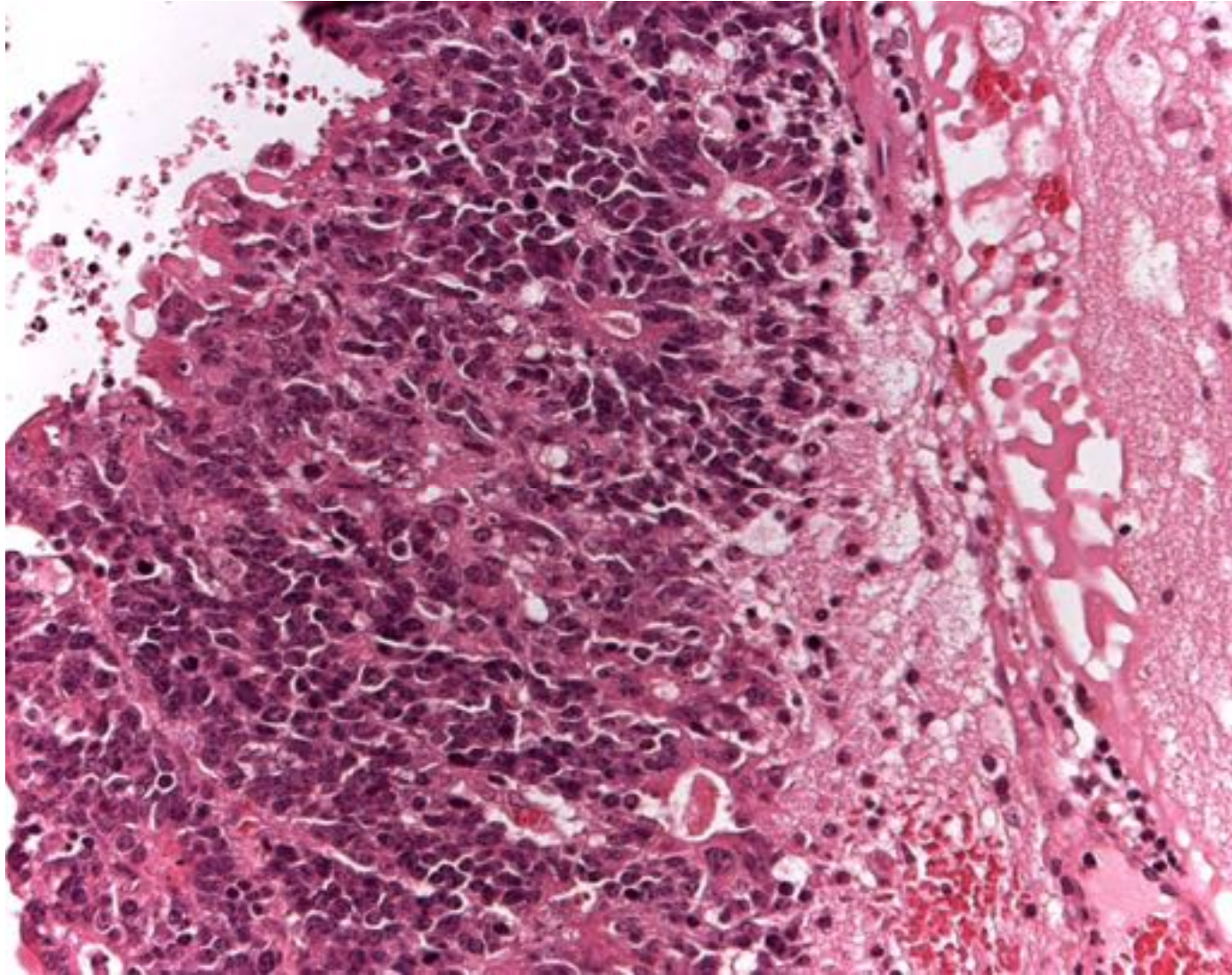
# Ependymoma

- Located around ependymal lining
- Uniform basophilic sheets of cells with scanty cytoplasm
- Rosette/ pseudorosettes
- Cytokeratin +, microvilli/ blepharoblasts on em

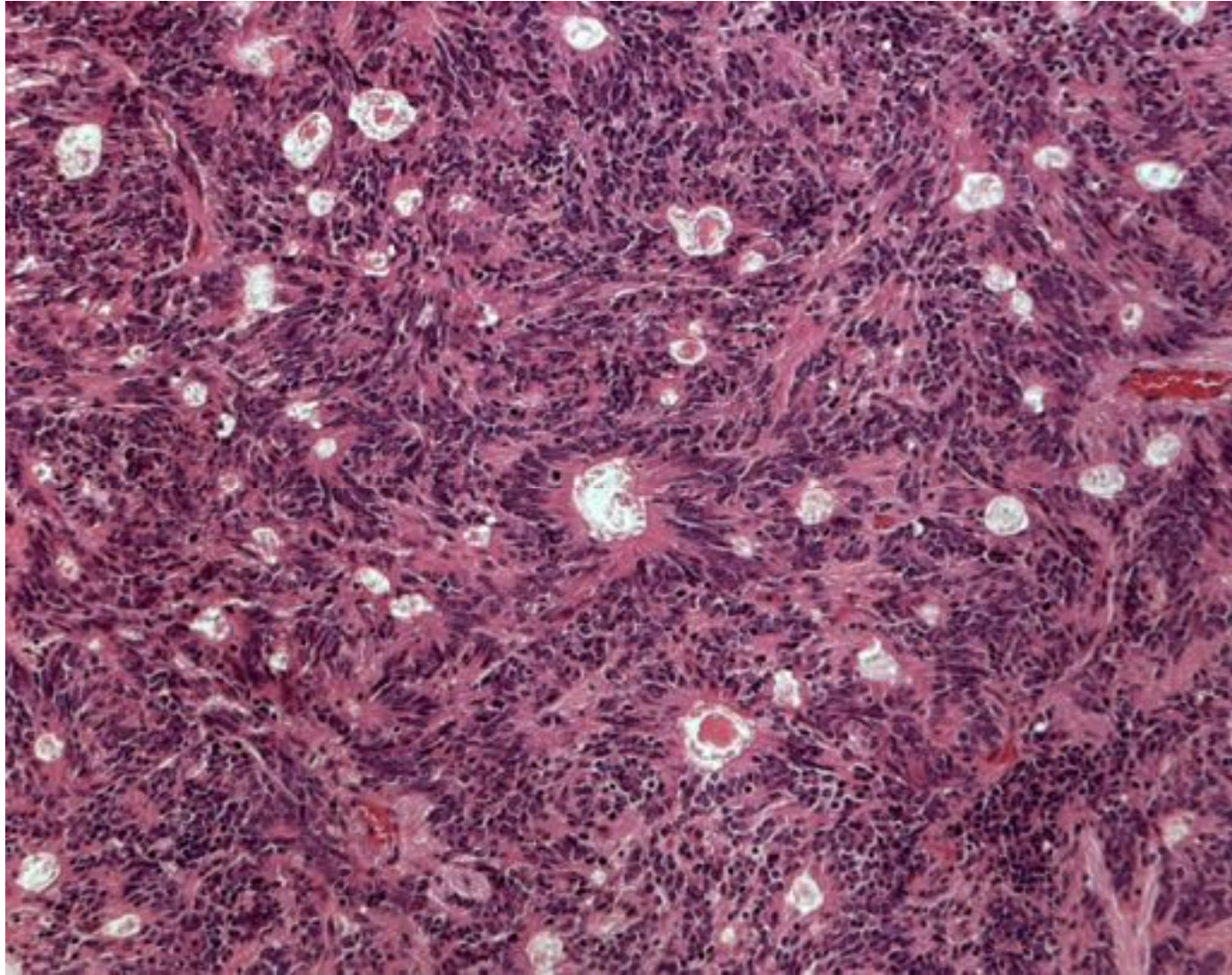
# Ependymoma



# Ependymoma



# Ependymoma



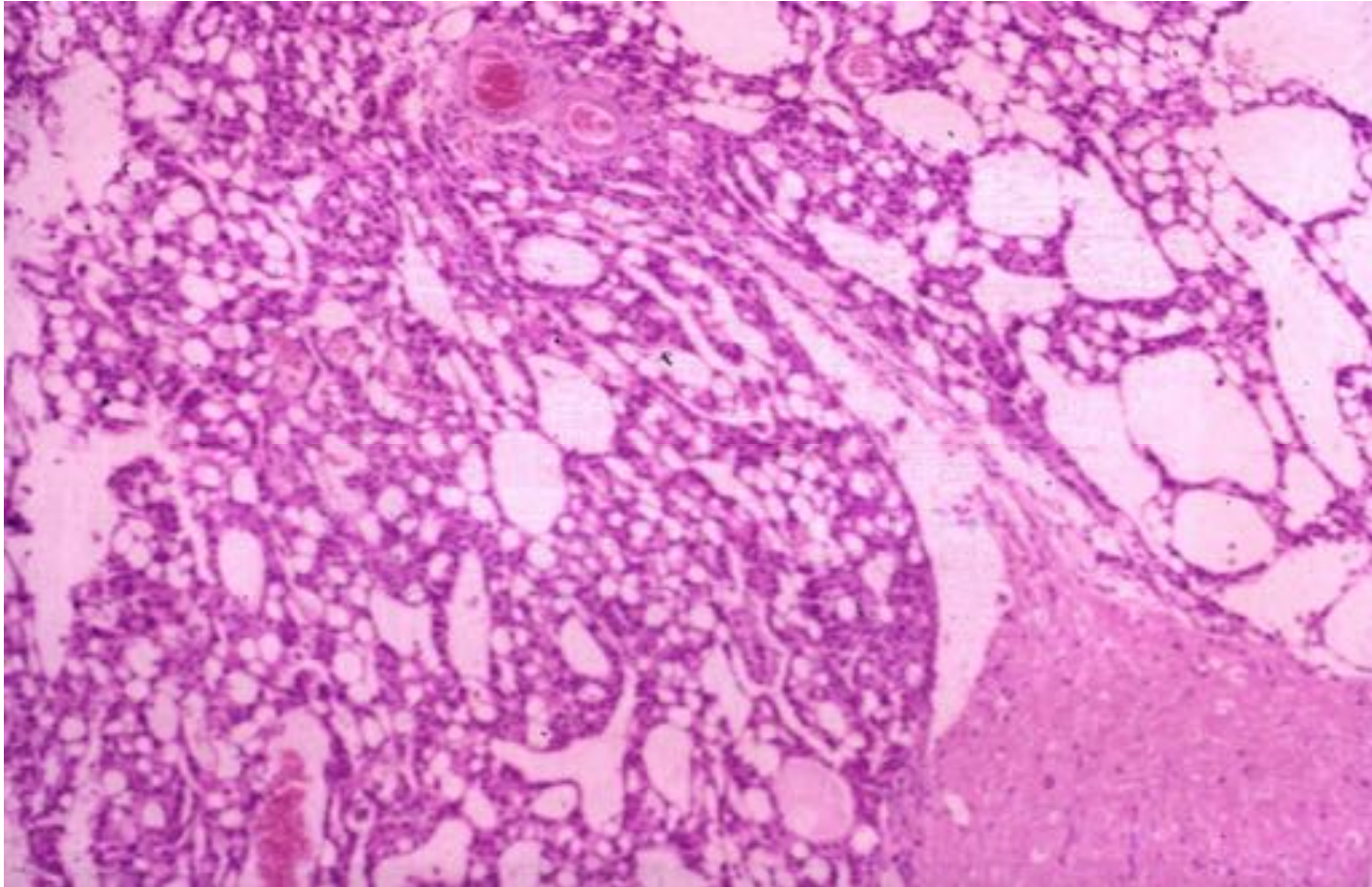
# Choroid plexus papilloma

- Papillary growth in ventricles
- Vascular stroma
- Eosinophilic cells with abundant cytoplasm
- Frequently single cell layer

## Choroid plexus carcinoma

- Papillary growth in ventricles with local invasion
- Cells are cuboidal/columnar often multilayered

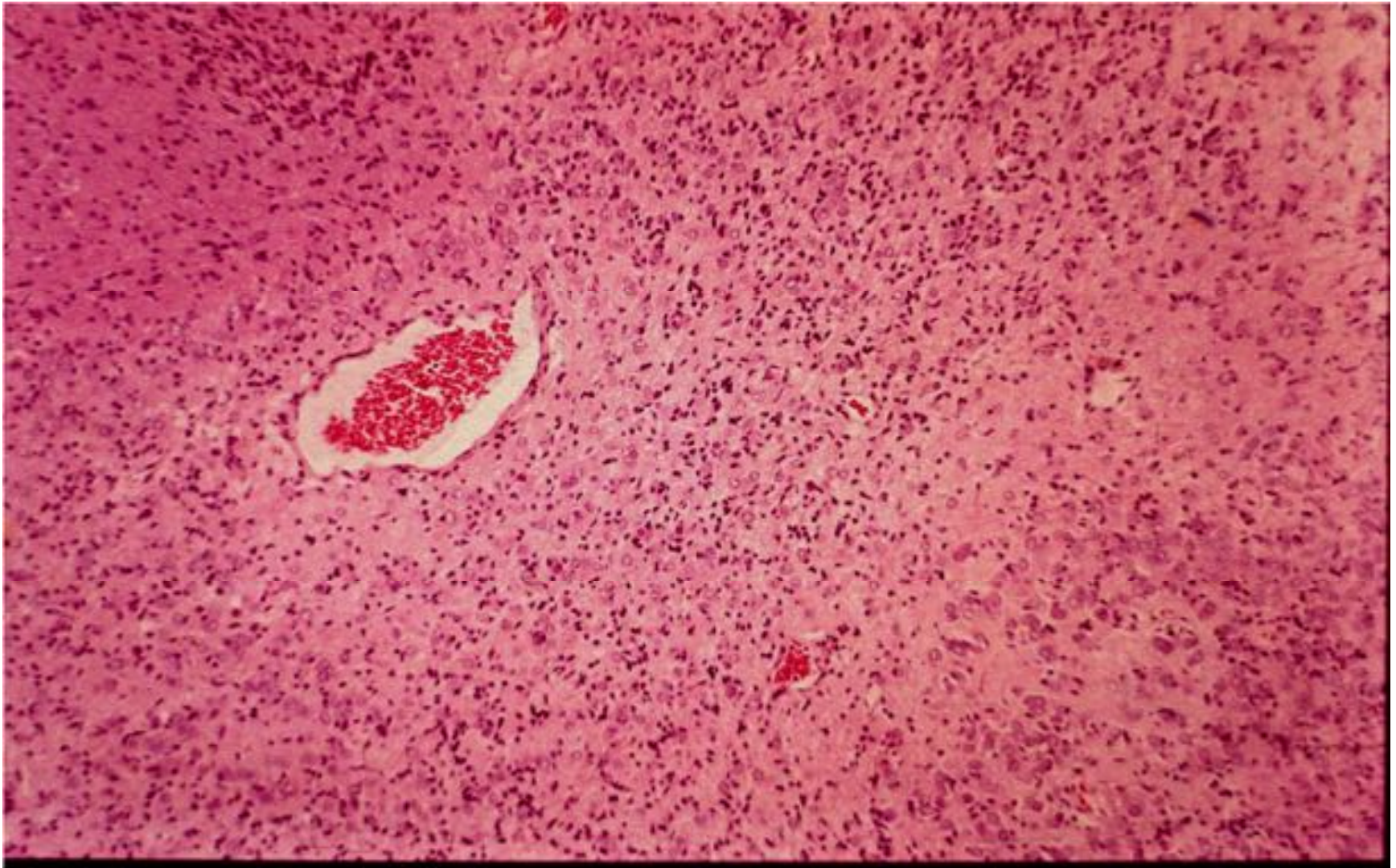
## Choroid plexus carcinoma, papillary



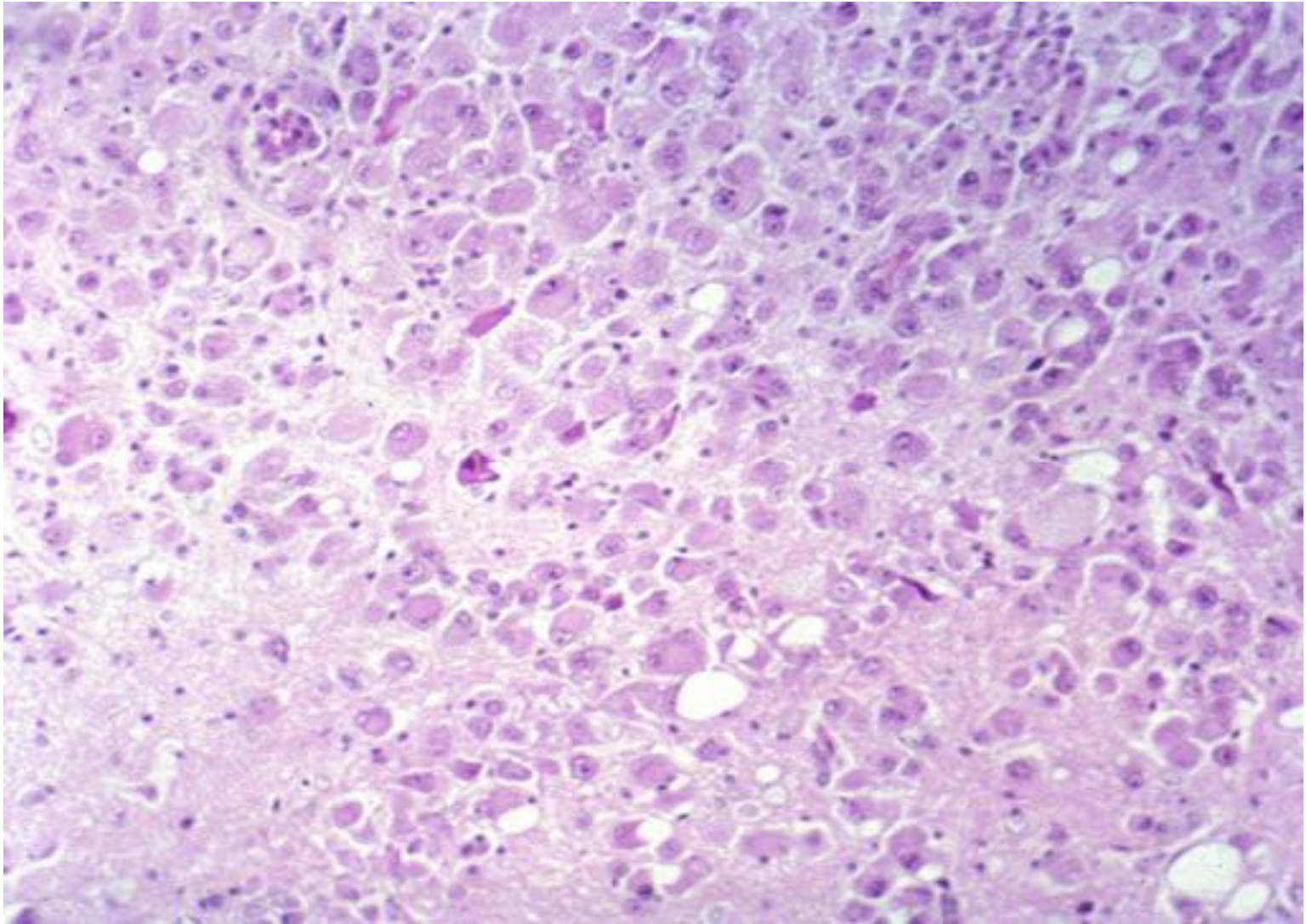
# Ganglioneuroma

- Ganglion/neurons embedded in neuropile within brain
- Similar to those occurring in adrenal medulla

# Ganglioneuroma- brain



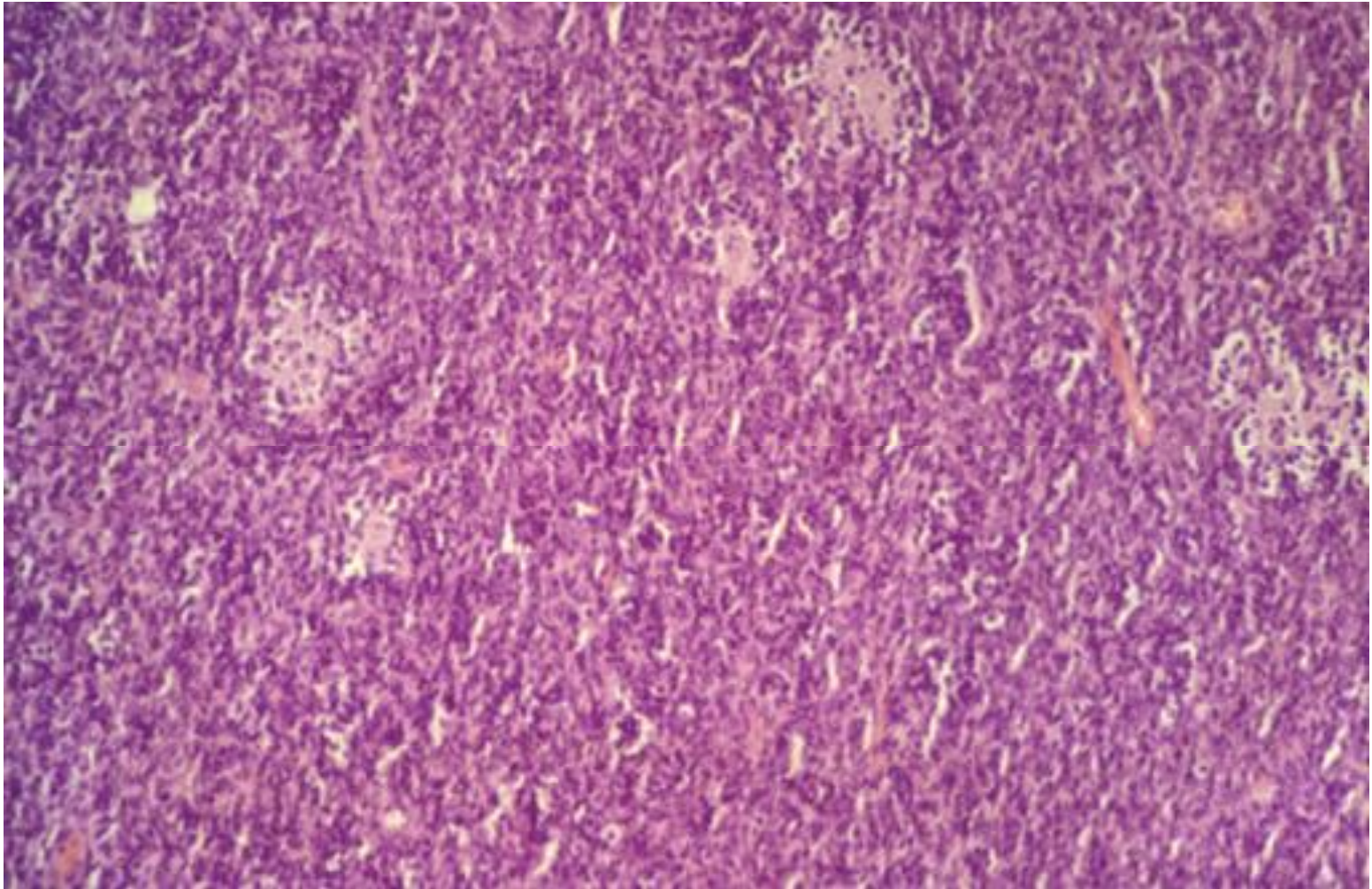
# Ganglioneuroma- adrenal



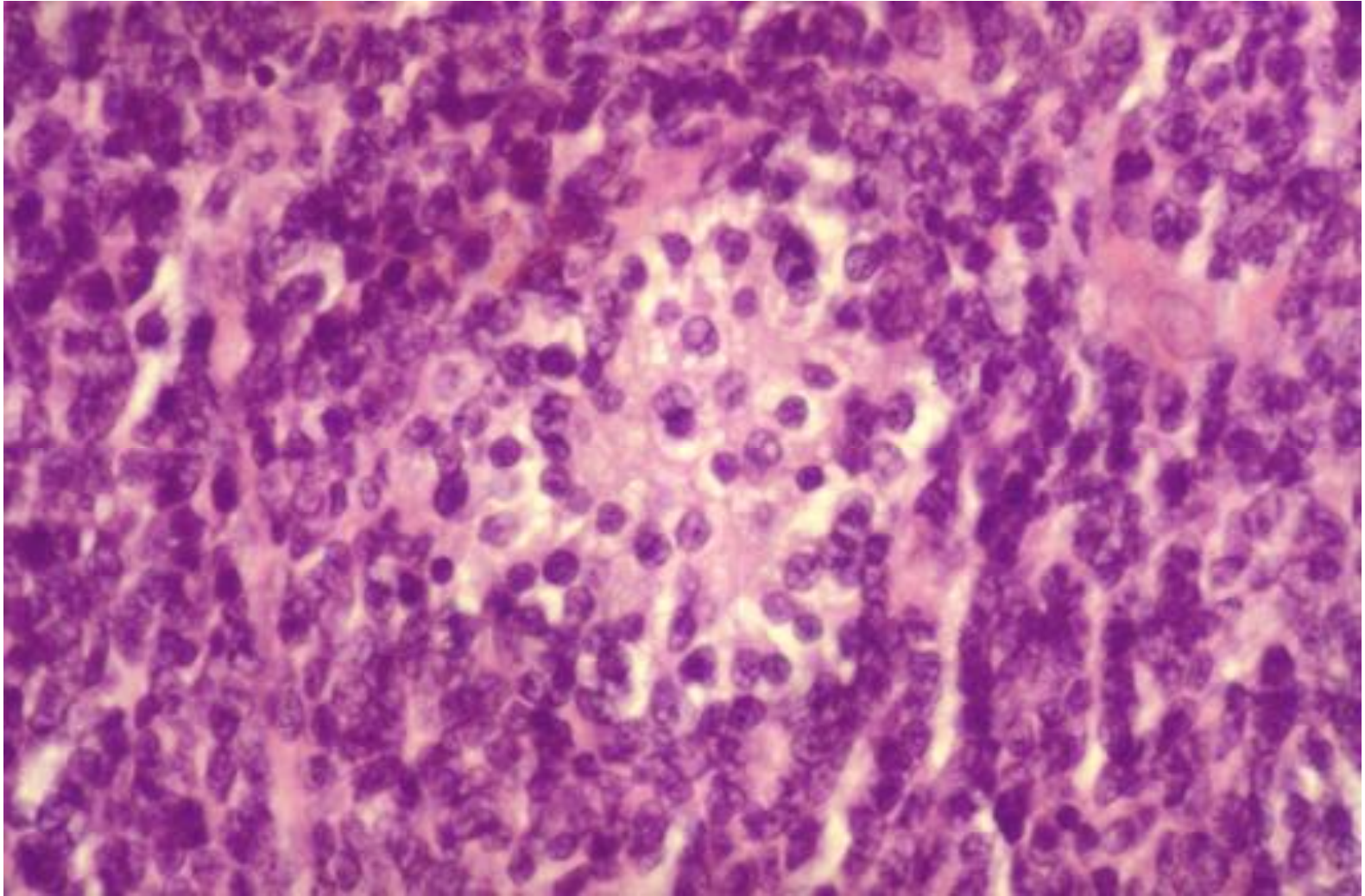
# Medulloblastoma

- Highly cellular, undifferentiated, basophilic, primitive cells, scanty cytoplasm, round/elongated nuclei, forming sheets
- Occasional rosetts/ pseudorosettes
- Neuronal differentiation is reported
- Frequent in cerebellum

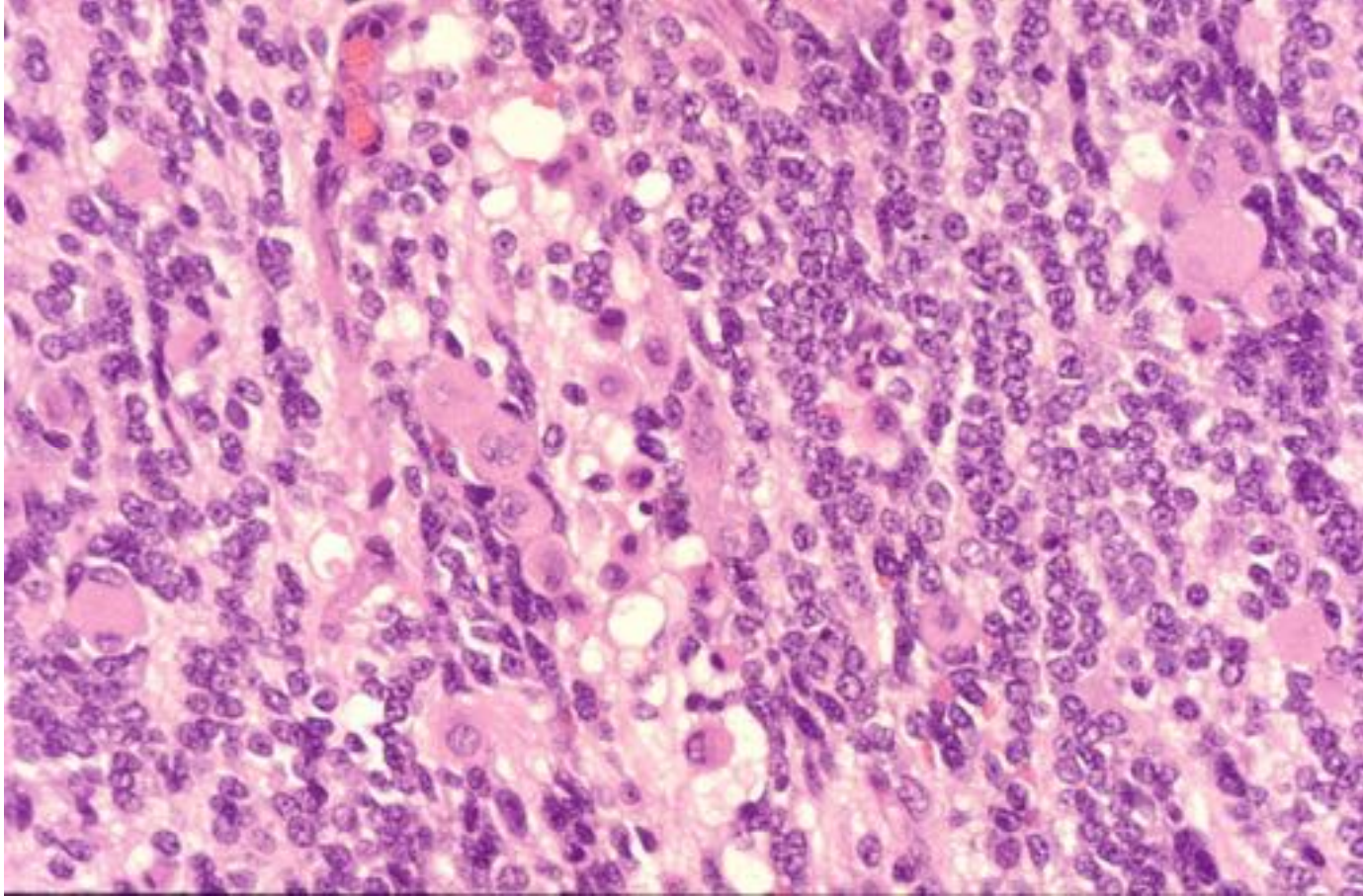
# Medulloblastoma



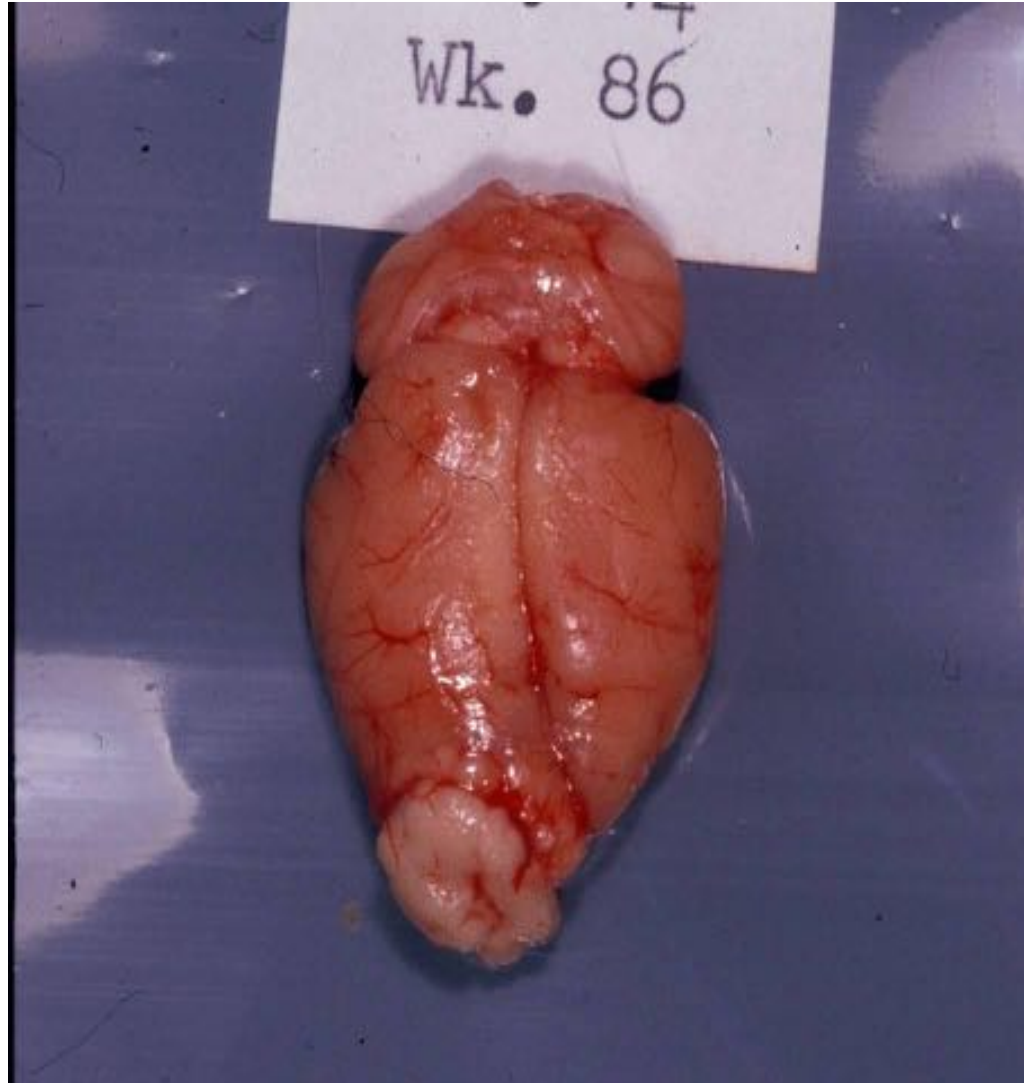
# Medulloblastoma



# Medulloblastoma

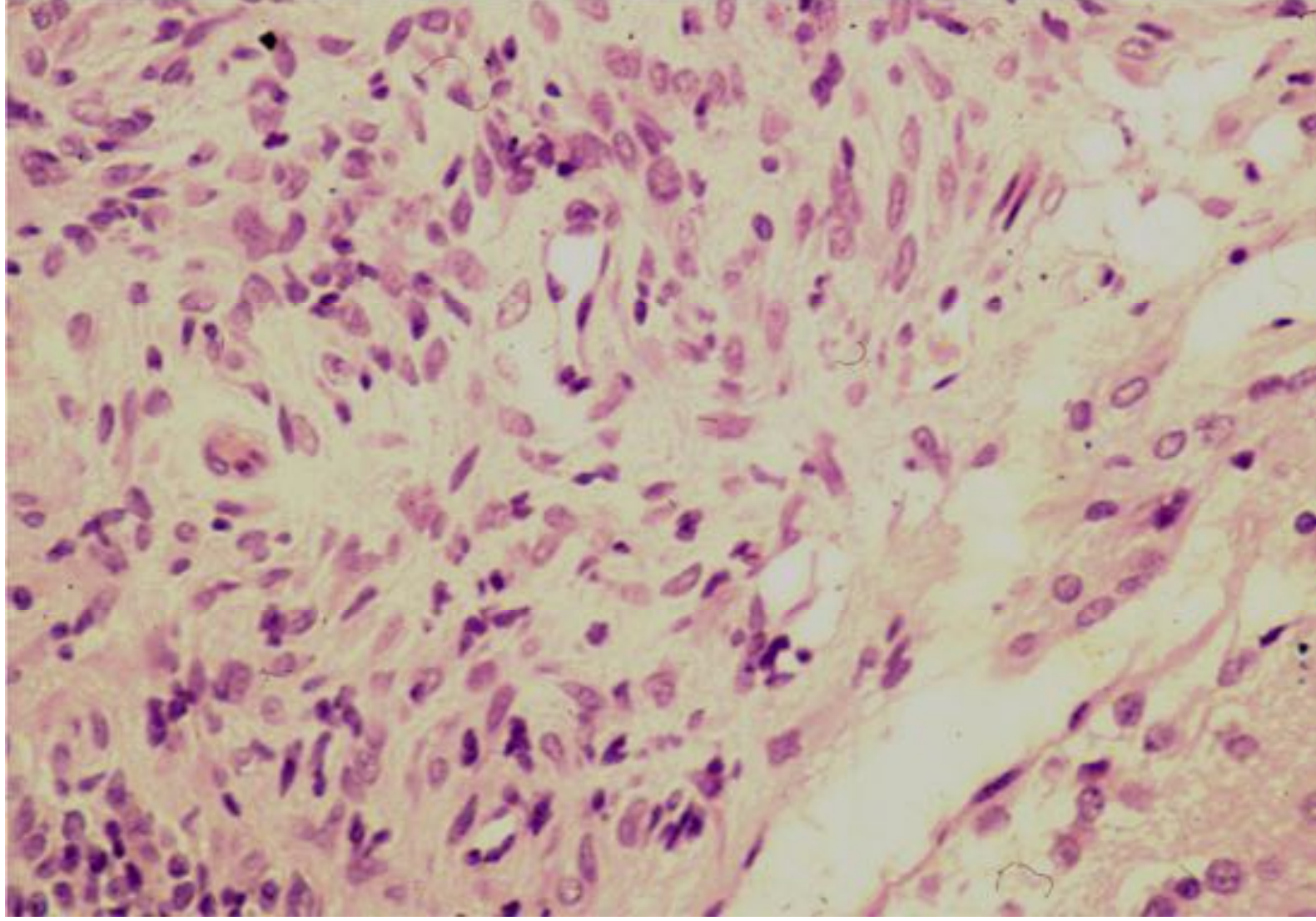


# Meningioma

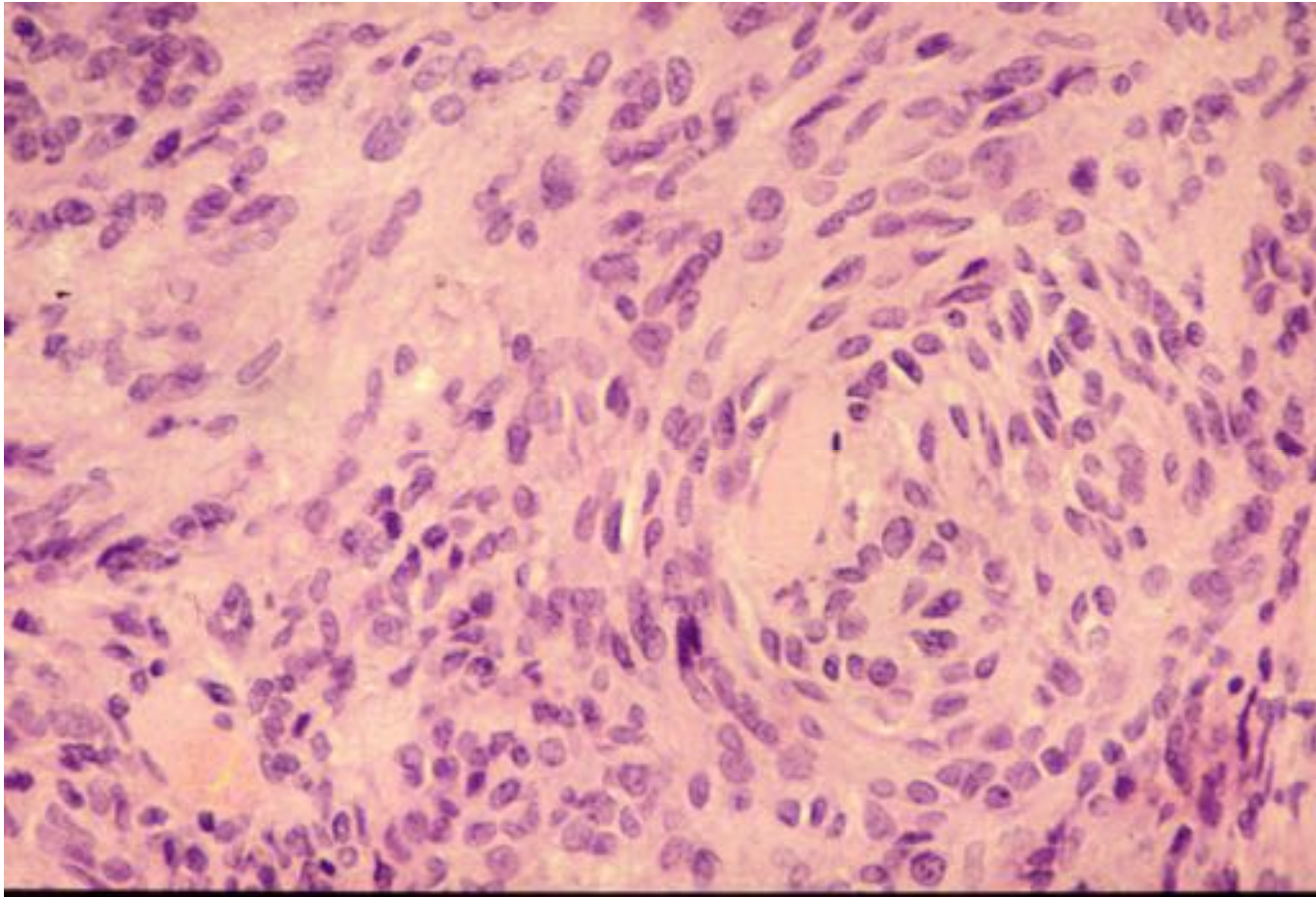


# Meningioma

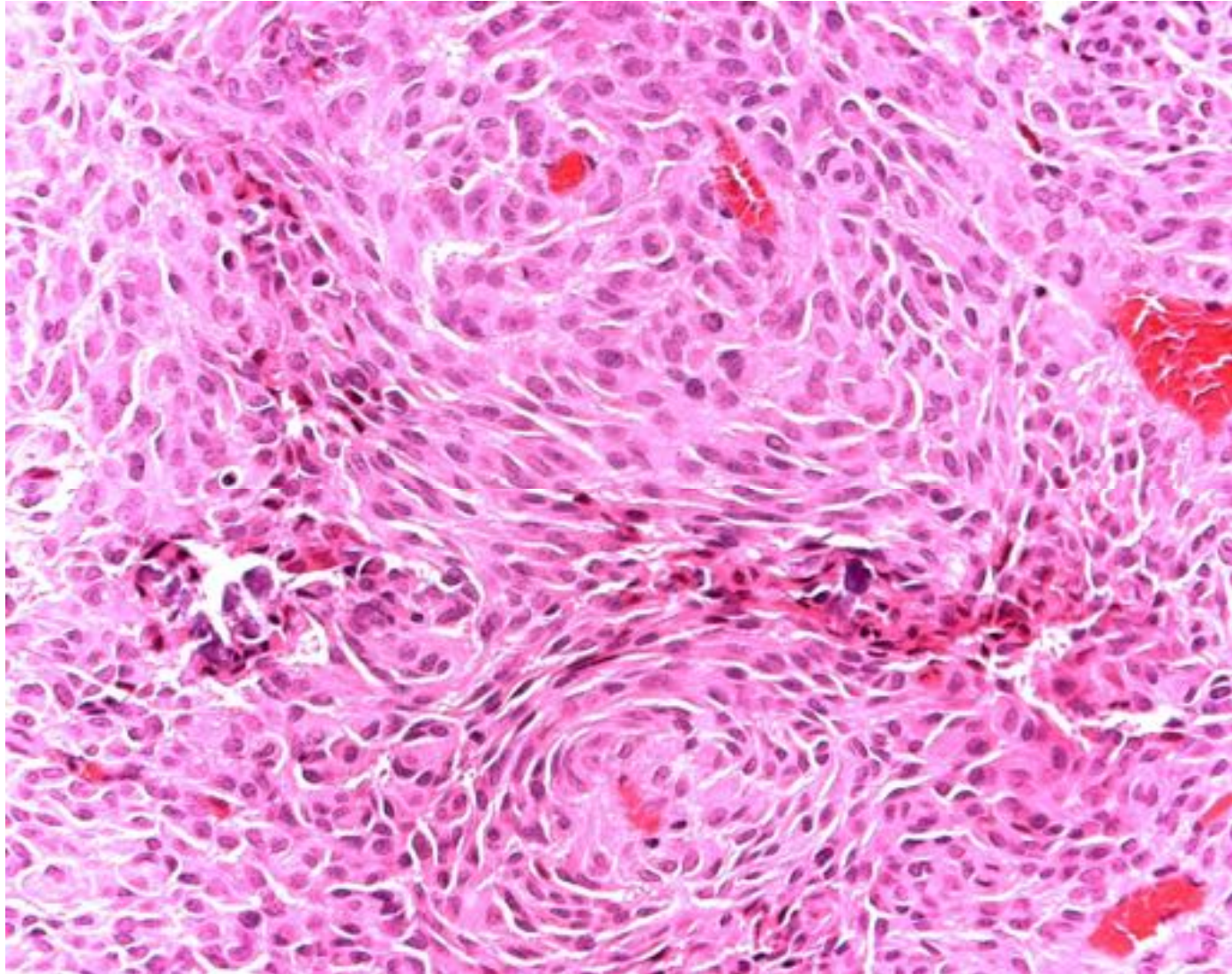
- Well circumscribed lesion of meninges, with distinct edge causing compression on brain.
- Fibroblastic: elongated cells fusiform dark nucleus, varying amounts of collagen, grows along the meninges
- Meningiothelial: Epitheloid cells with abundant cytoplasm and open nucleus. Lobulated, interlacing or whorl patterns
- Admixtures also possible



# Meningioma



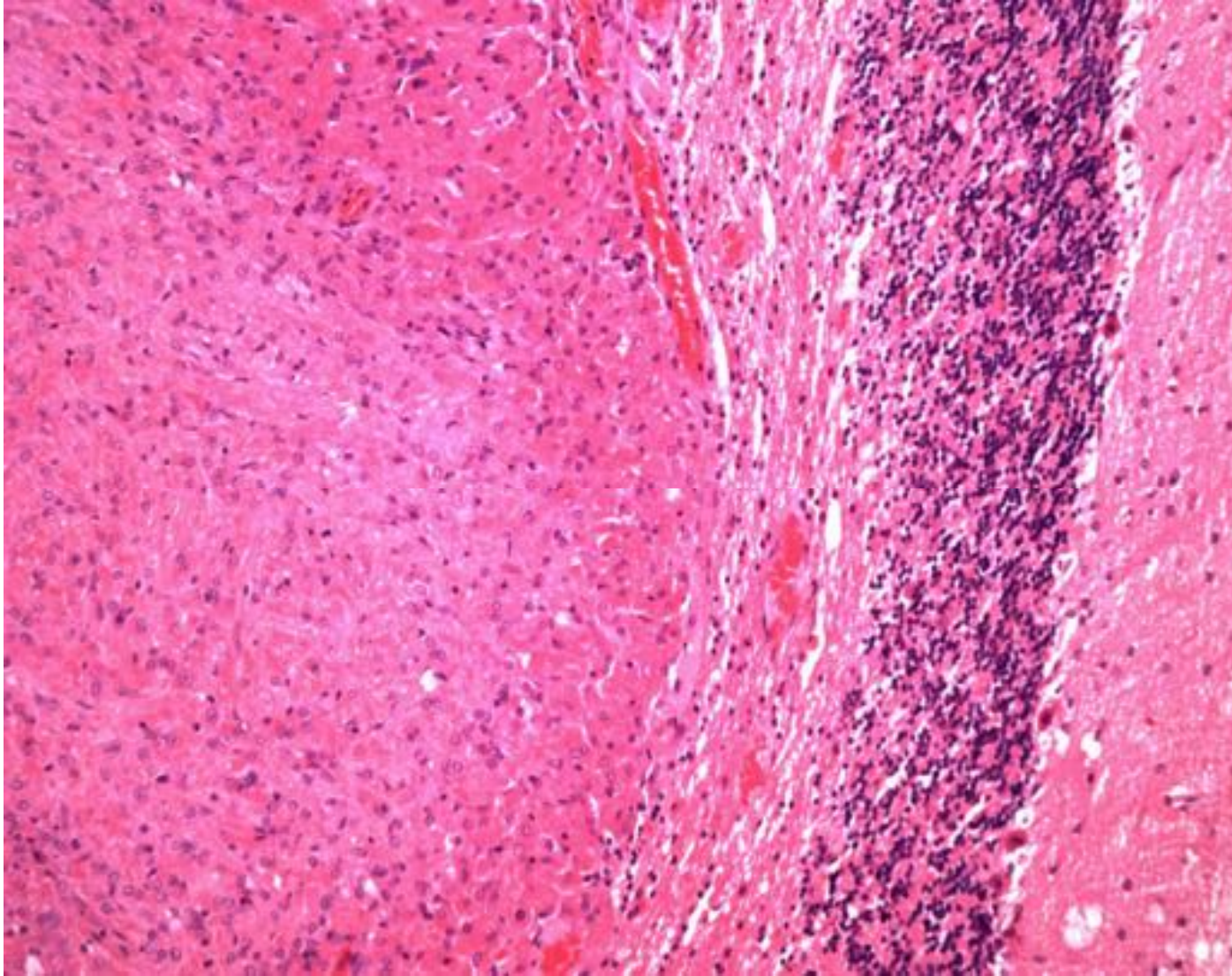
# Meningioma



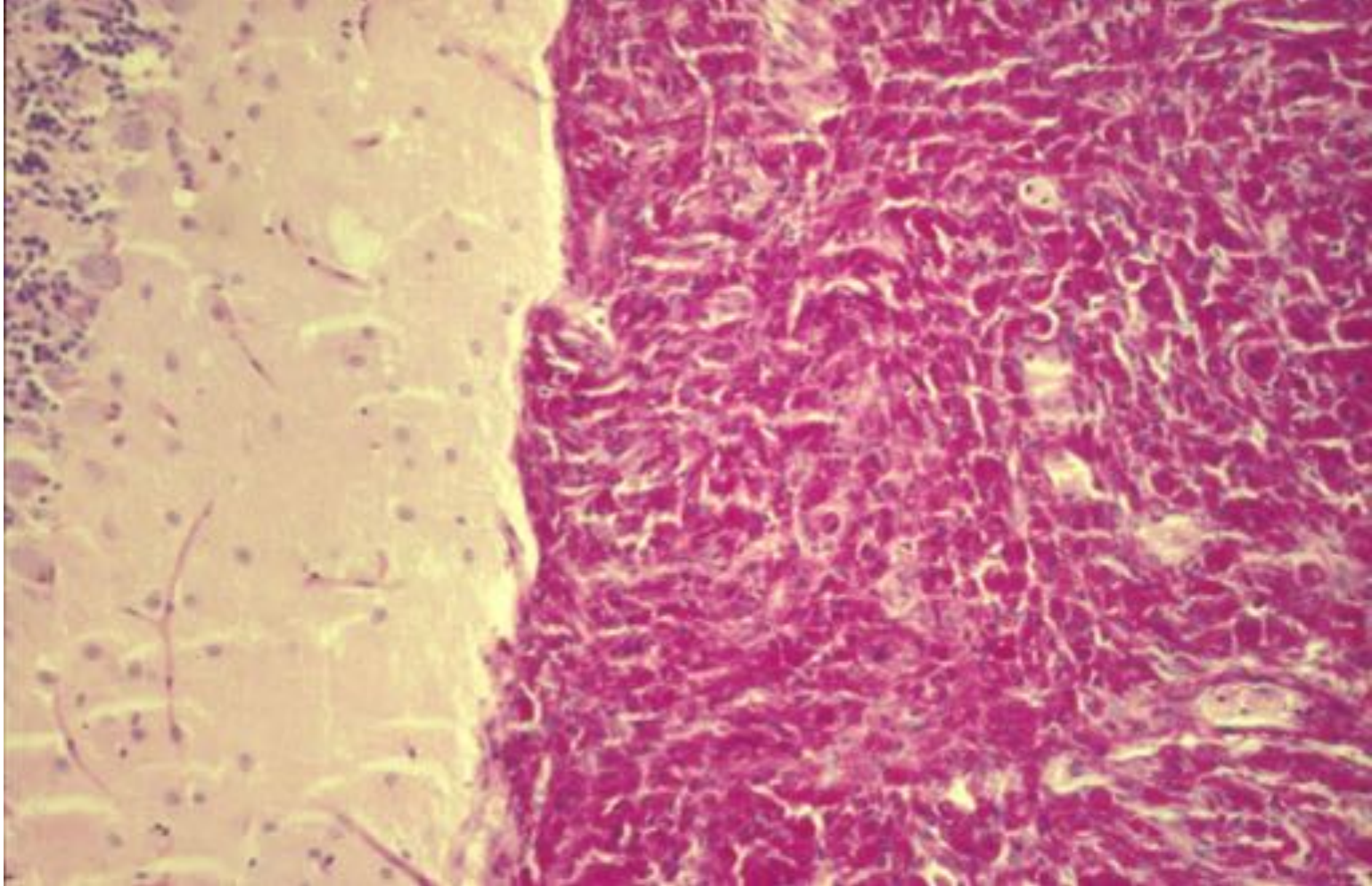
## Granular cell tumour

- A well circumscribed growth arising from or attached to meninges.
- Abundant cytoplasm with eosinophilic granules, stain PAS +
- Outgrowths into brain parenchyma noted on occasions
- Considered meningeal in origin

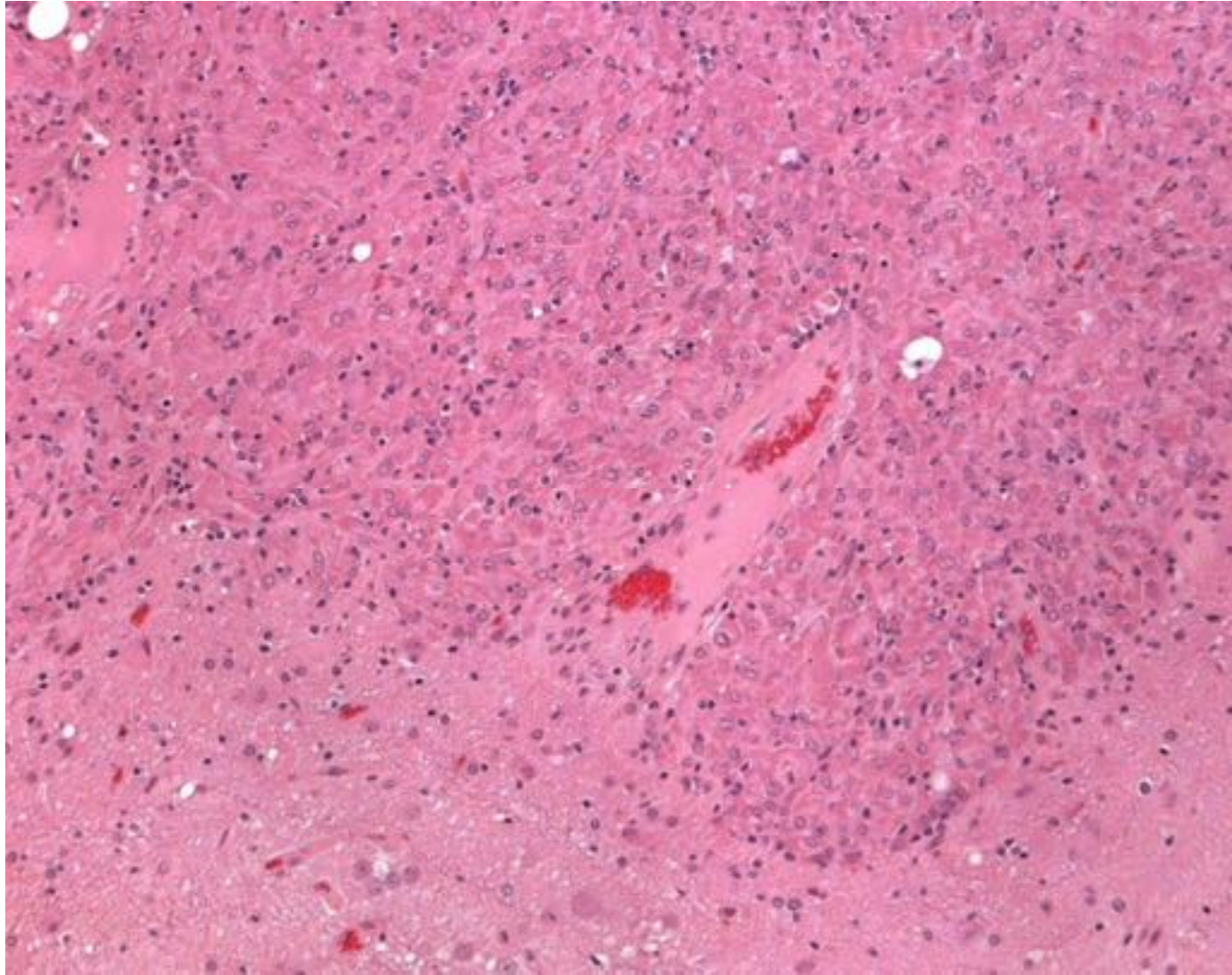
## Gr cell tumour



## Granular cell tumour- PAS



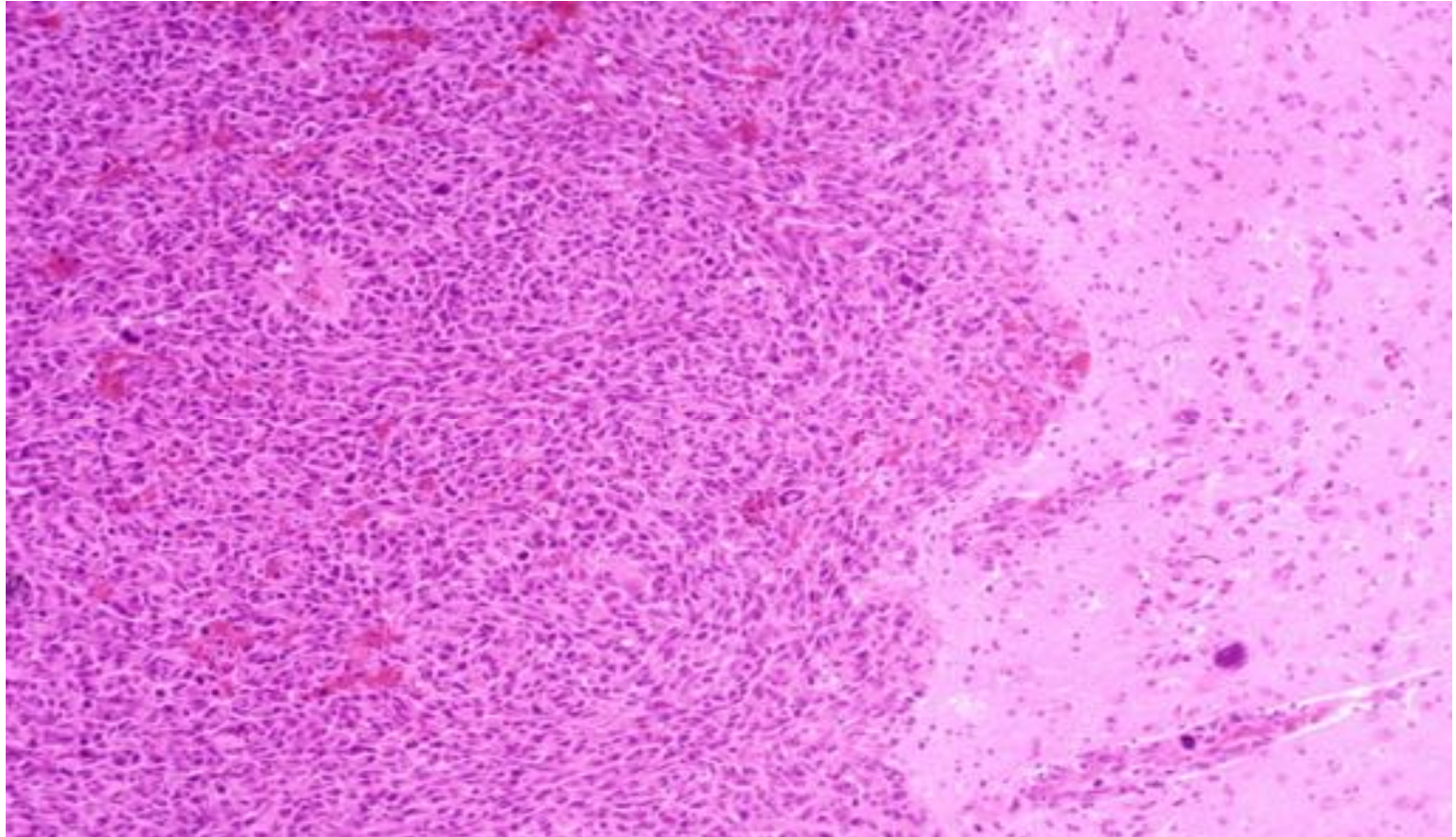
## Gr cell tumour Malignant?



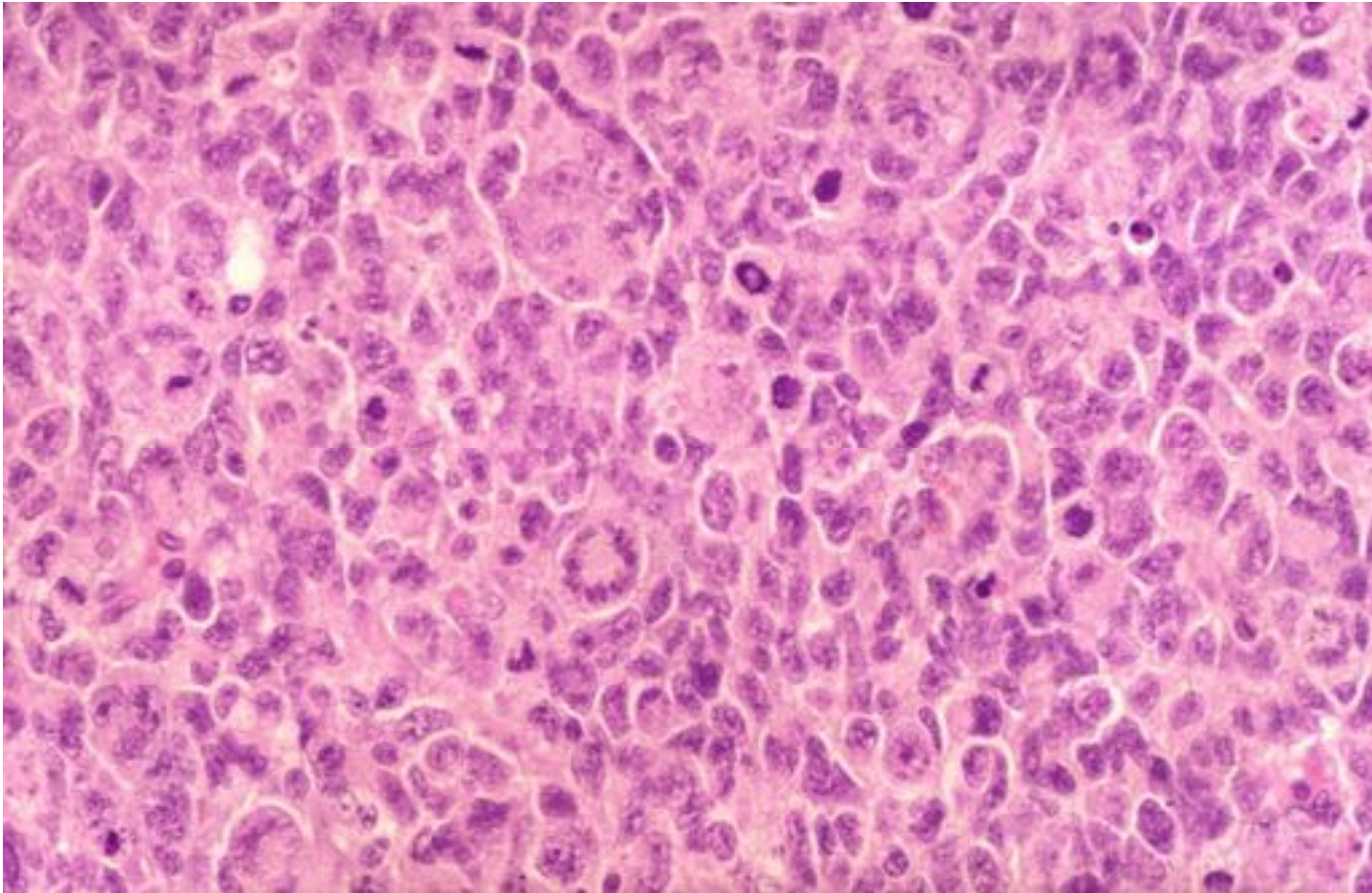
## Meningeal sarcoma

- Highly cellular, pleomorphic growths from meninges show local invasion and perivascular spread into the brain
- Fibrosarcoma patterns
- Pleomorphic patterns with giant cells

# Meningiosarcoma



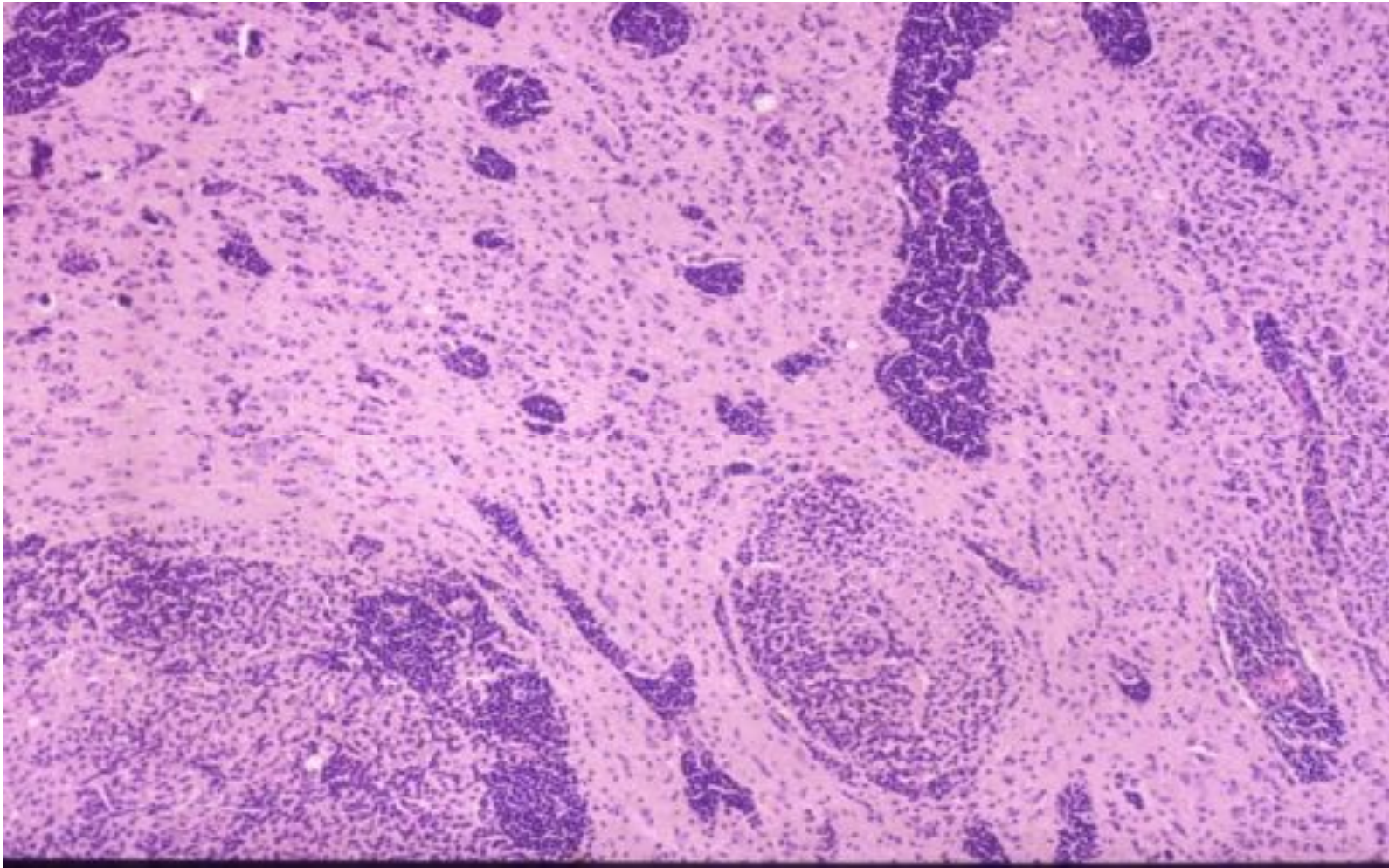
## Meningiosarcoma, polymorphic



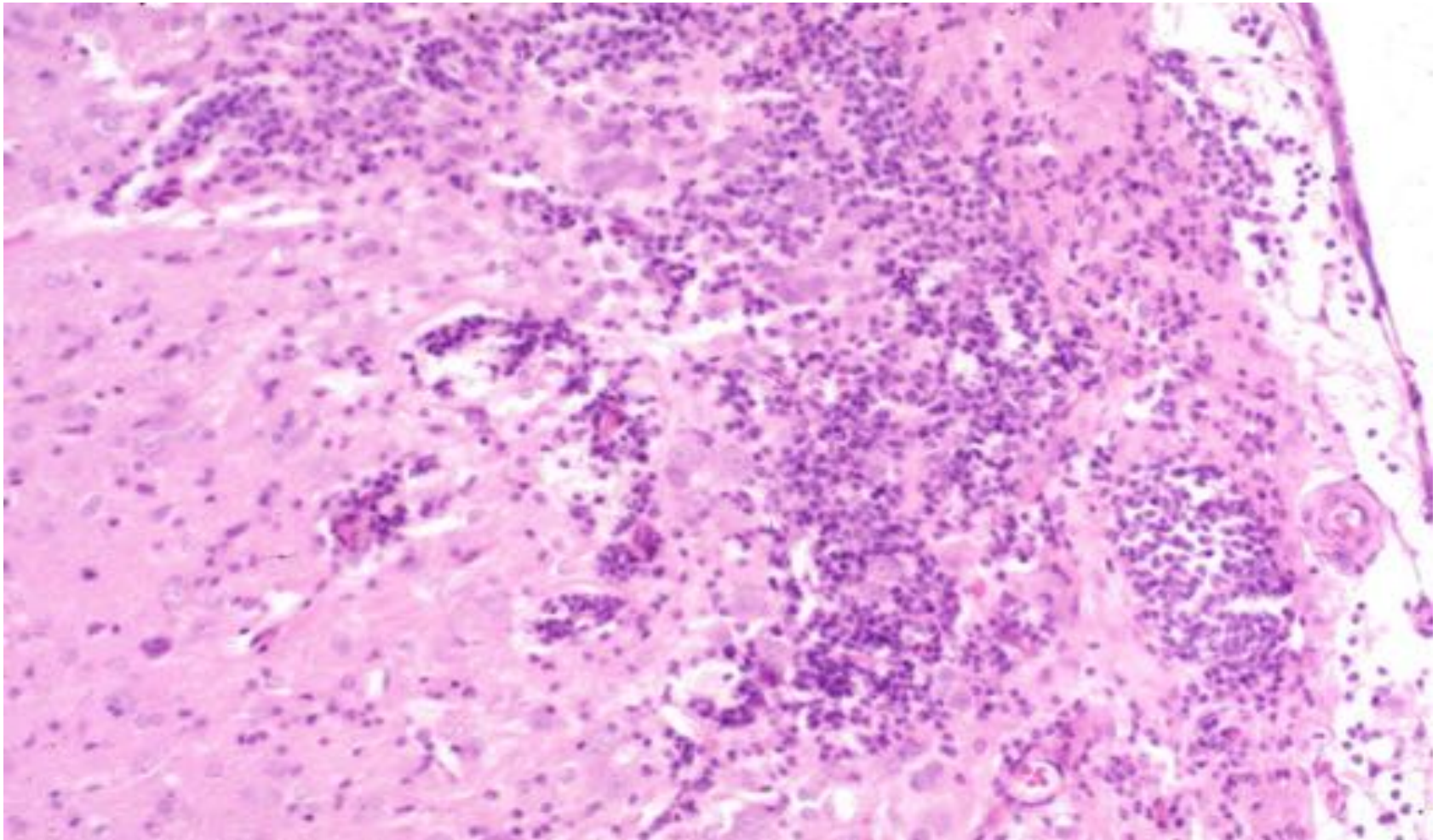
## Malignant reticulosis

- A disseminated / widespread lesion of mixed cell population consisting of microglial cells, lymphocytes, histiocytes, plasma cells.
- Poor edge, perivascular cuffing, leptomeningeal infiltration.
- Differential diagnosis from astrocytoma

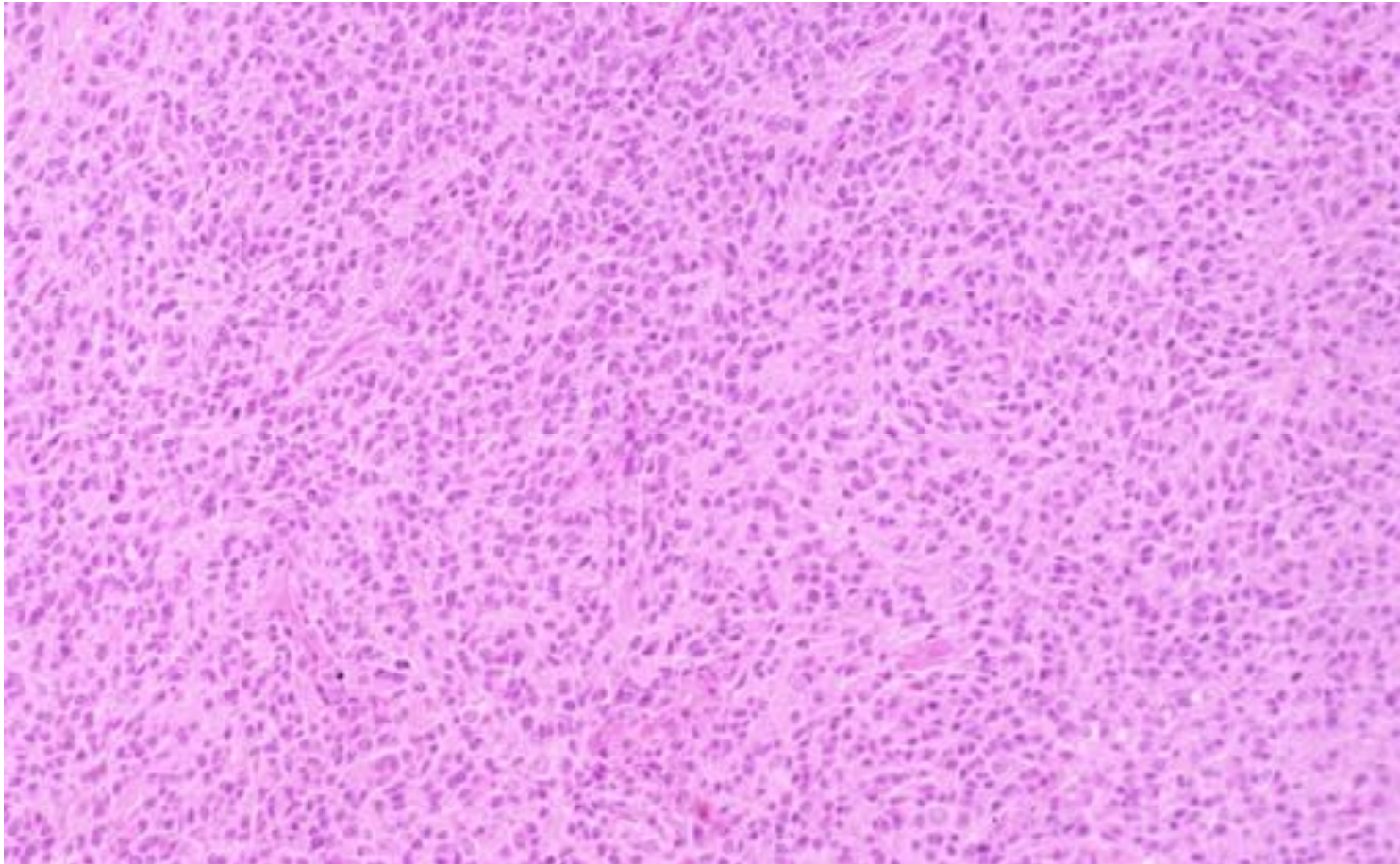
# Malignant reticulosis



# Malignant reticulosis



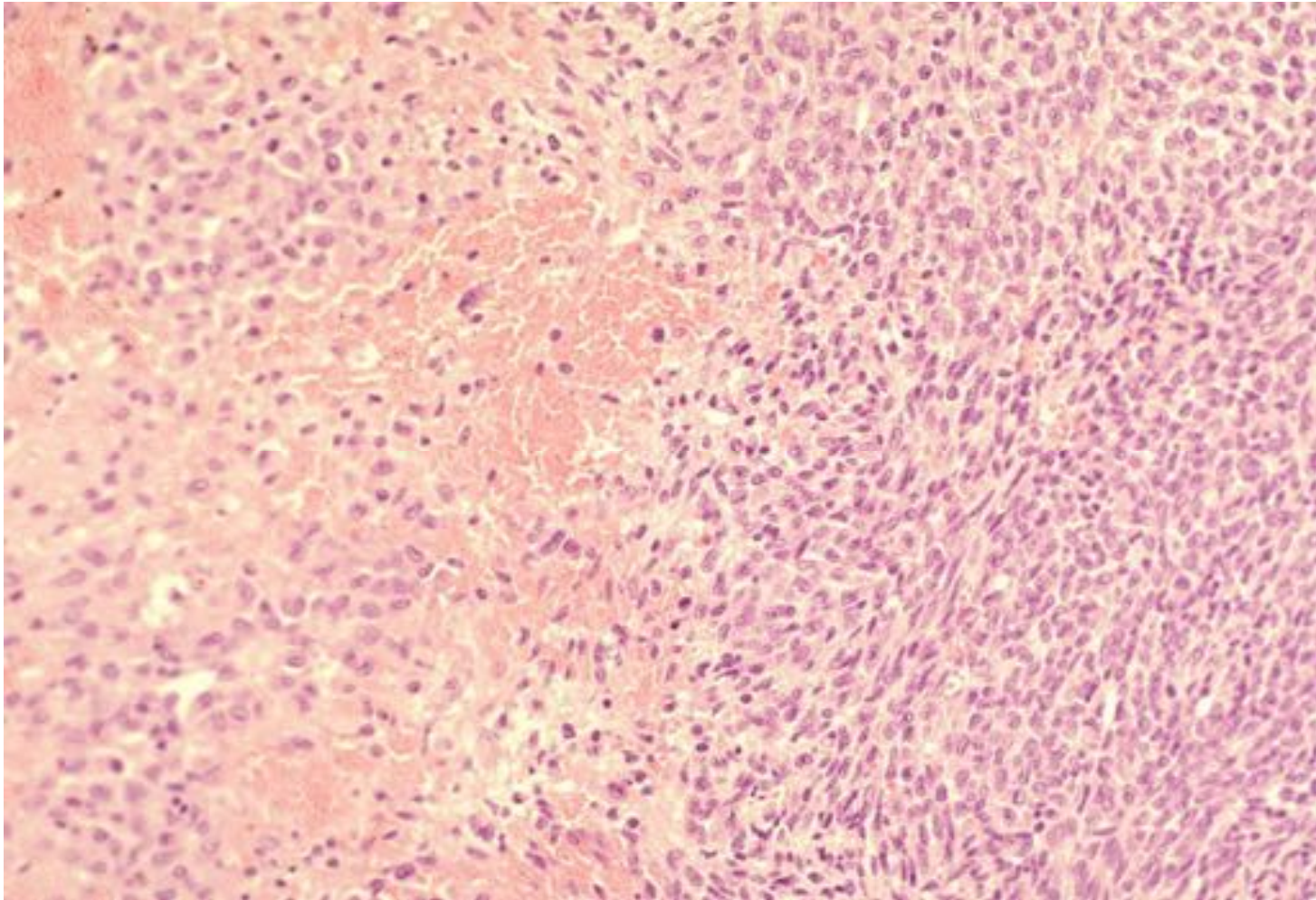
# Astrocytoma



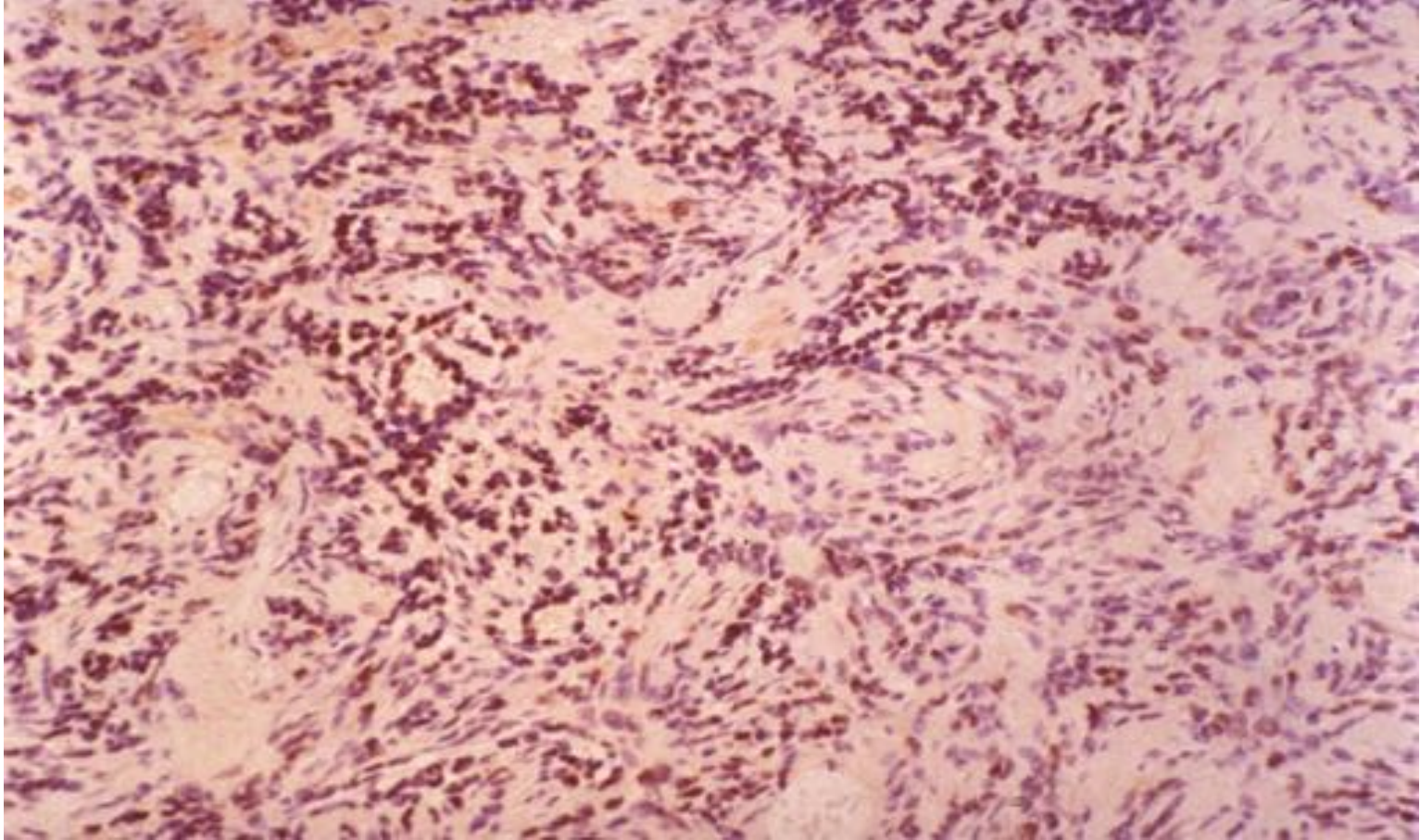
## Malignant Schwannoma

- Tumour of the PNS, can be seen rarely in the brain usually arising from cranial nerves and around pituitary gland
- Spindle shaped cells in sheets, interlacing bundles or palisading patterns as in type A or appear as poorly differentiated small cells embedded in oedematous or myxoid matrix Antoni type B, show haemorrhage necrosis and microcysts. S-100 +

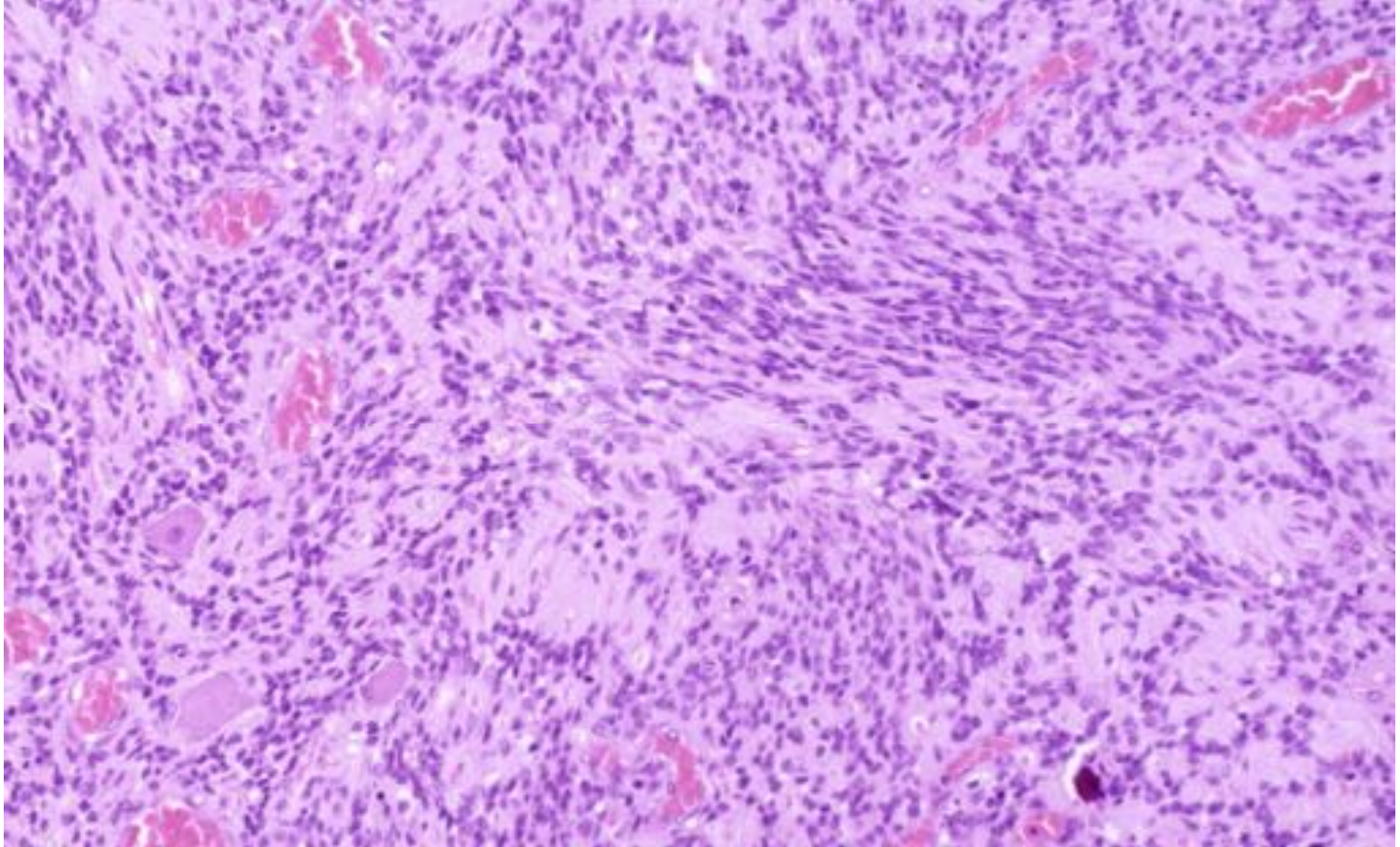
# Mal Schwannoma



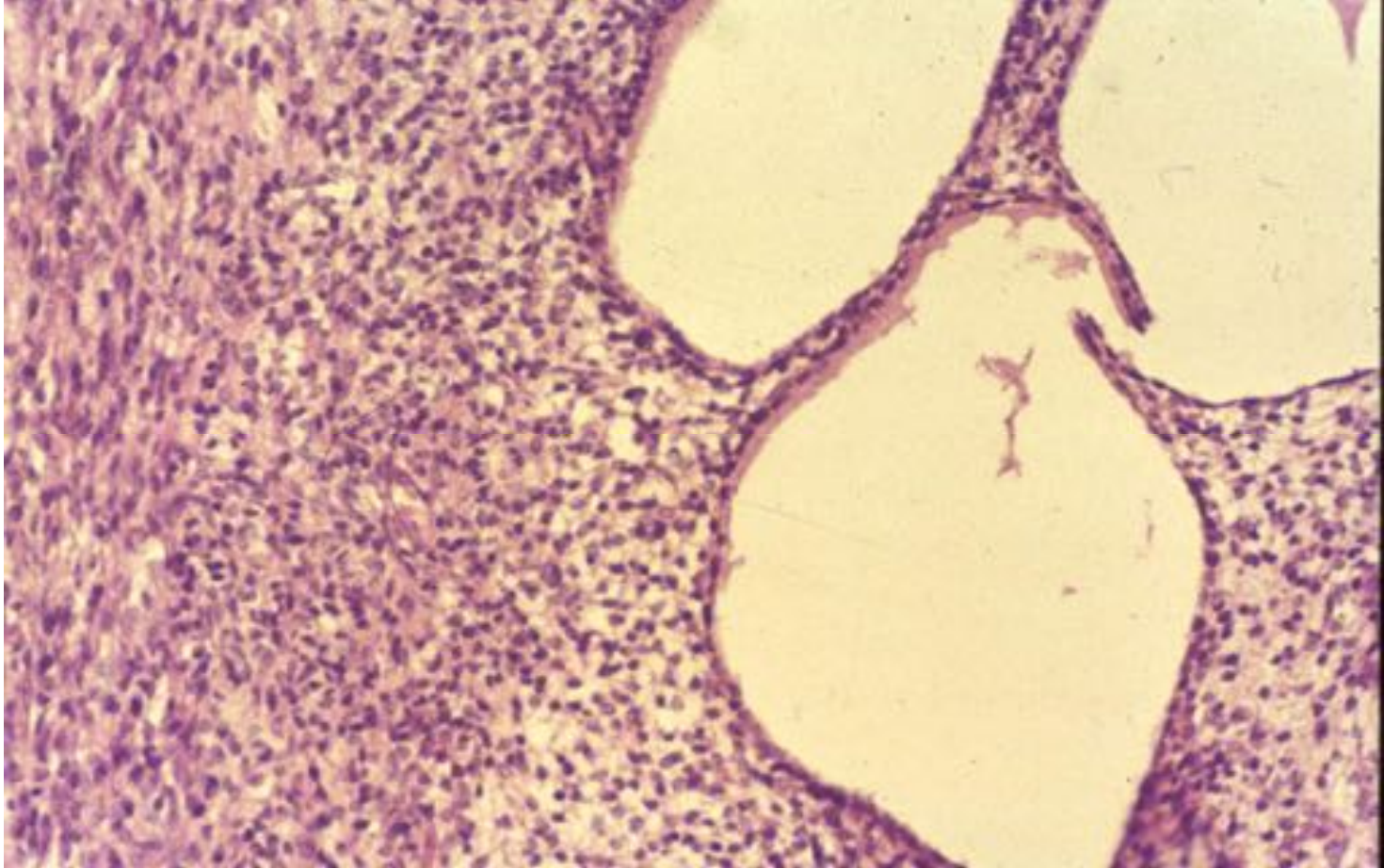
## Mal Schwannoma, S-100+



# Mal Schwannoma



# Mal Schwannoma



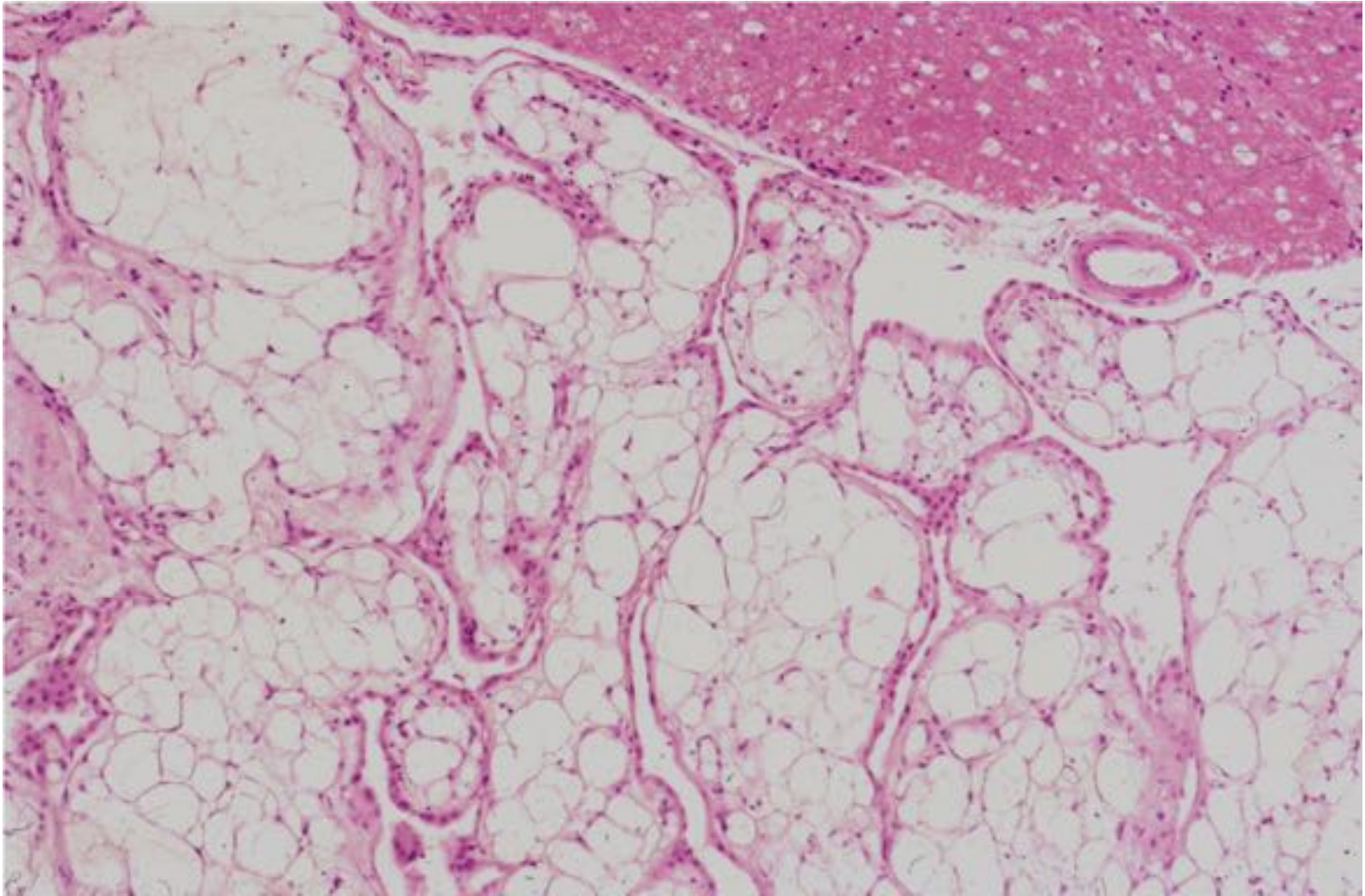
## Schwannoma, sp cord



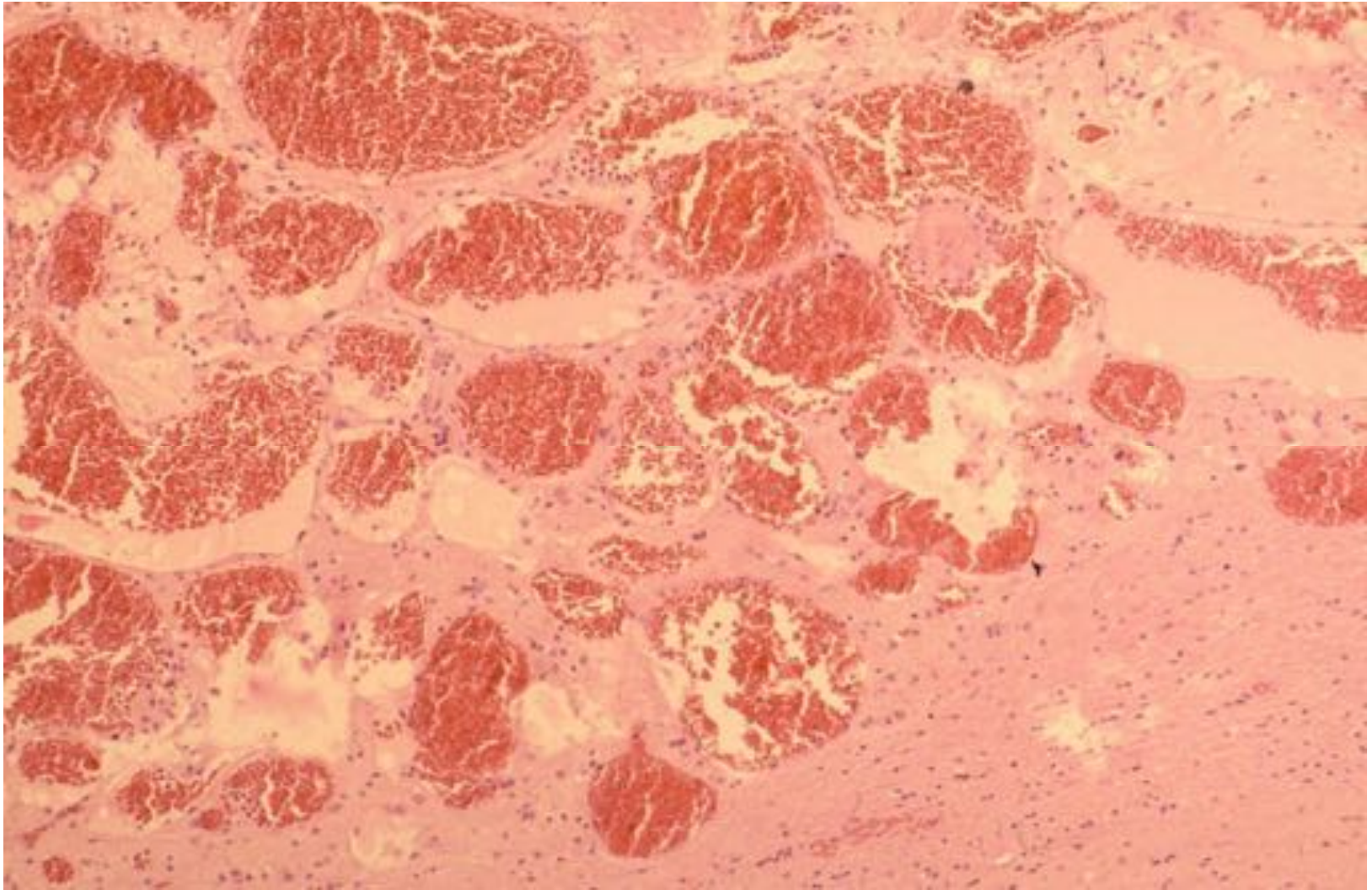
## Others

- Lipoma ( choroid plexus)
- Haemangioma (meningeal or brain)
- Meningeal melanoma
- Primary lymphoma
- Secondary as: pituitary, pineal gland, Zymbal's gland, osteosarcoma, lymphoma, leukaemia and histiocytic sarcoma

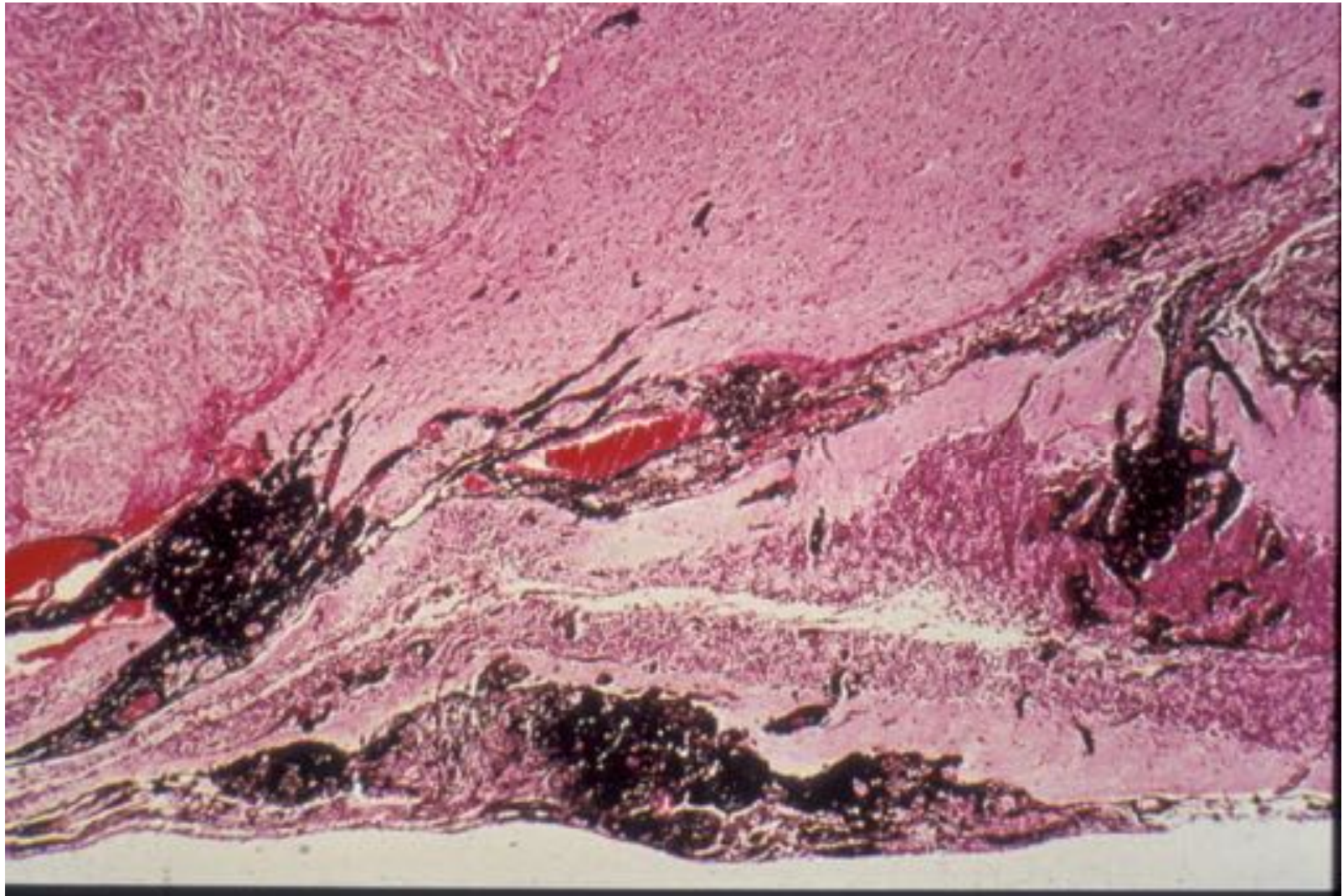
## Lipoma- choroid plexus



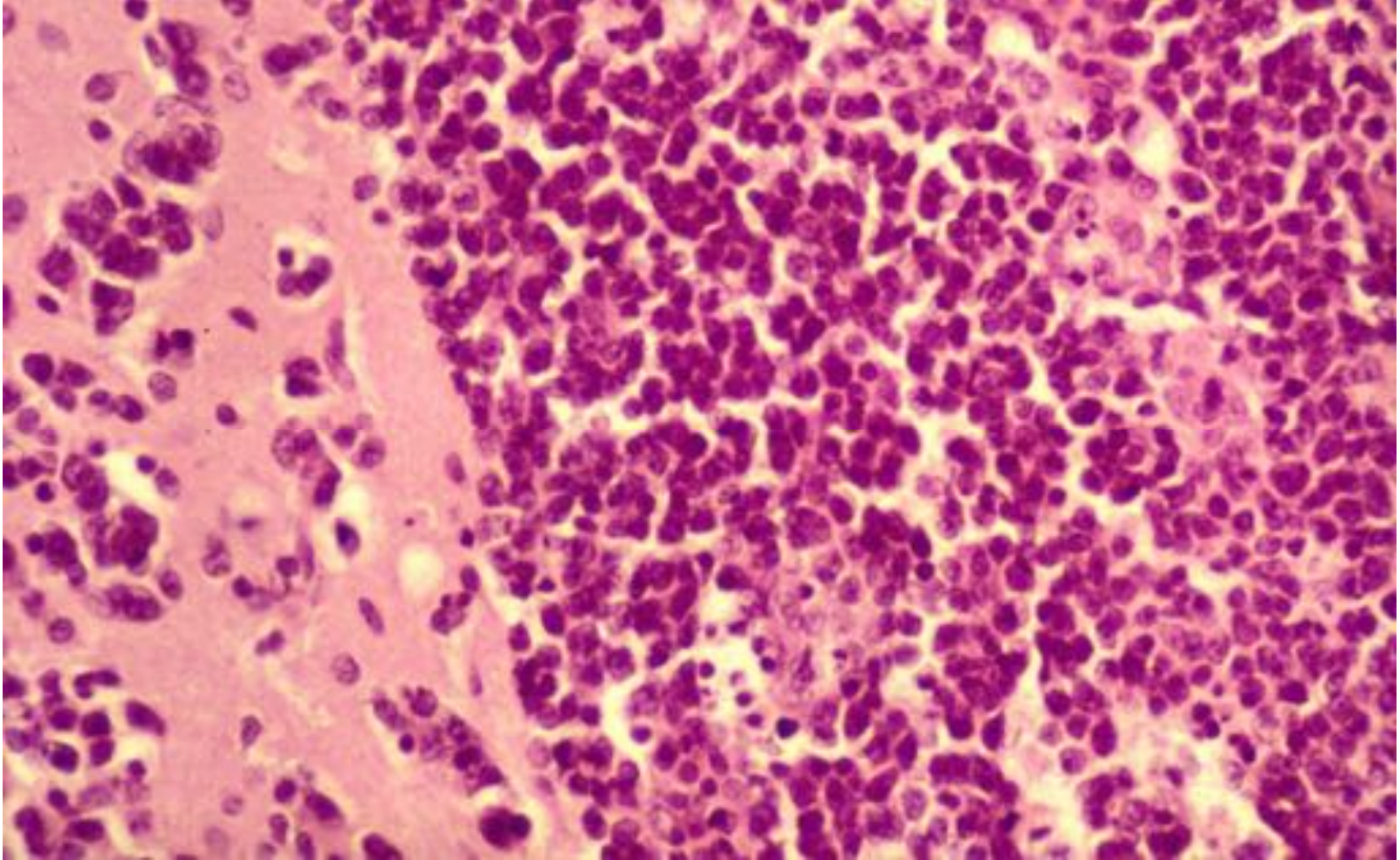
# Haemangioma



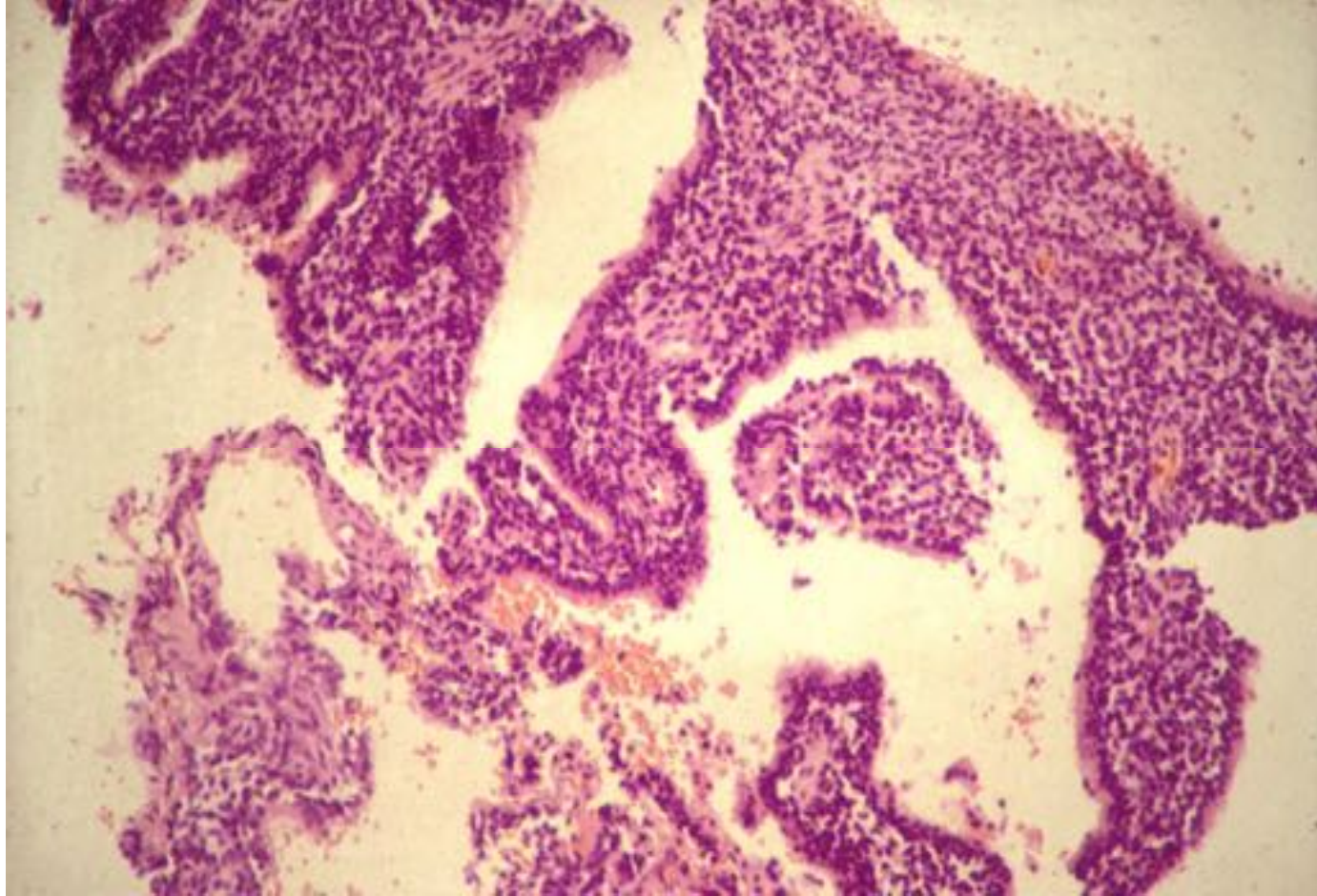
## Malignant melanoma, meninges



# Lymphoma



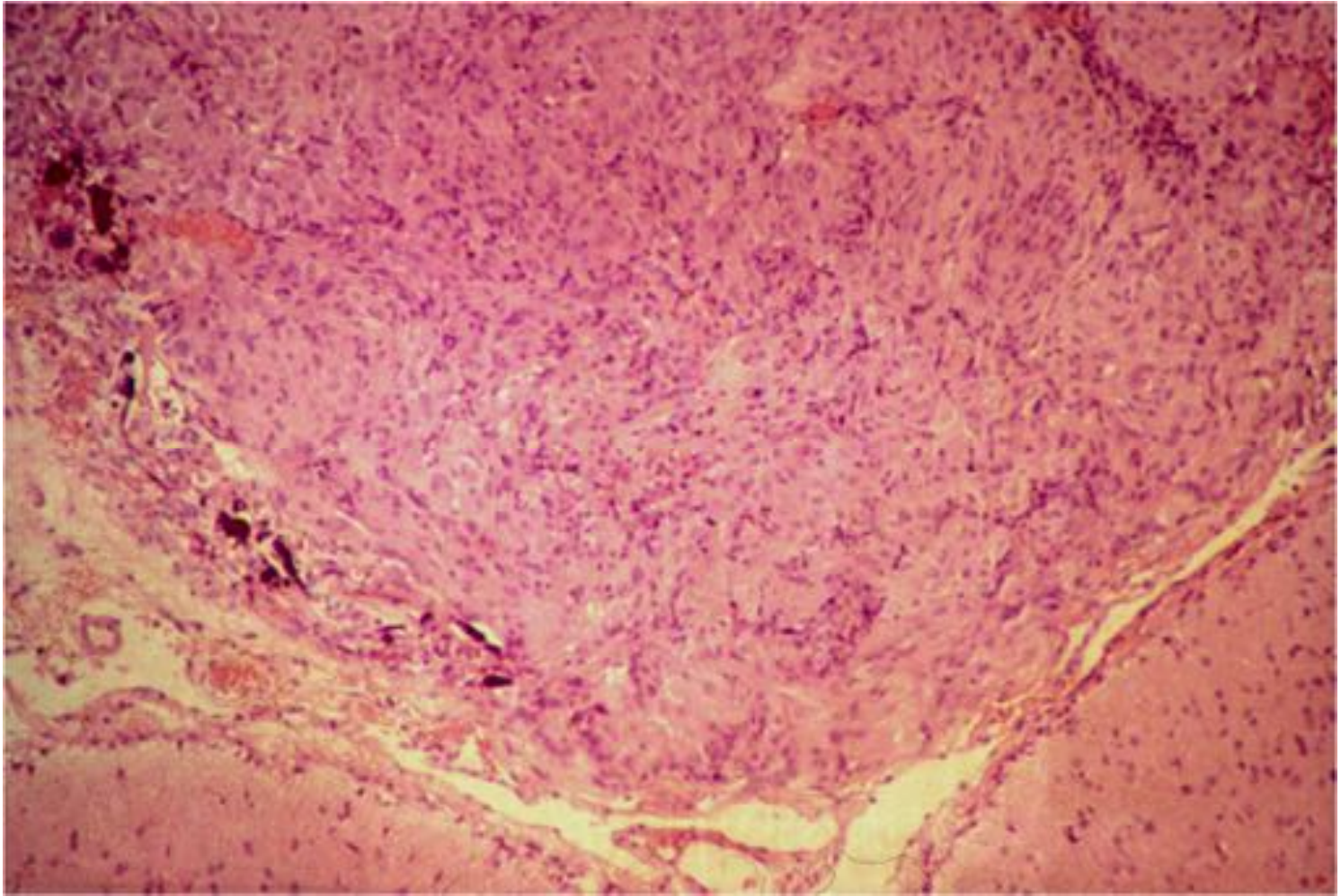
# Craniopharyngioma

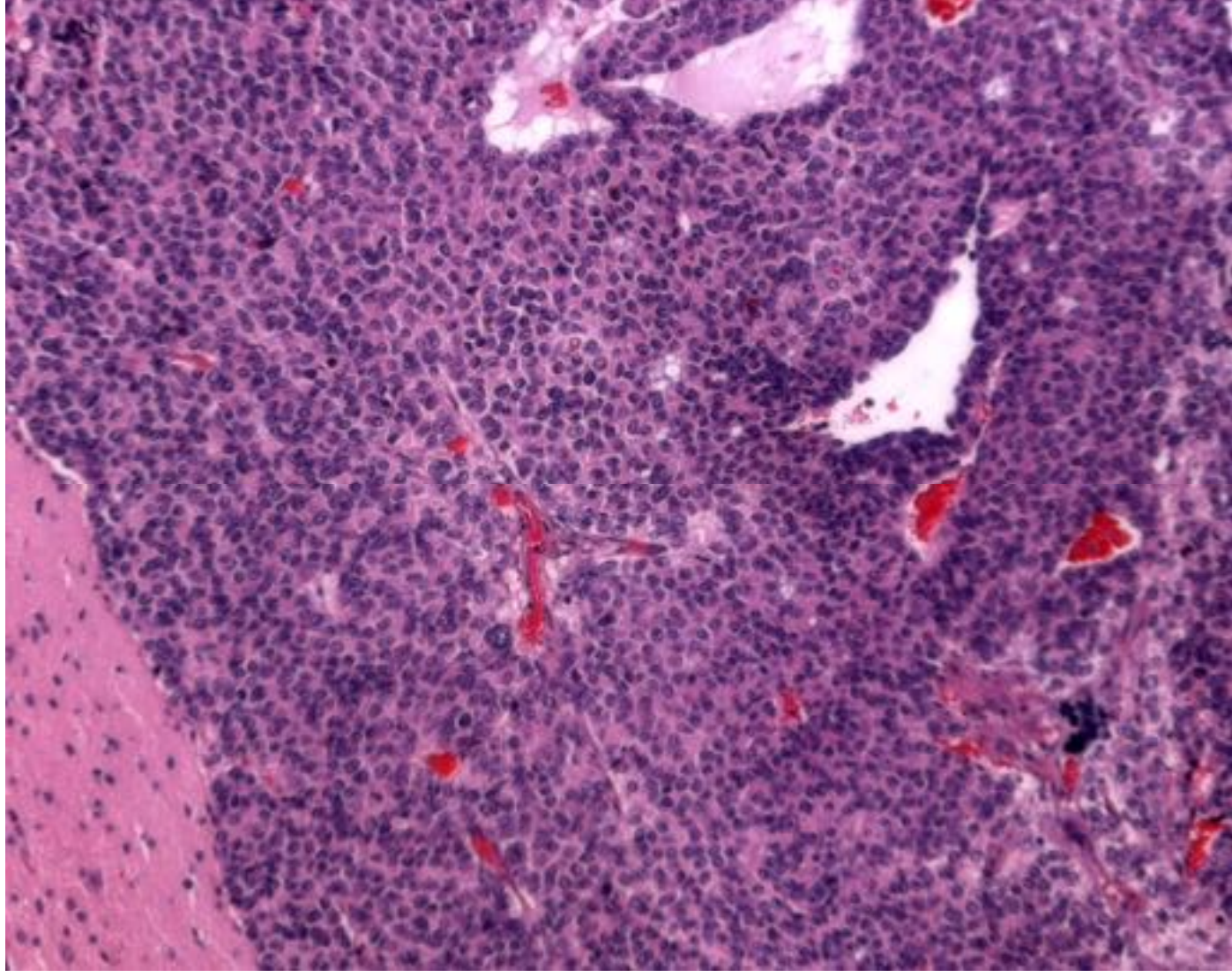


## Pineal gland tumours

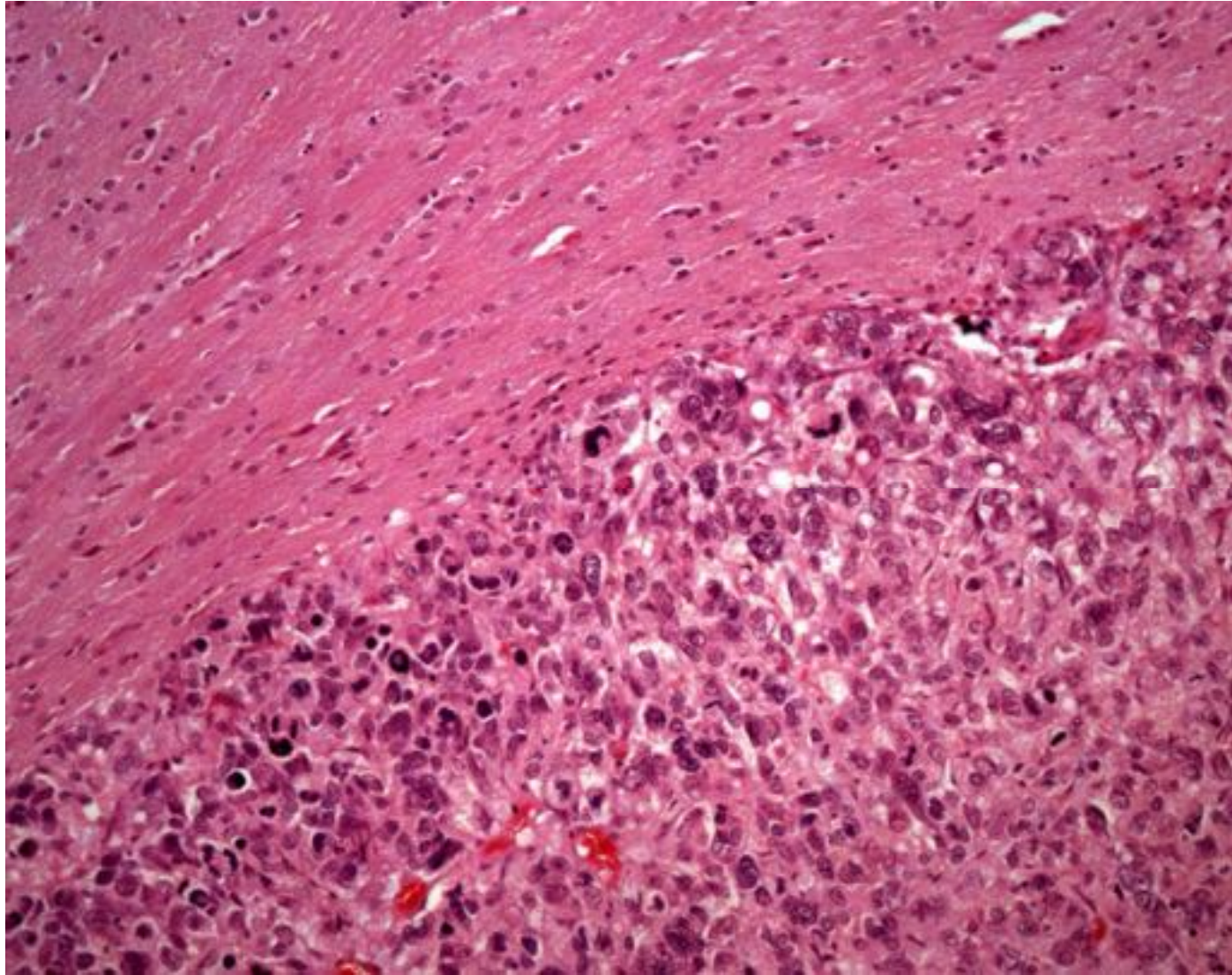
- Pinealoma: A circumscribed growth causing compression
- Cells are large, faintly basophilic and show lobulation.
- Pineal gland carcinoma: Highly cellular, pleomorphic/undifferentiated, giant cells with bizarre nuclei. Invade locally.
- Location helpful for diagnosis

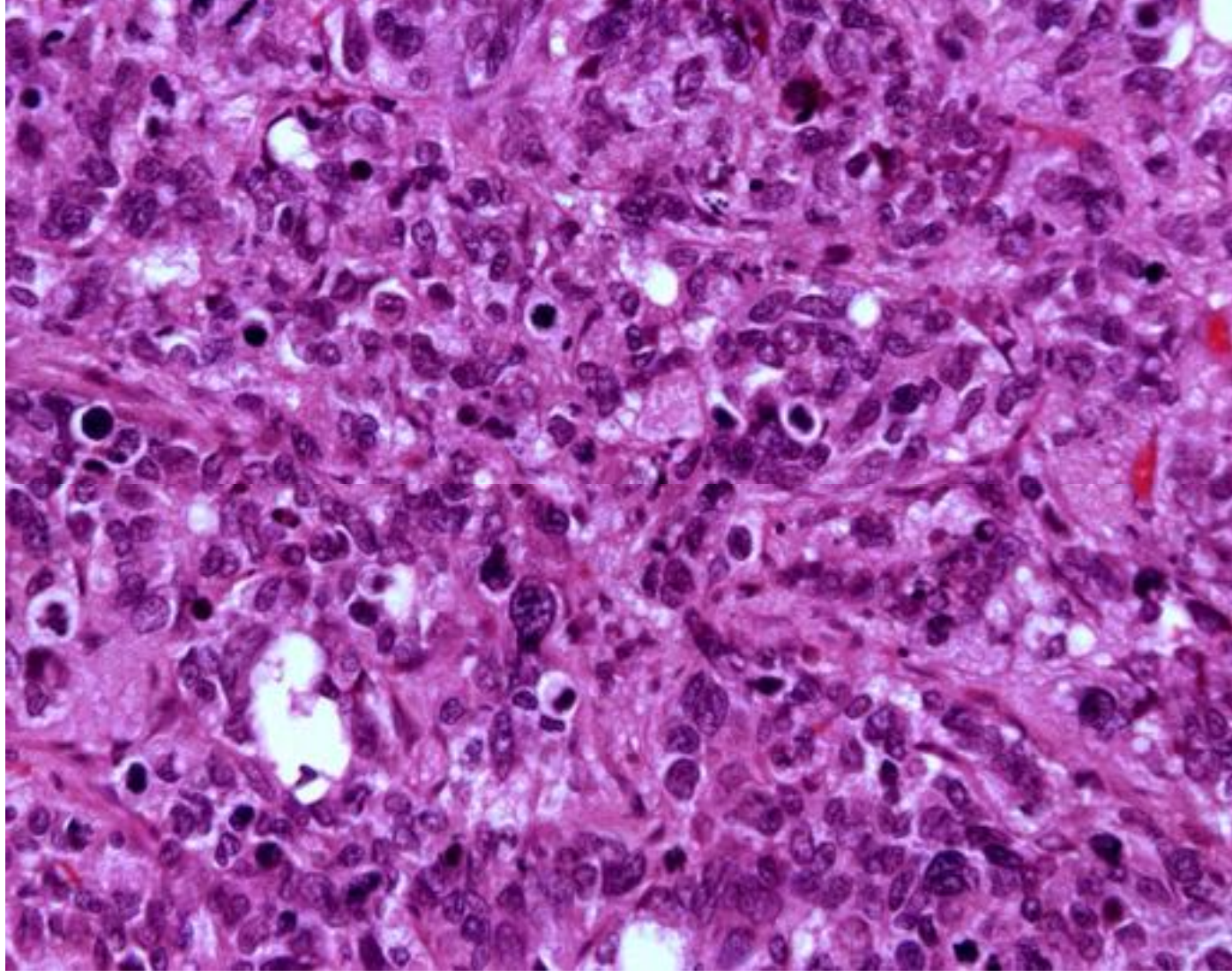
# Pinealoma



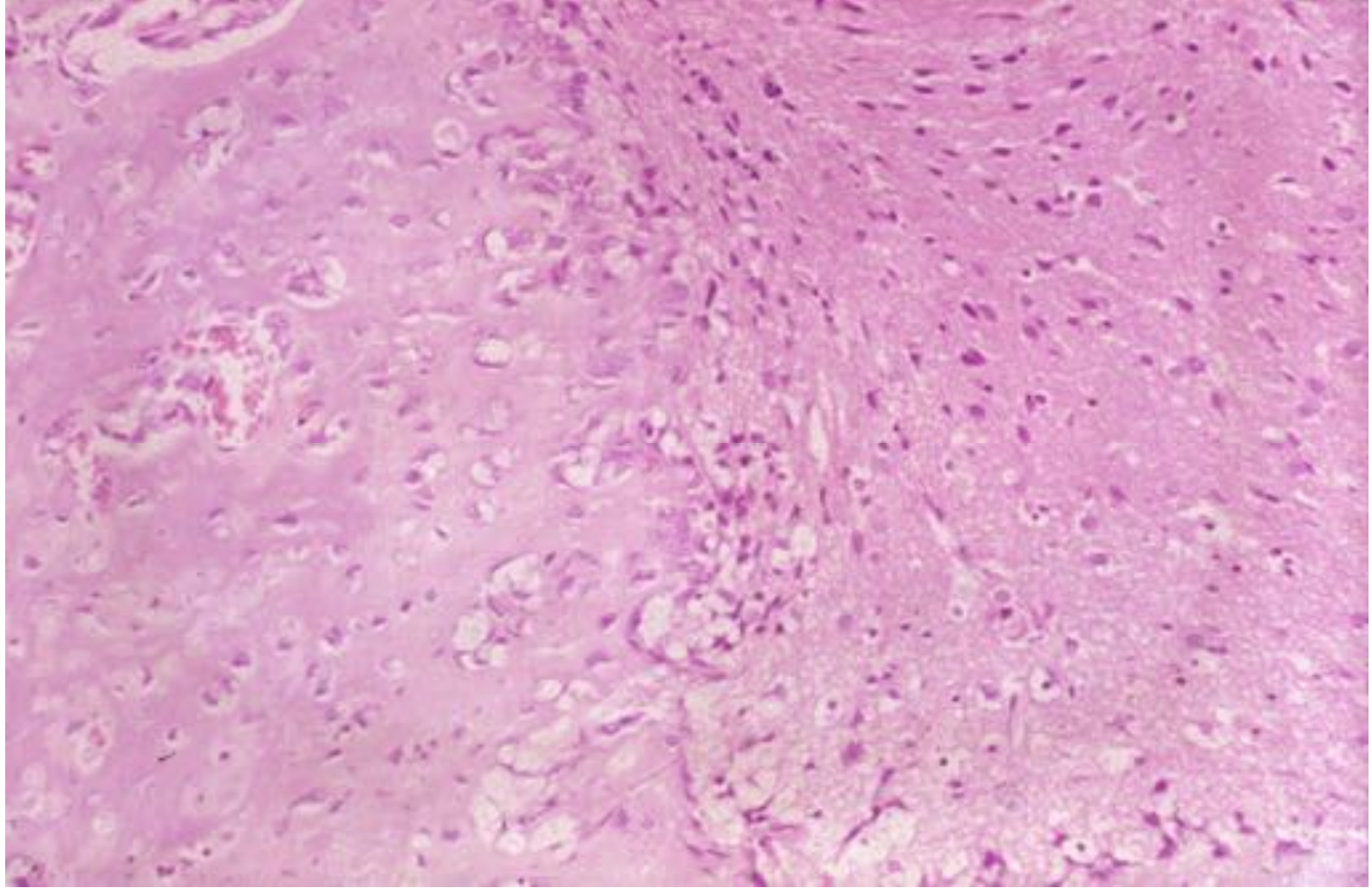


# Pin gl carcinoma

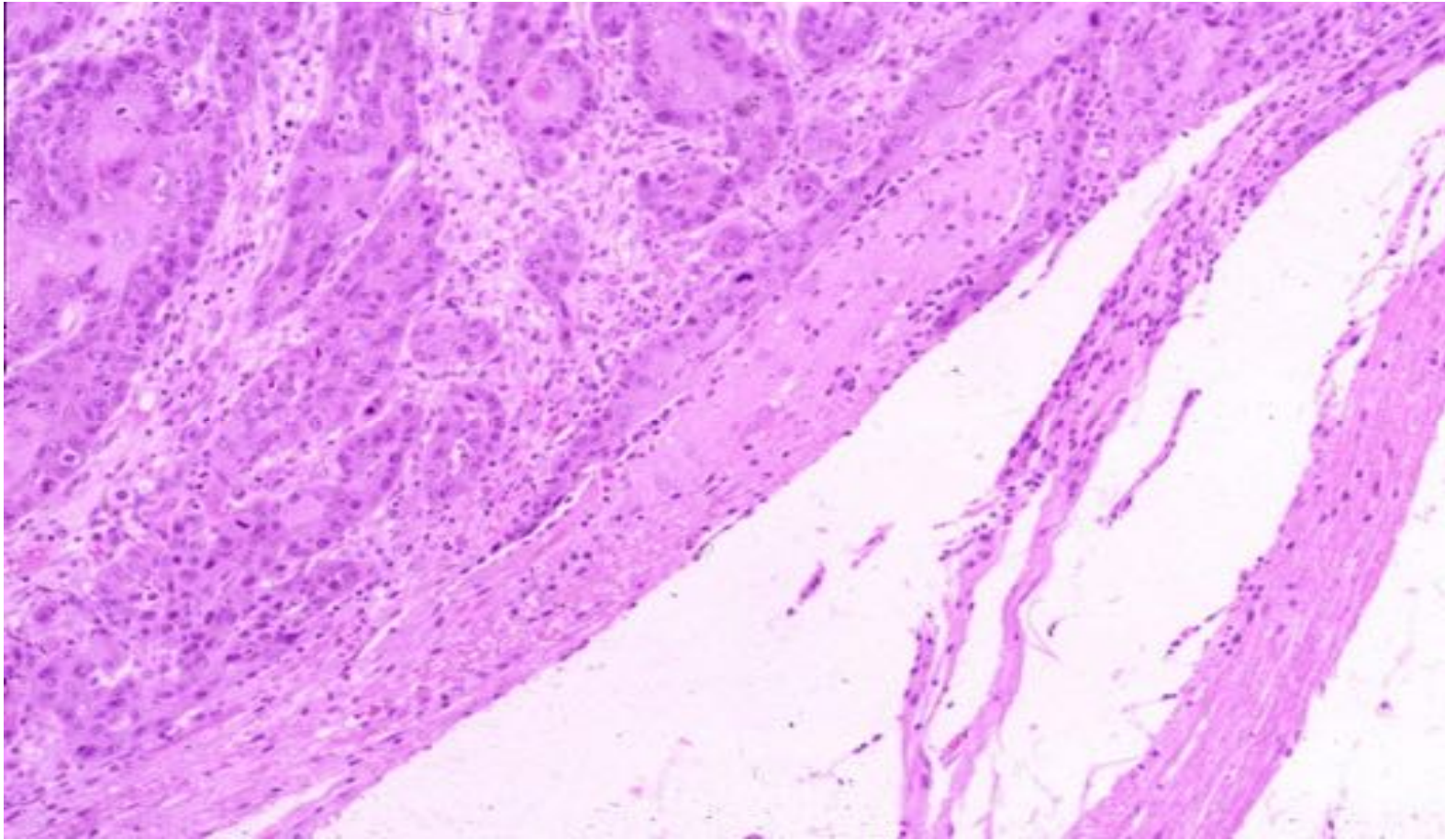




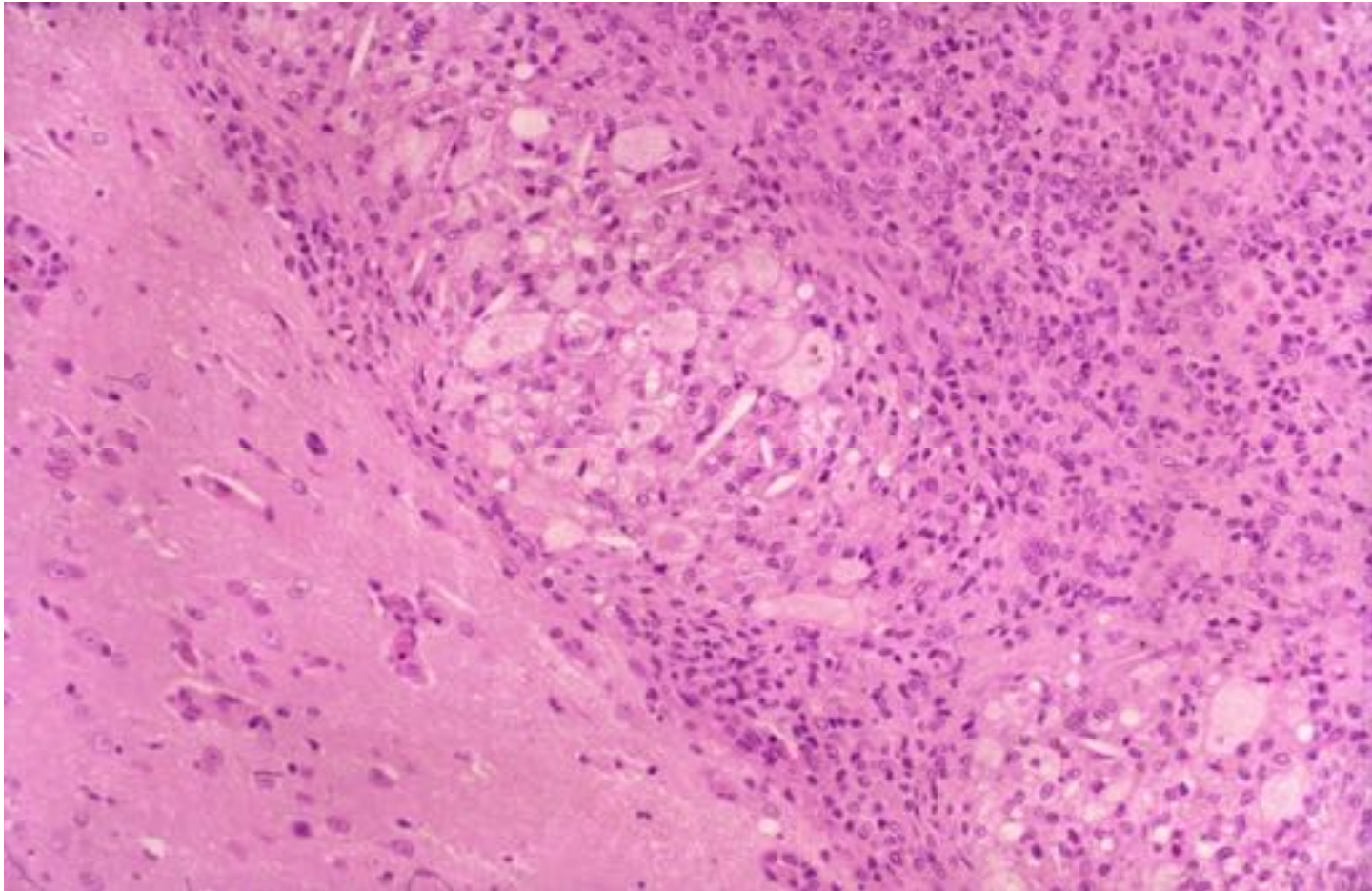
# Osteosarcoma

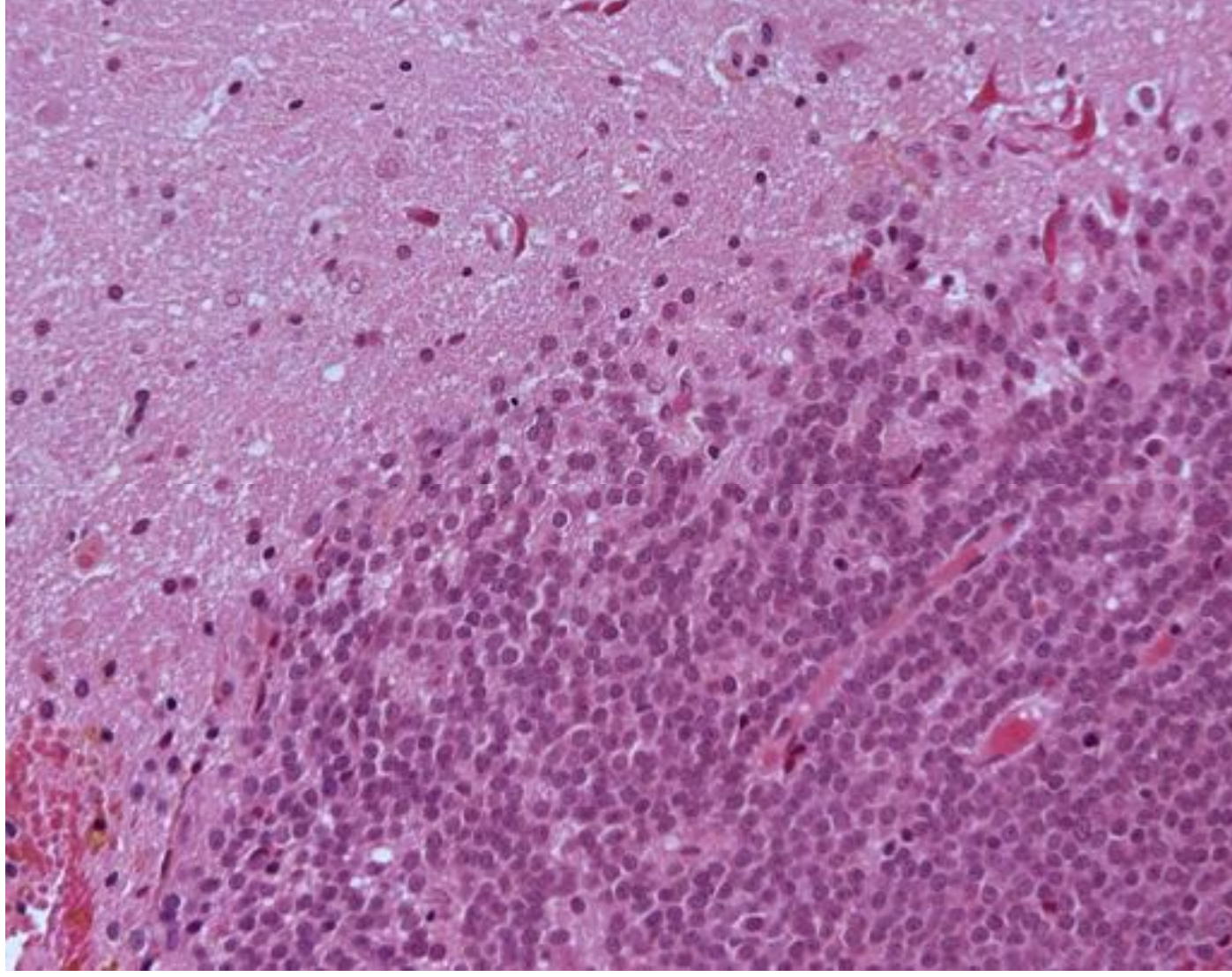


# Zymbal's gland carcinoma

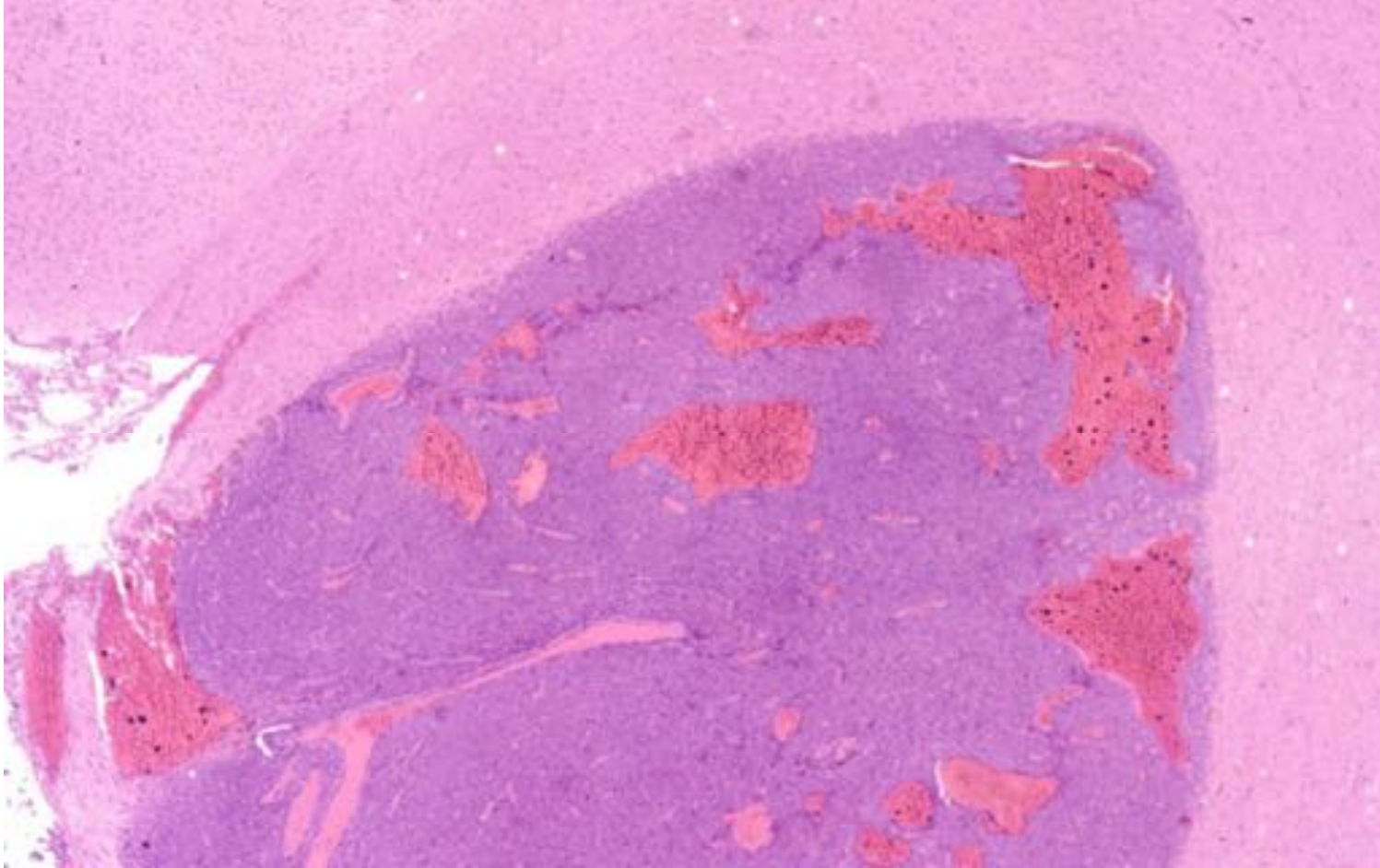


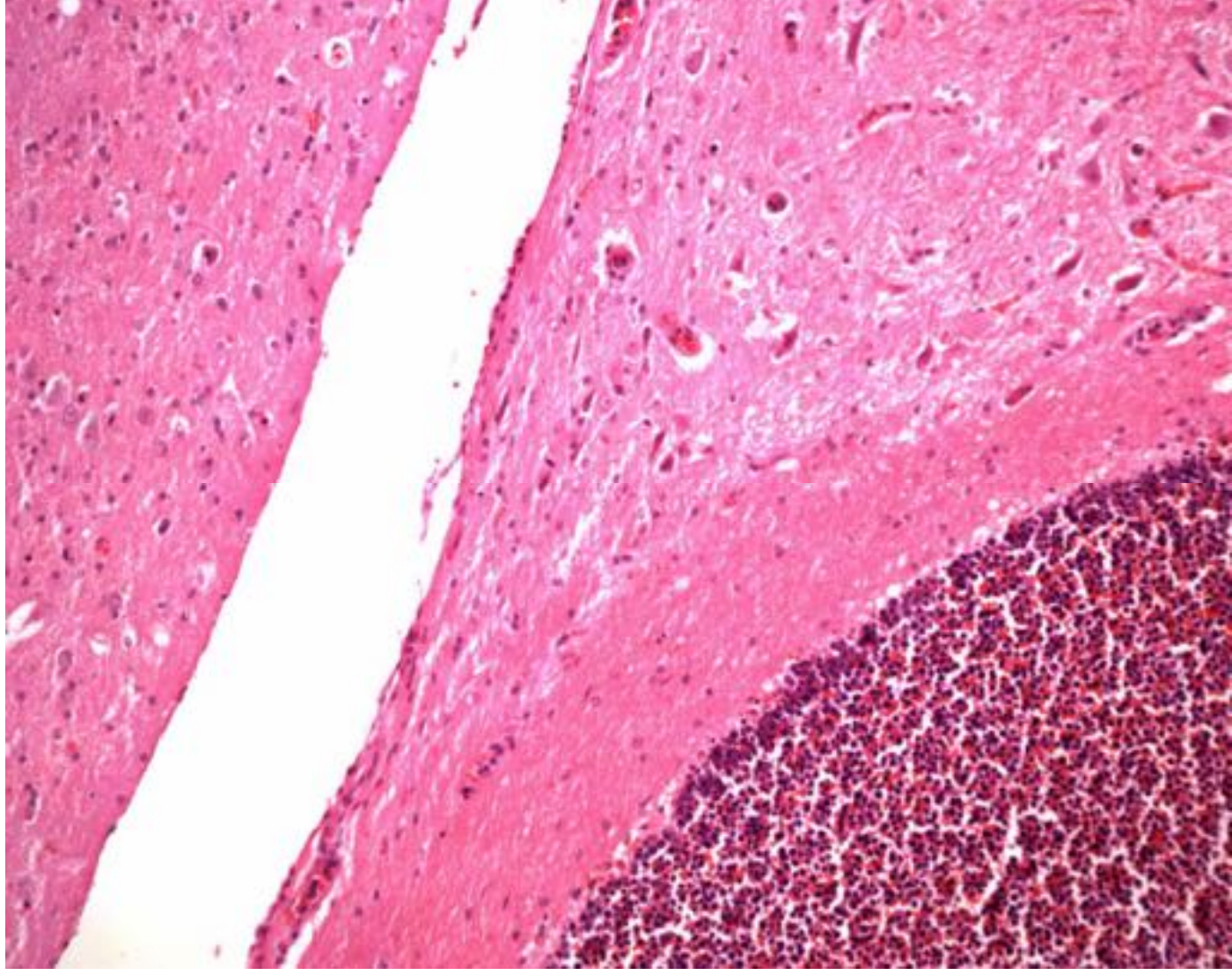
# Histiocytic sarcoma





# Pituitary carcinoma



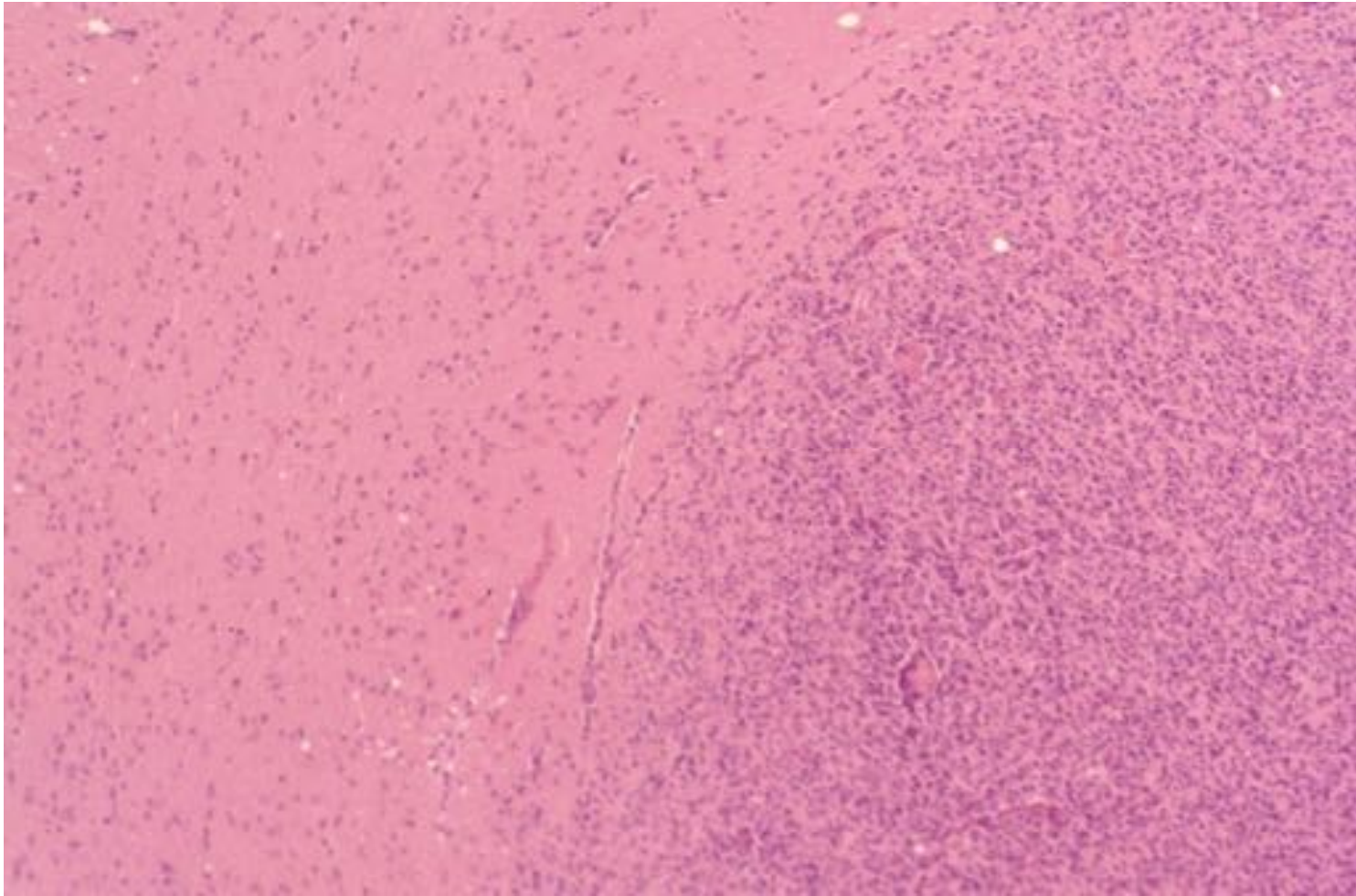


## Brain tumours- mouse

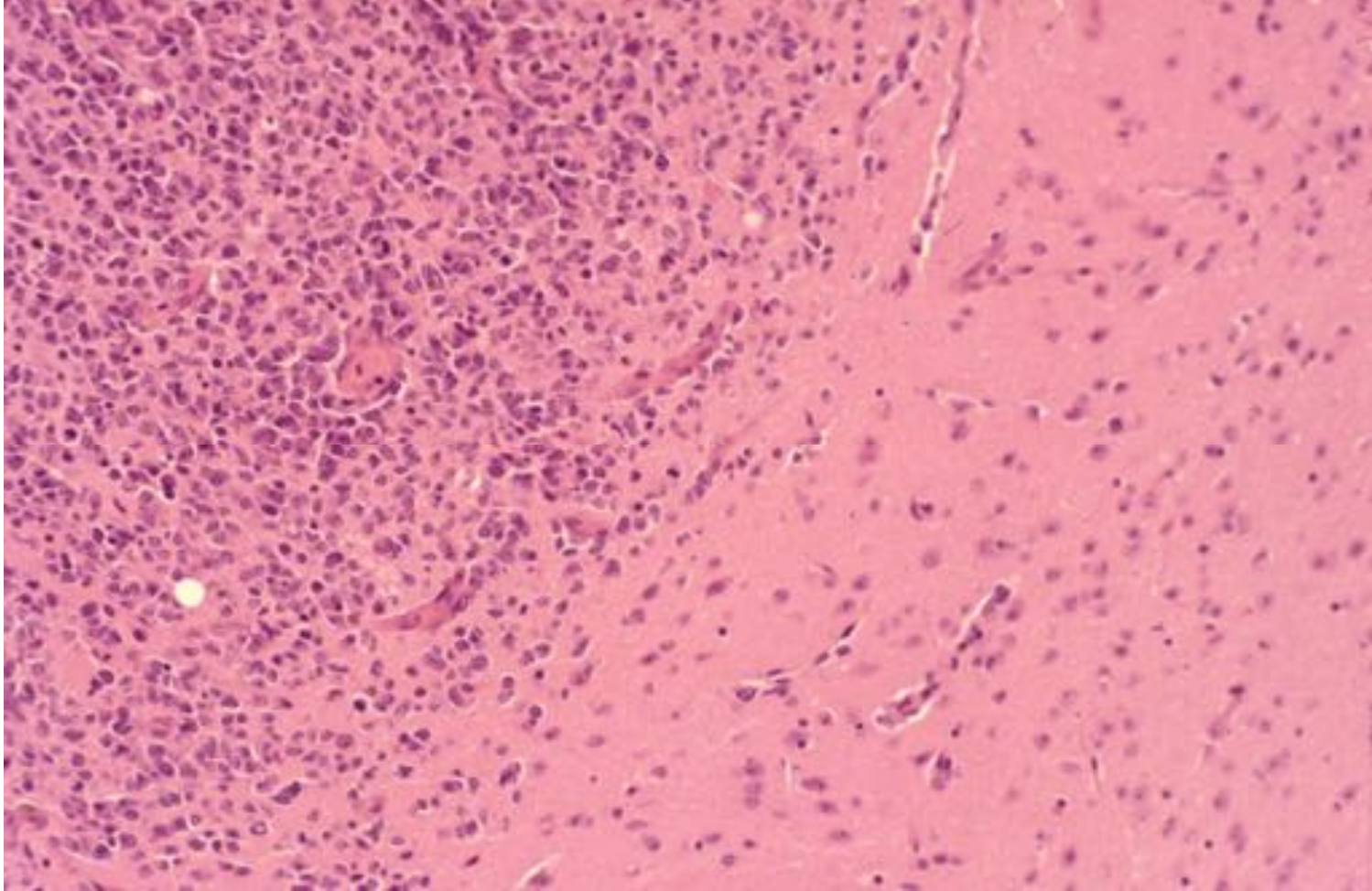


- Similar in morphology

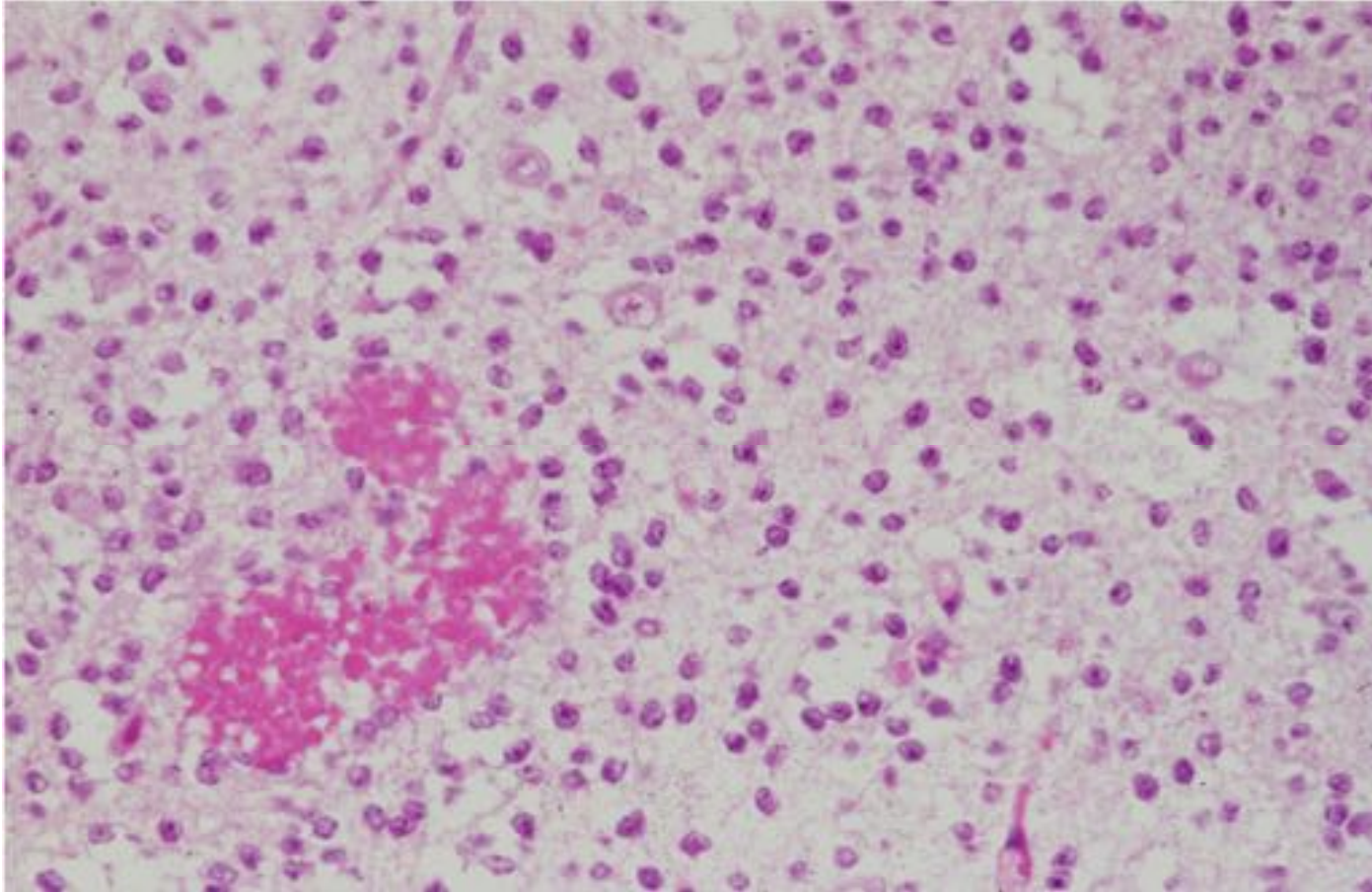
# Astrocytoma



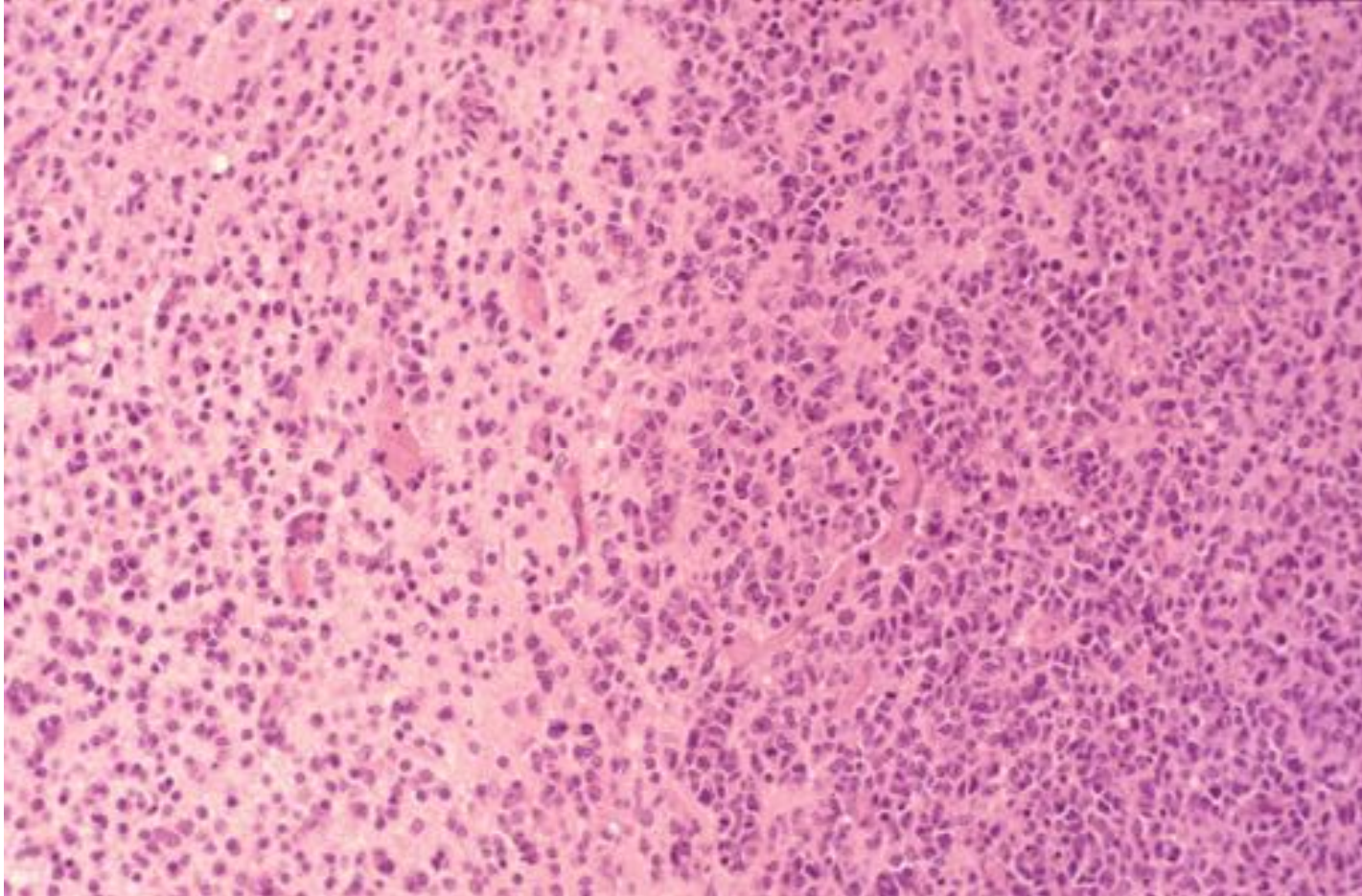
# Astrocytoma



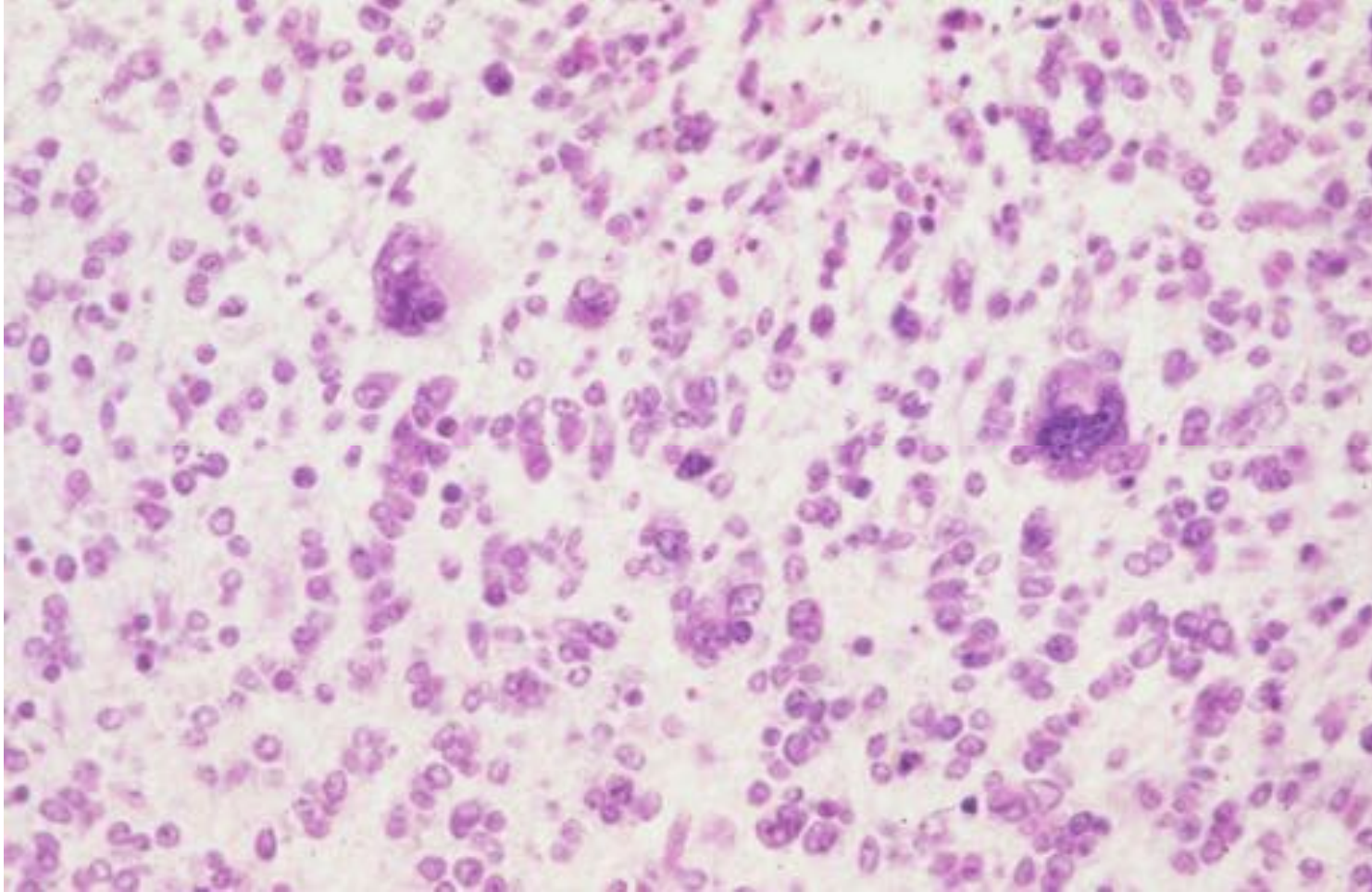
# Oligodendroglioma



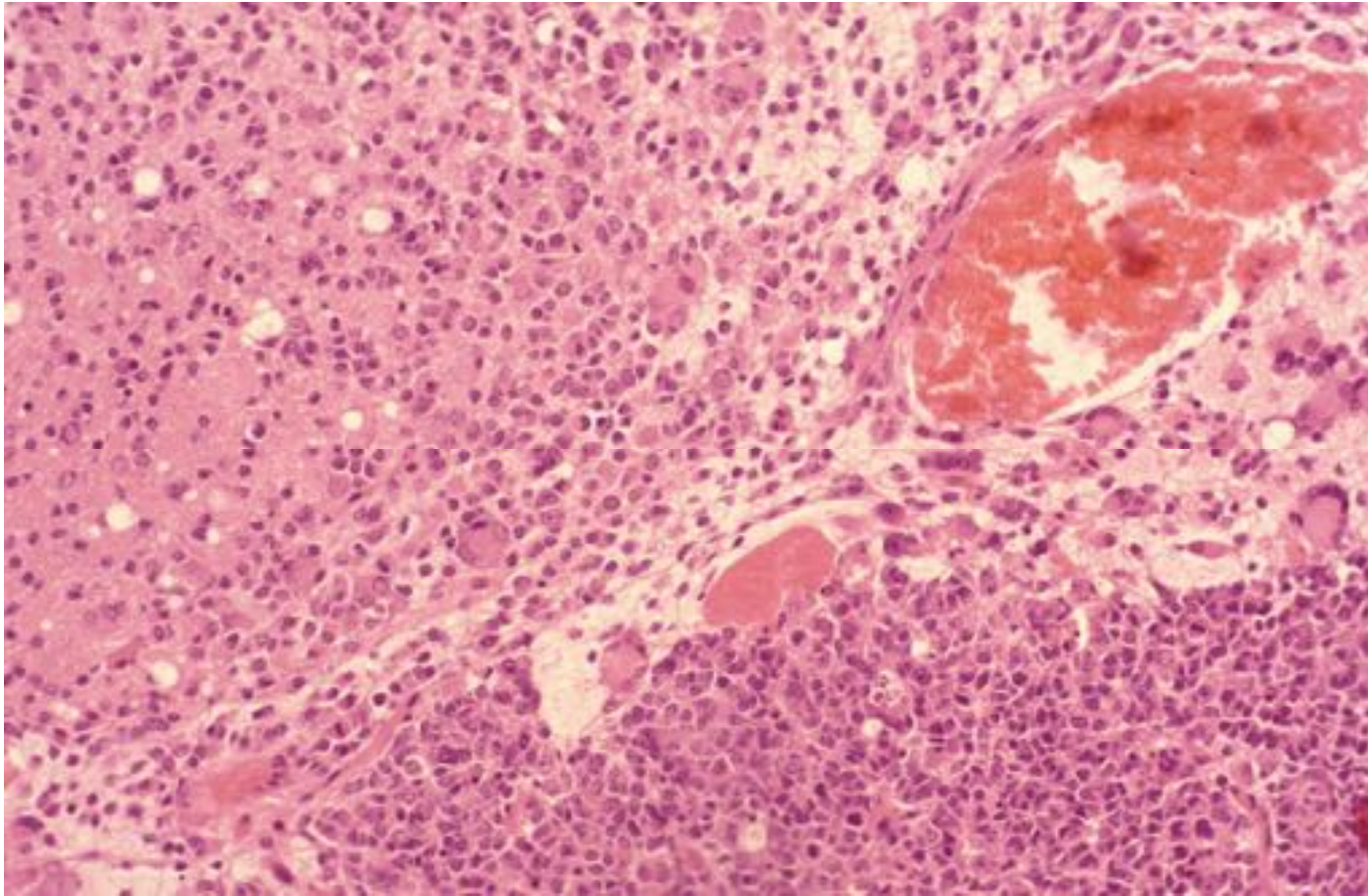
# Mixed glioma



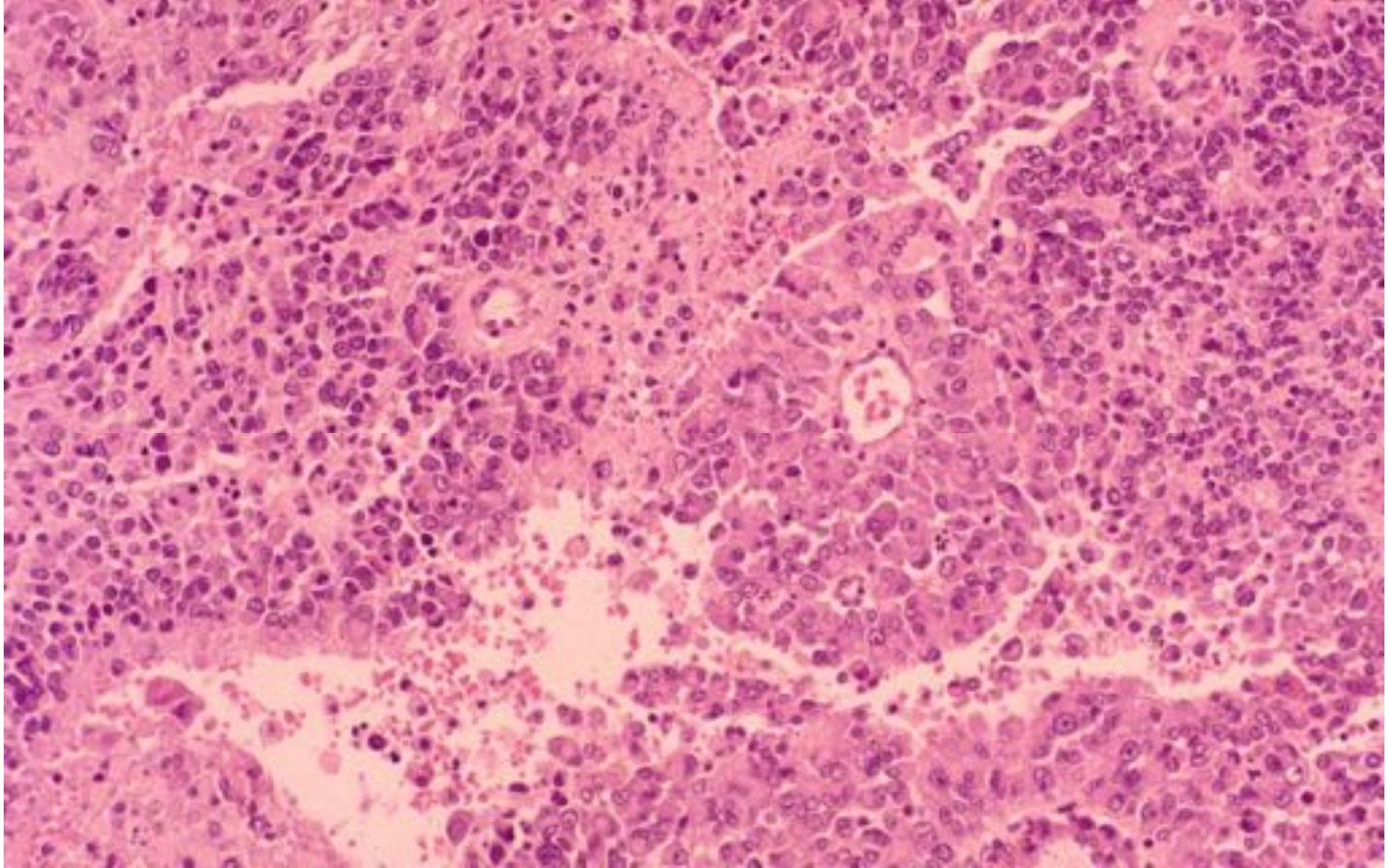
# Anaplastic glioma



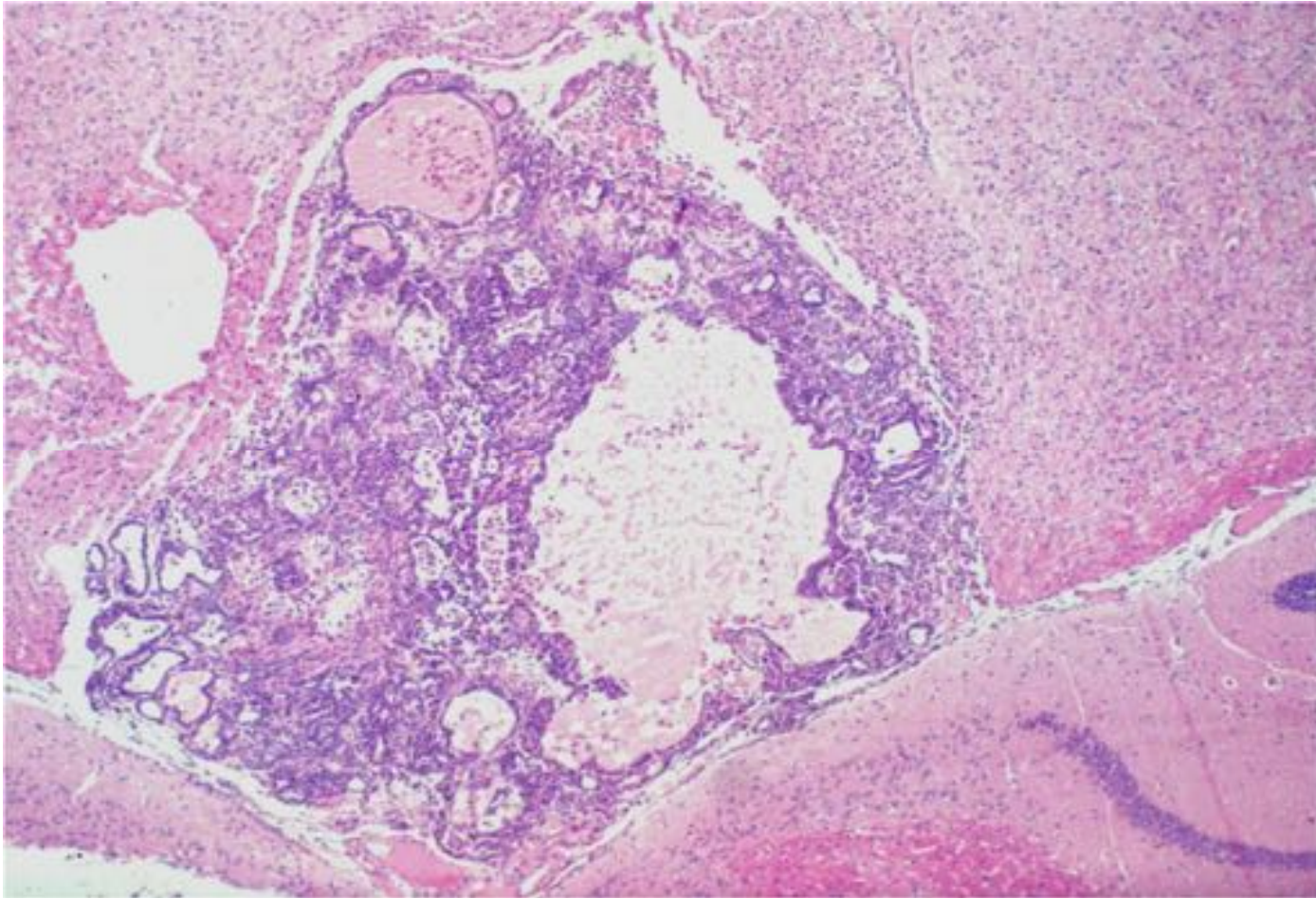
# Anaplastic glioma



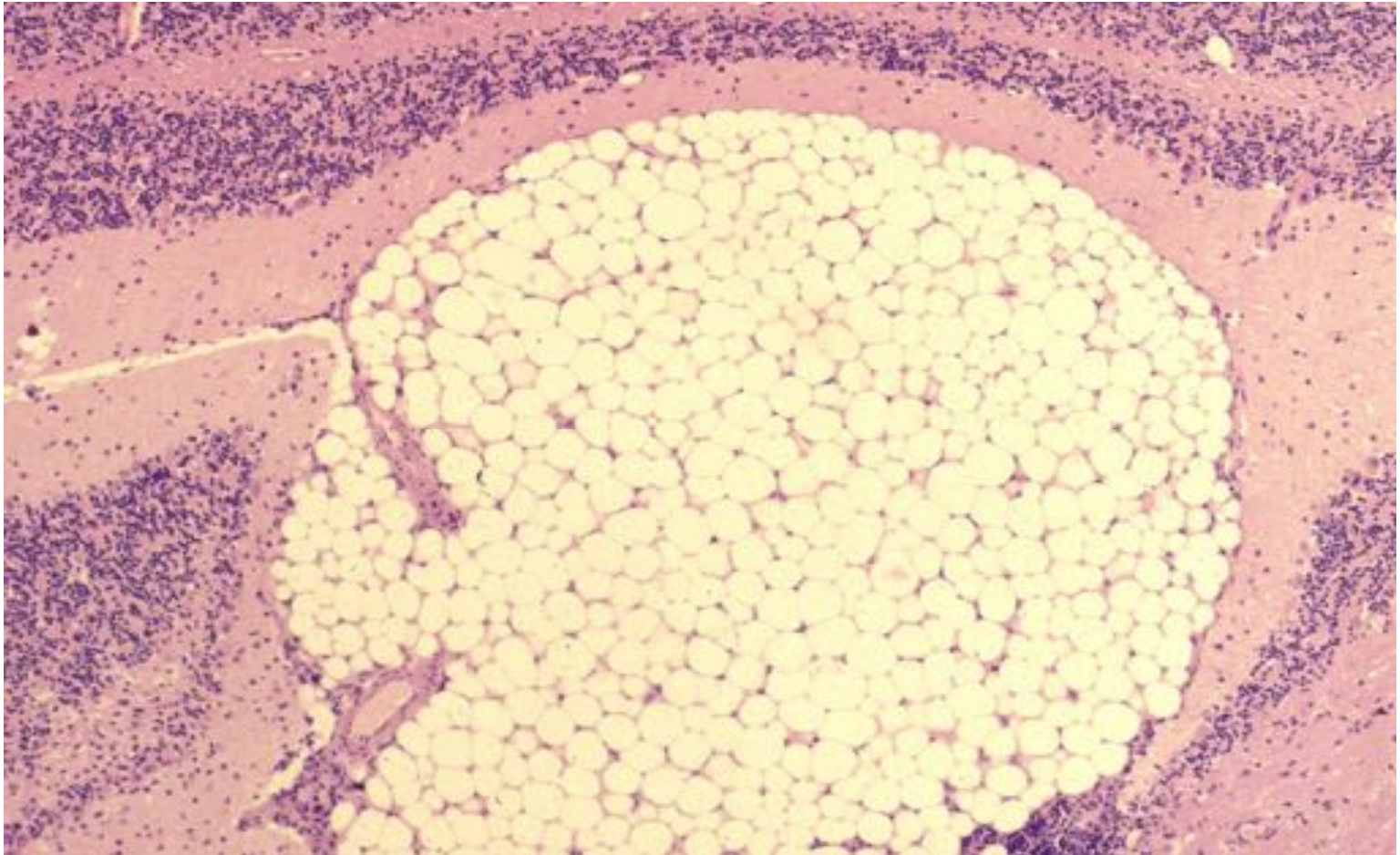
# Anaplastic glioma



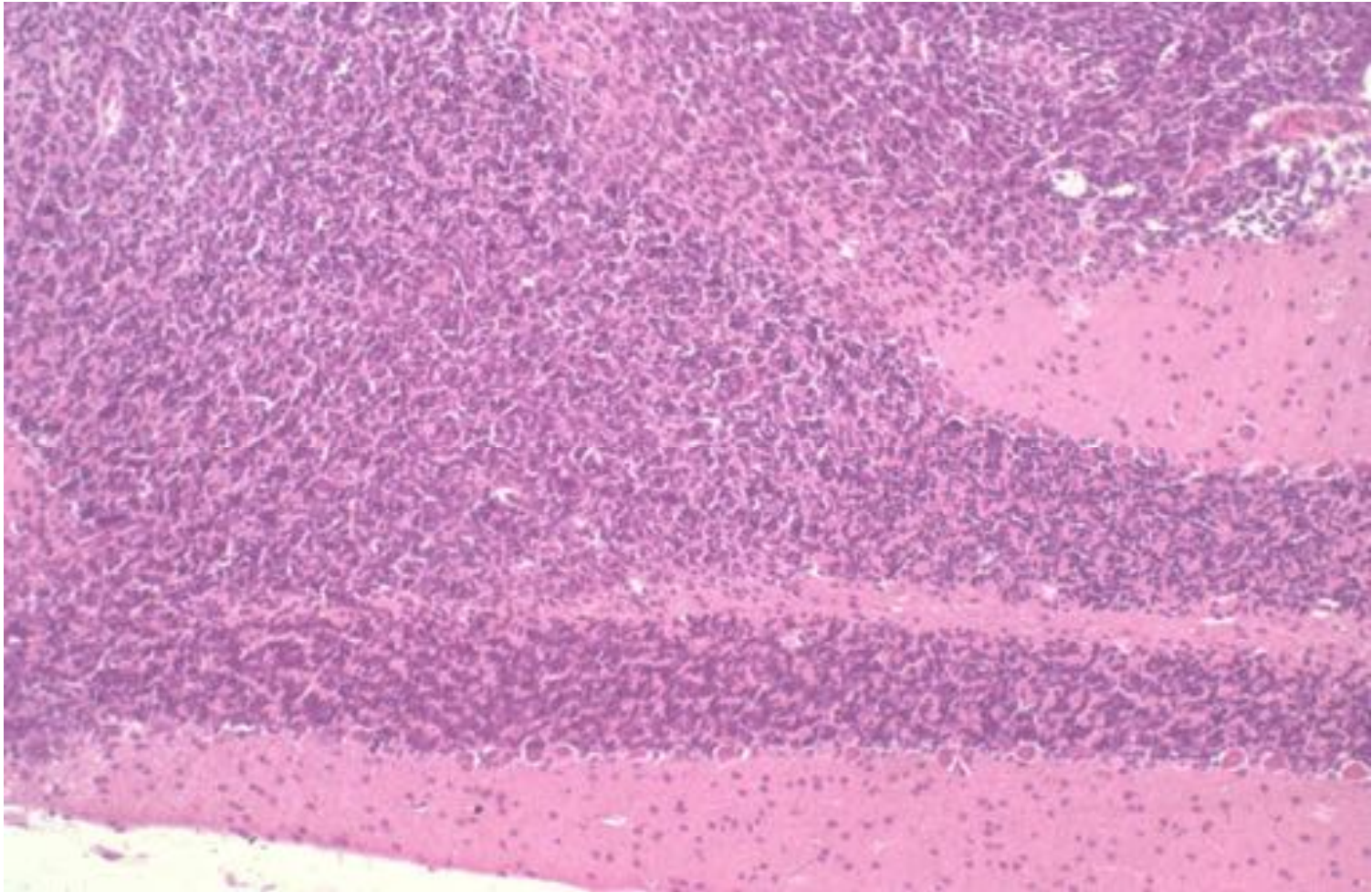
# Choroid plexus tumour



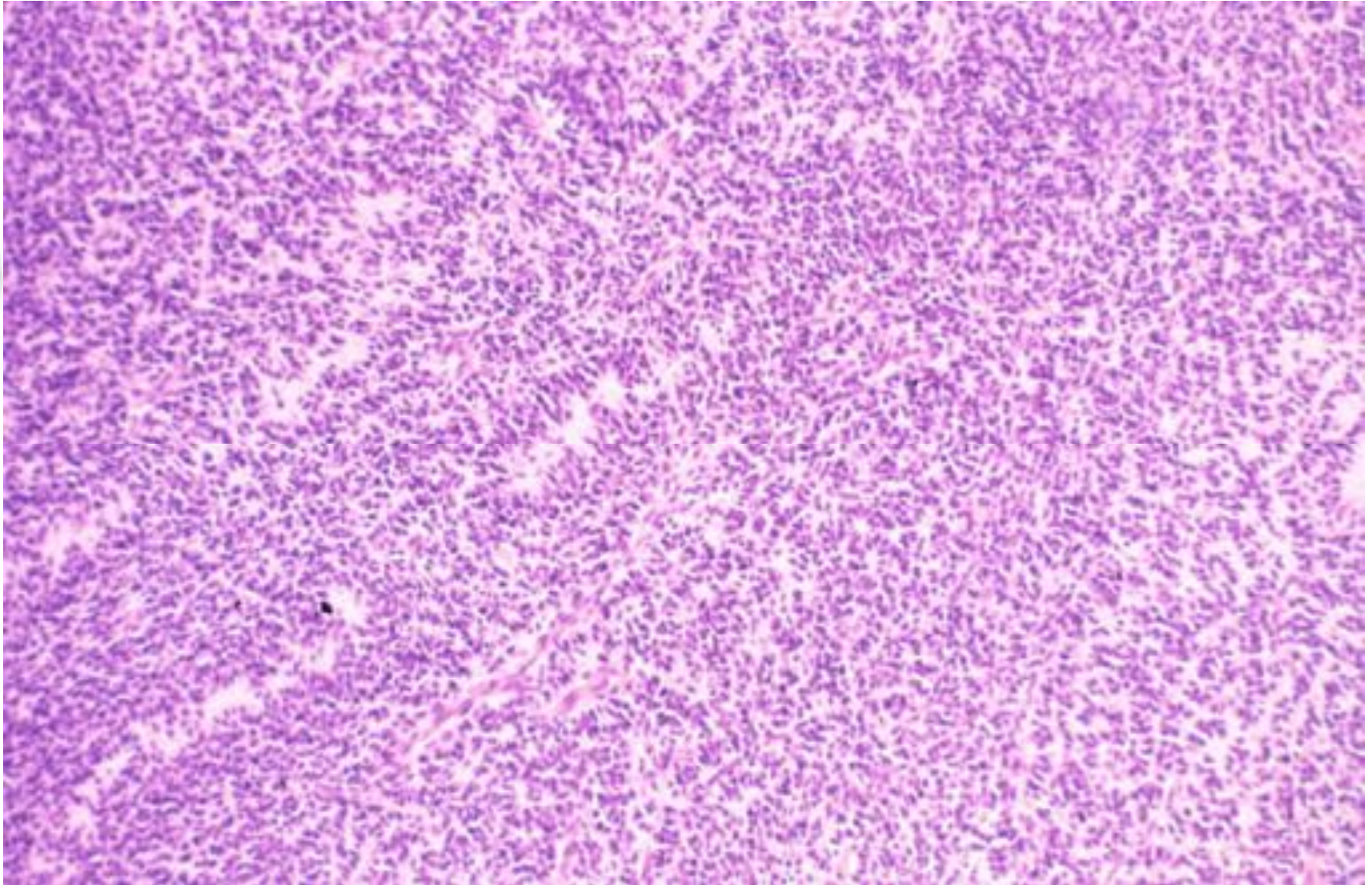
# Lipoma



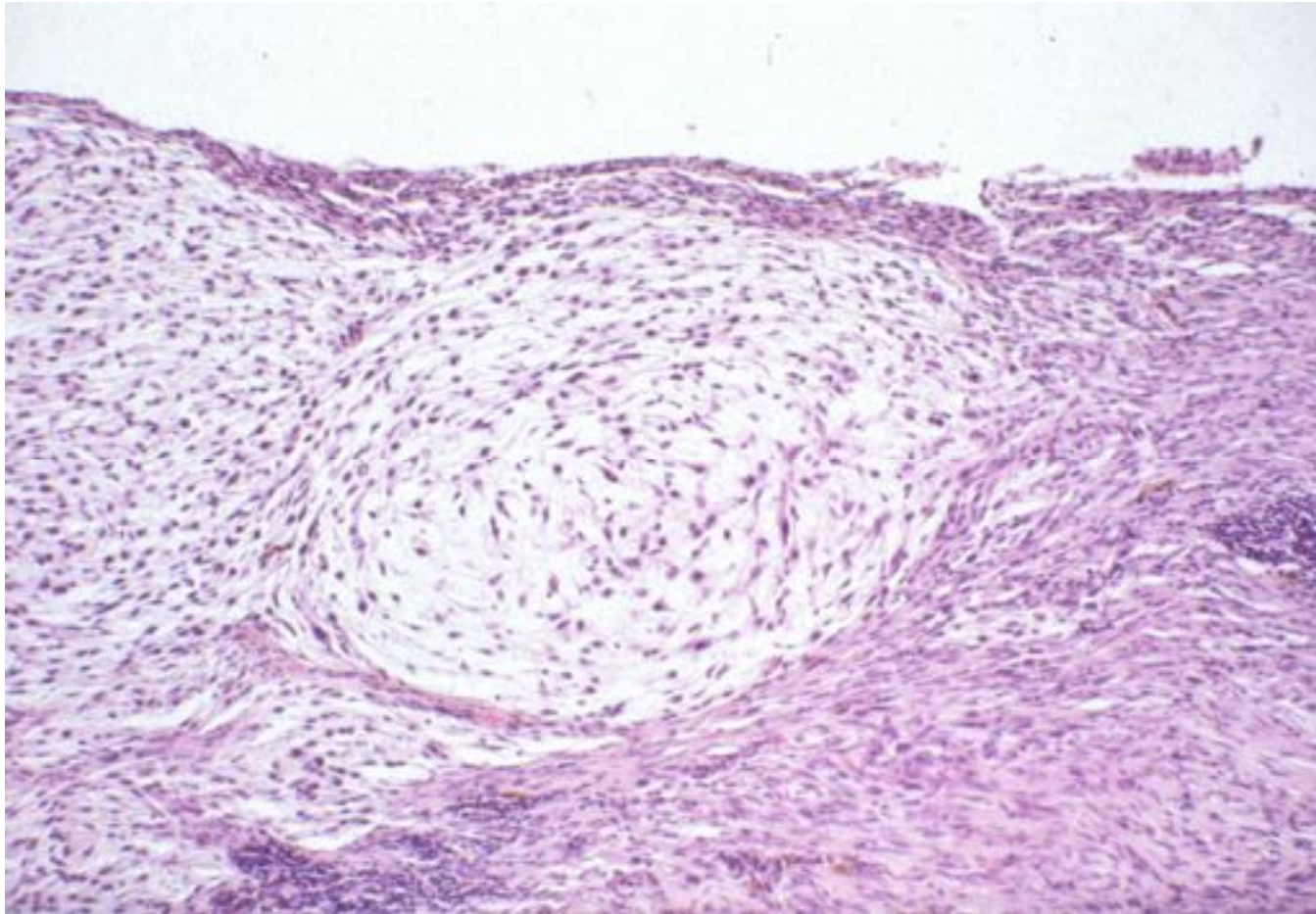
# Medulloblastoma



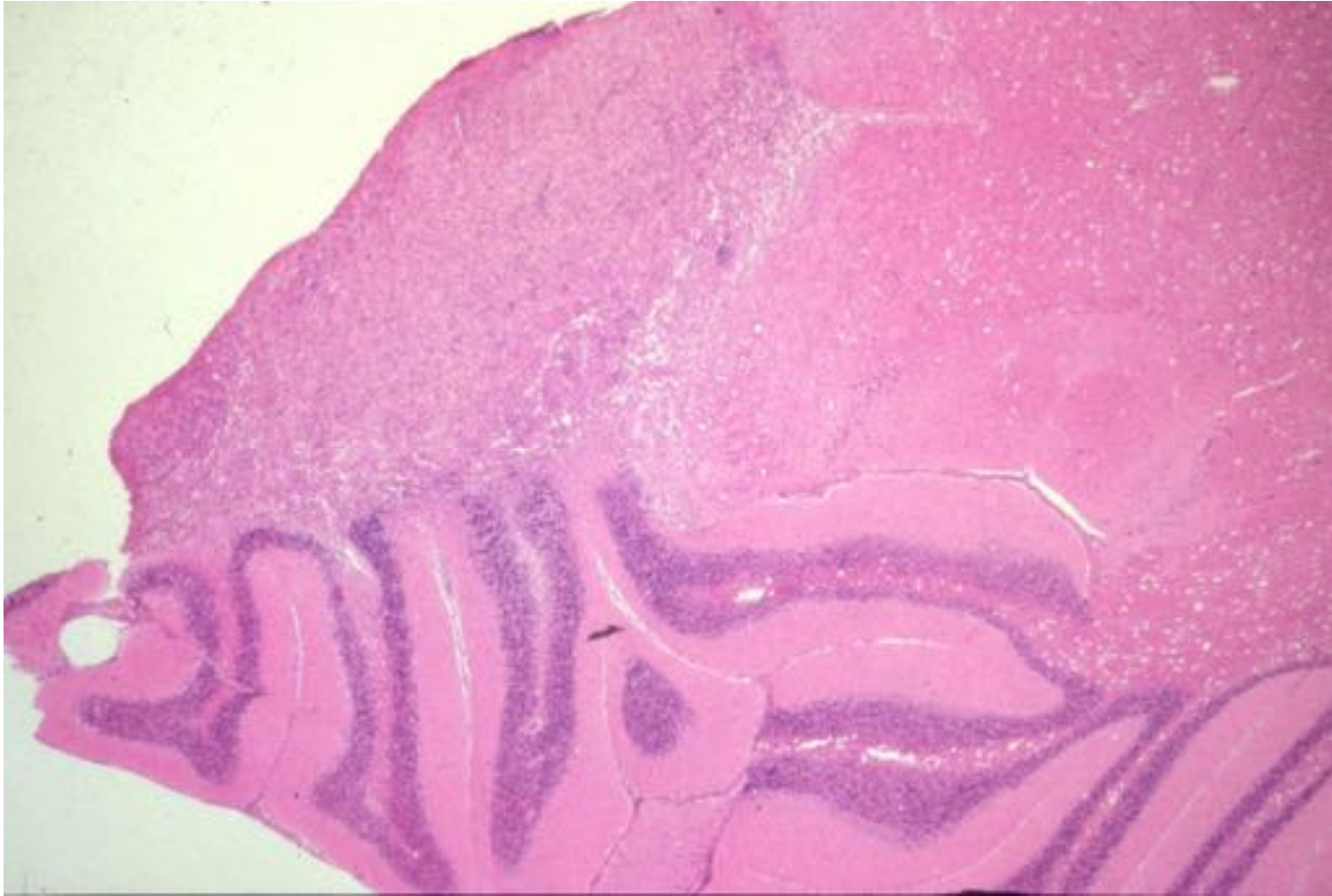
# Medulloblastoma



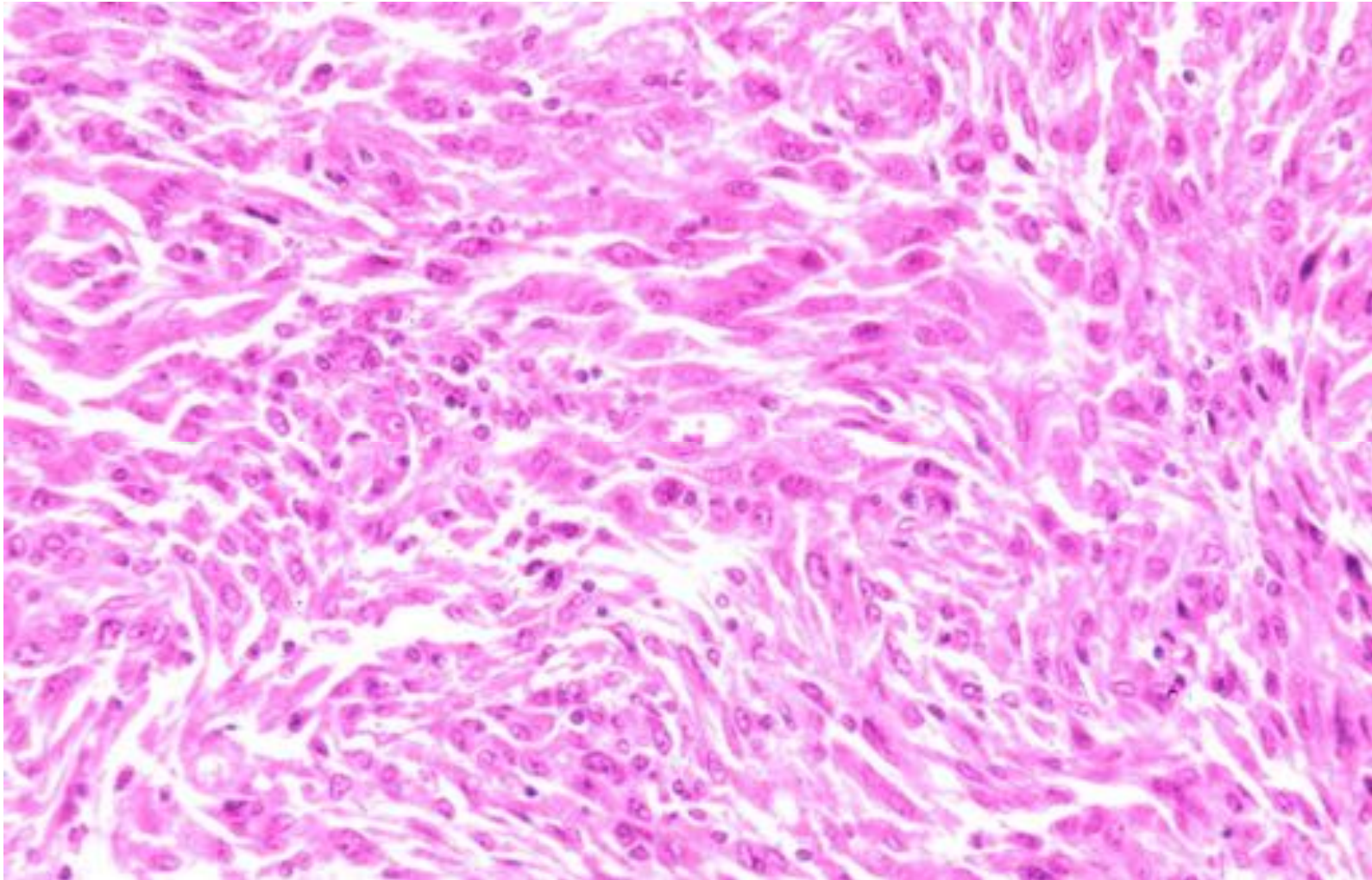
## Meningioma- fibroblastic



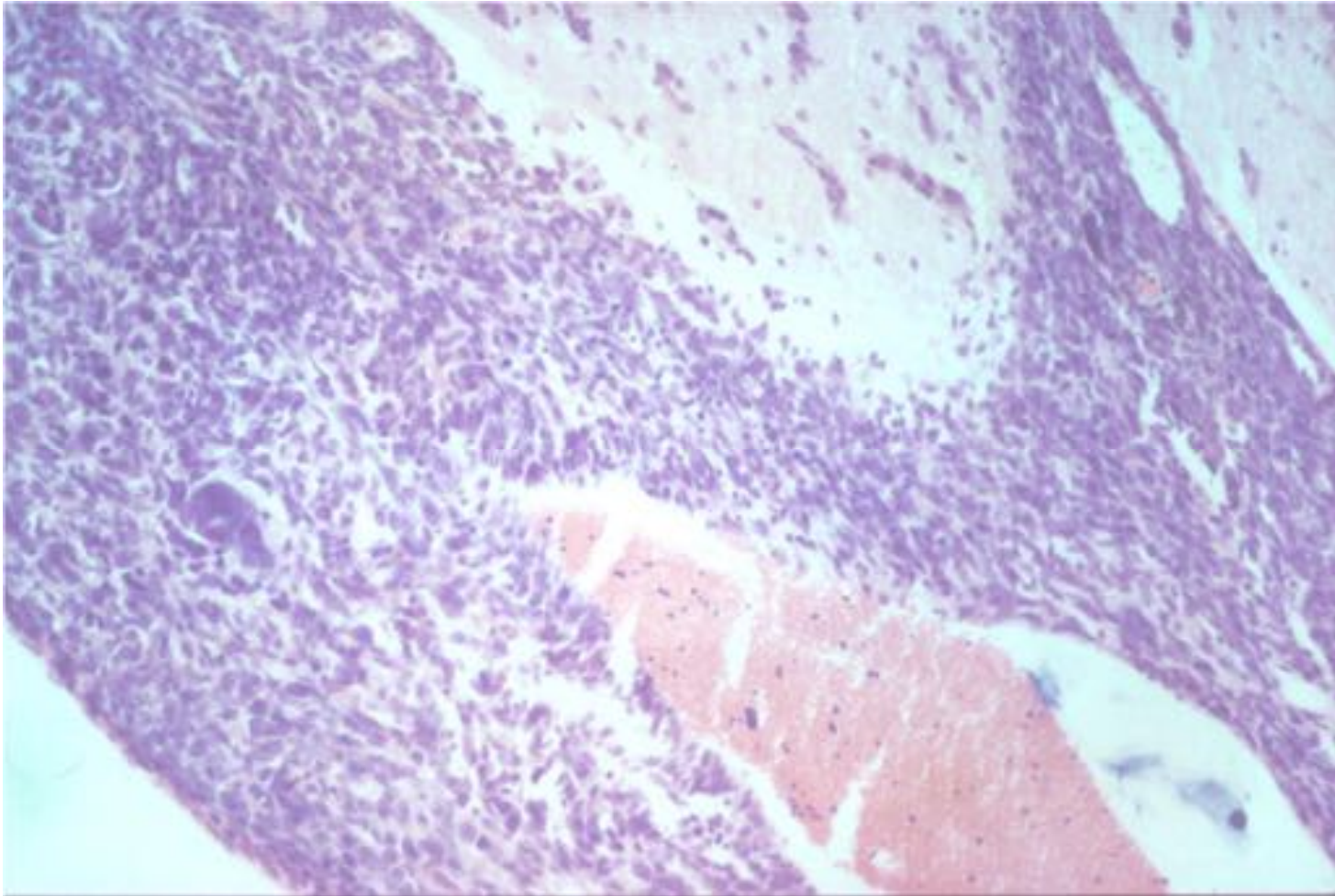
## Meningioma- gr cell

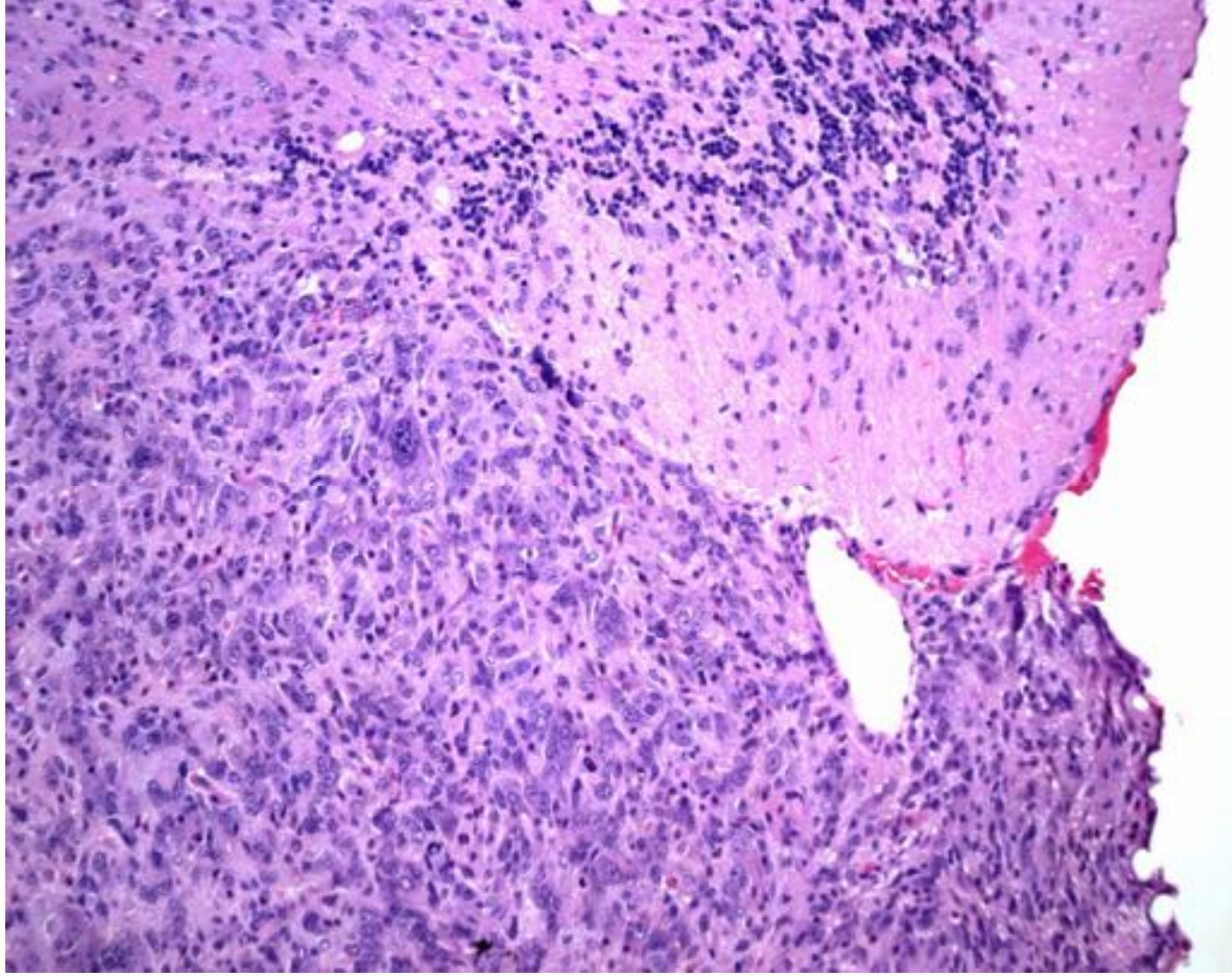


## Meningioma- granular cell

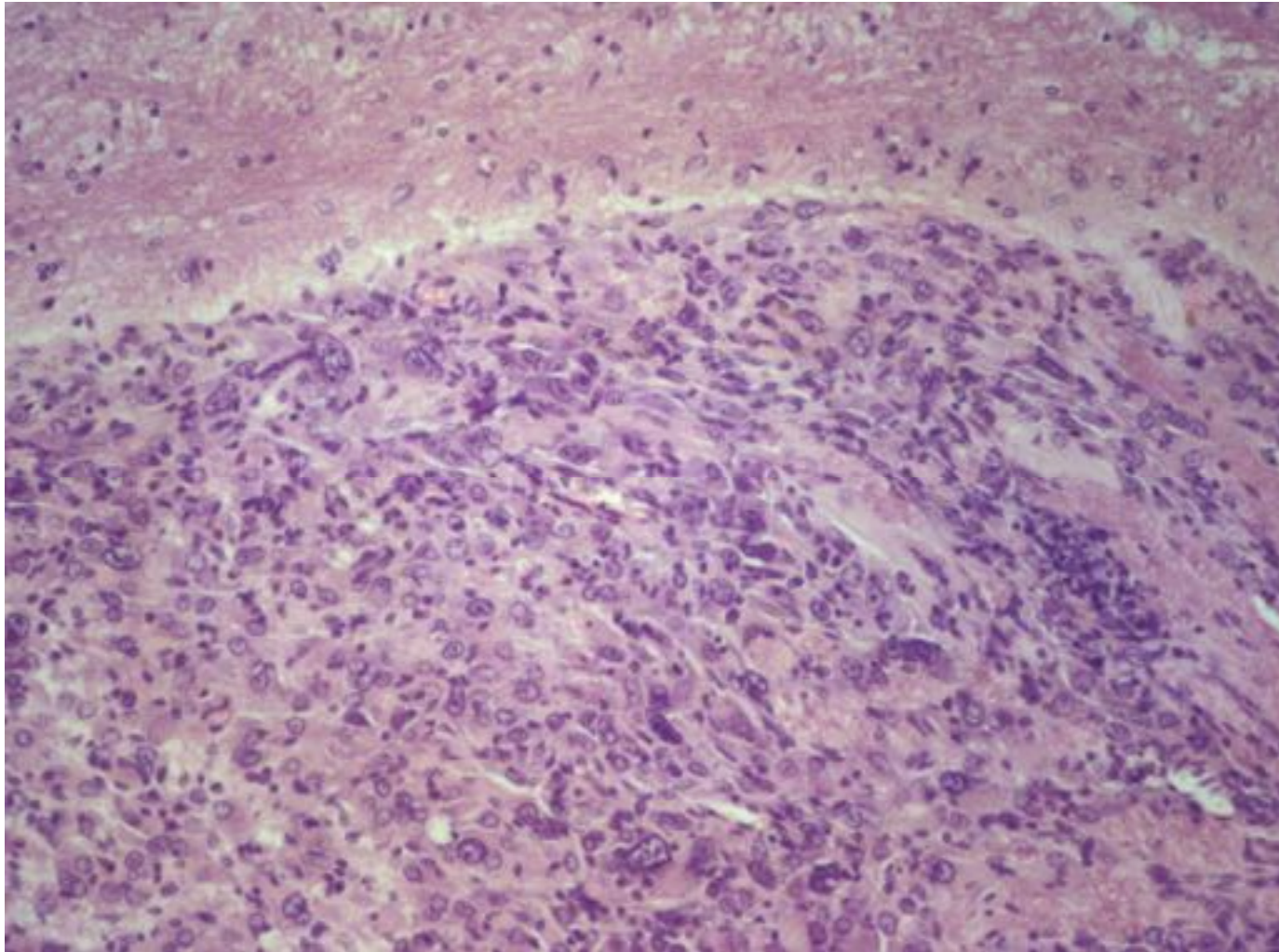


# Meningiosarcoma

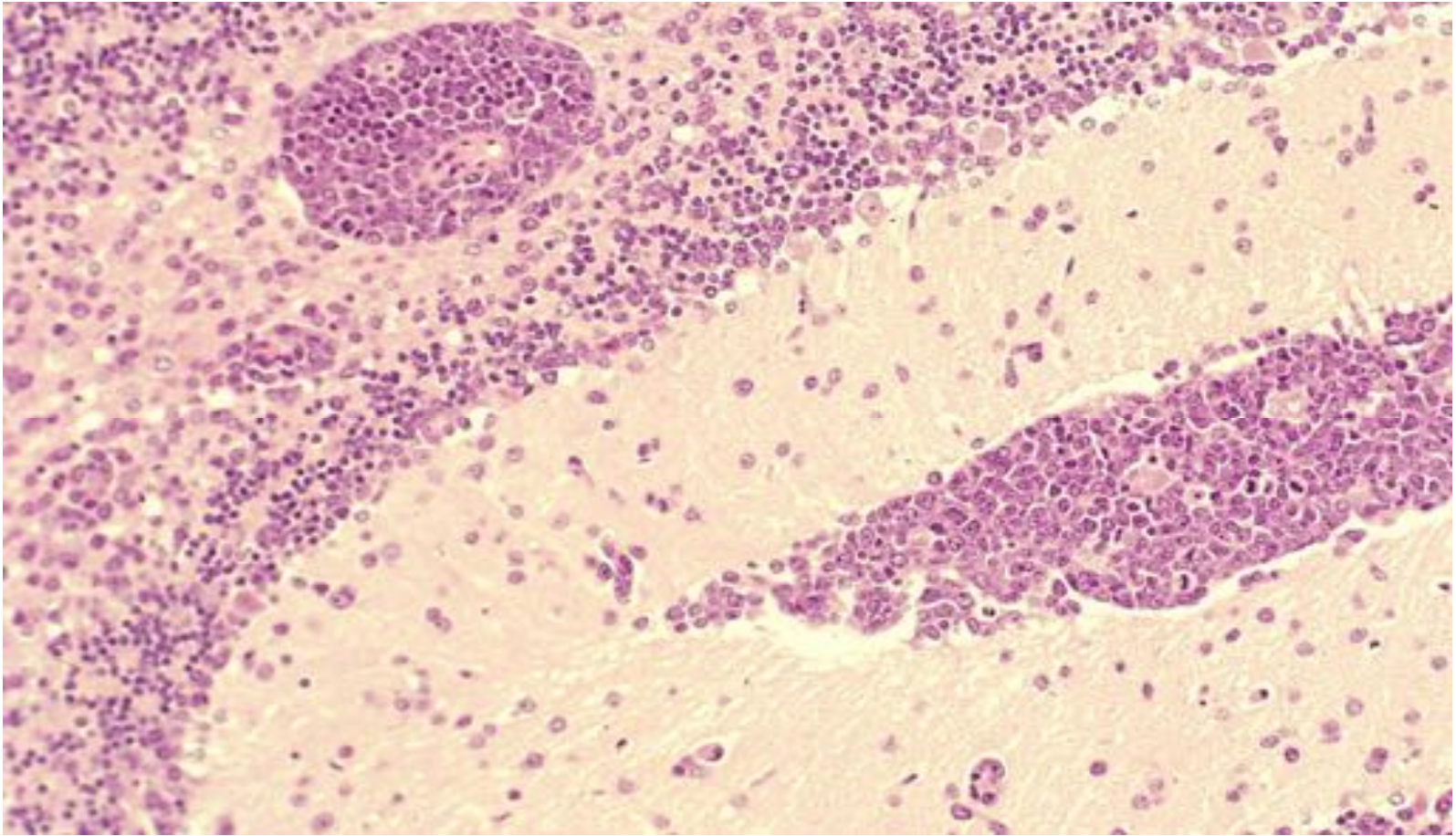




## Meningiosarcoma- polymorphic



# Lymphoma



## Brain tumours- chemical induction

- Nitroso- compounds
- Ethyl nitrosourea ENU: I/V to pregnant rats (last semester), single inj of 20mg results in mixed glioma, oligo, and anaplastic neurinoma (Schwannoma)
- MNU: I/V results in anaplastic glioma, oligo and non-neuro specific tumours
- Mice are resistant

## Chemical induction

- Polycyclic hydrocarbon: i/cerebral, trans placental, parenteral or oral results in glioma, sarcoma, ependymoma, meningioma and medulloblastoma
- DMBA: i/v on 21<sup>st</sup> d of gestation results in tumours of NS in offspring
- Triazenes, hydrazine, and procarbazine are neurocarcinogenic in rats

## Chemical induction

- Acrylonitrile: oral/inhalation results in astrocytoma in rats
- Ethylene oxide inhalation low inc of glioma in rats
- Acrylamide, glycidol, inorganic lead are all implicated

## Chemical induction- some mechanisms involved

- Not clearly established but:
- Electrophilic agents/ or metabolites covalently bind with proteins- DNA □ RNA. Alkylation of O6 position of guanine occurs. The DNA-adduct O6 alkyl guanine is formed, accumulates and persist in brain of rats treated with E/MNU. Formation/ persistence is important Little known about selection/ amplification of initiated cells or promotion in brain! Multistep hypothesis is valid; microenvironment after initiation is important.

## Brain tumours: Oncogenic viruses

- RNA- oncornaviruses  
ASV, MuSV, SSV
- DNA-papovavirus human papovavirus, PML-1, Bk SV40, murine polyoma
- DNA-adenovirus human adenovirus type 12, Sa7 CELO
- Intra cerebral/parenteral
- Astrocytoma, glioblastoma, sarcoma
- Medulloblastoma, ependymoma, choroid plexus tumours
- Neuroblastoma, retinoblastoma, ependymoma

## Biological criteria for evaluation of neurocarcinogens

- Increased incidence beyond expected control level
- Shift of tumour appearance to a younger age
- Dose- effect / relationship
- Trend towards anaplasia
- Presence of pre-neoplastic lesions
- Multiplicity of tumours in affected animals

## Continued

- Tumour occurrence in both sexes
- Occurrence also in PNS
- Occurrence outside nervous system
- Genotoxicity
- Higher incidence after trans placental exposure
- Weight of evidence

# Thank you

