BRAIN TUMORS

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INTRODUCTION

- **Intracranial tumors can be divided into**

- primary brain tumors vs. Metastasis
- intra-axial(parenchymal) vs. extra-axial
- supratentorial vs. infratentorial
- adult vs. pediatric

- **can be divided into**

- benign: non invasive, but can be devastating due to mass effect in fixed volume of skull (e.g. most meningiomas, WHO Grade I)
- Malignant: implies rapid growth, invasiveness, possibly drop-metastases to spinal cord from a primary CNS tumour (rare)

Epidemiology

Table 8. Tumour Location: Etiology and Clinical Feature

	Supratentorial	Infratentorial (Posterior Fossa)
Epidemiology		
Age <15 yr Incidence: 2-5/100,000/yr 60% infratentorial	Astrocytoma (all grades) (50%) Craniopharyngioma (2-5%) Others: pineal region tumours, choroid plexus tumours, ganglioglioma, DNET	Medulloblastoma (15-20%) Cerebellar astrocytoma (15%) Ependymoma (9%) Brainstem astrocytoma
Age >15 yr 80% supratentorial	High grade astrocytoma (12-15%, e.g. GBM) Metastasis (15-30%, includes infratentorial) Meningioma (15-20%) Low grade astrocytoma (8%) Pituitary adenoma (5-8%) Oligodendroglioma (5%) Other: colloid cyst, CNS lymphoma, dermoid/epidermoid cysts	Metastasis Acoustic neuroma (schwannoma) (5-10%) Hemangioblastoma (2%) Meningioma

Clinical Feature		
Shared Features (from elevated ICP)	**H/A**: usually worse in AM and made worse with straining, coughing **N/V** **Papilledema** **Diplopia** - CN VI palsy	
Distinguishing Features	**Seizure**: commonly the first symptom Progressive neurological deficits (70%) Frontal lobe: hemiparesis, dysphasia, personality changes, cognitive changes Temporal lobe: auditory/olfactory hallucinations, memory deficits, contralateral superior quadrantanopsia **Mental Status Change**: depression, apathy, confusion, lethargy **"Tumour TIA"** (transient ischemic attack) stroke like symptoms caused by a) occlusion of vessel by tumour cells b) hemorrhage c) 2° to "steal phenomenon" - blood is shunted from ischemic regions to non-ischemic regions Endocrine disturbance - with pituitary tumours (see Endocrinology, E20)	**Brainstem involvement**: cranial nerve deficits and long tract signs **N/V**: compression on vagal nucleus/area postrema **Diplopia**: direct compression CN VI **Vertigo** **Nystagmus** **Truncal ataxia + titubation**: cerebellar vermis lesions **Limb ataxia, dysmetria, intention tremor:** cerebellar hemisphere lesions **Obstructive hydrocephalus** more common than supratentorial lesions

Etiology and pathogenesis

- As any neoplastic process in the body . there must be :

  Induction , promotion and progression

- Carcinogenesis process on molecular level
  - oncogene
  - tumor suppressor gene

Risk Factors

1. no genetic predisposition except in certain inherited syndromes
    1. **NF1** : optic nerve glioma , peripheral neurofibroma
    2. **NF2** :bilateral acoustic neuroma , multiple meningioma
    3. **Tuberous sclerosis** : subependymal glioma
    4. **Li-fraumeni disease:** glioma , ependymoma and medulloblastoma
    5. **Von hippel lindau disease:** hemiangioma and hemiangioblastoma

Risk Factors

2. radiation of head
3. immunosuppresion
4. viral infection
5. Chemicals as anthracen and nitrosurea
6. Head trauma

WHO Classification

- In 2007 , the WHO Classification of CNS tumours was based solely on histology; an update was made in 2016 which bases the classification on a combination of histology (phenotype) and molecular genetics (genotype) for "integrated" diagnoses

- Last update published 2021 (5^{th} update) introduces major changes that advance the role of molecular diagnostics in CNS tumor classification

Classification

- WHO classification depend on cell of origin

- **neuroepithelia tumors**
  - **glial cells**
    - astrocytoma
    - oligodendroglioma
    - ependymoma
    - choroids plexus tumors
  - **neurons**
    - ganglioglioma
    - gangliocytoma
    - neuroblastoma
  - **pineal** tumors
  - **medulloblastoma**
- nerve **sheath tumors** : shwanomma , neurofibroma
- meningial tumors : meningioma
- microglial cells : primary CNS lymphoma
- pituitary tumors
- germ cell tumors :
  - germinoma
  - teratoma
- TUMOR LIKE MALFORMATION
  - Craniopharyngioma
  - Dermoid and epidermoid tumors
  - Colloid cyst
- Metastasis and extension from regional tumors .

Clinical presentation

- Gradual vs acute onset

1. **headache**

   result of :

   - increase in ICP
   - invasion or compression of pain sensitive
   - secondary to vision difficulties

Clinical presentation

2. other features of **increased ICP**
3. **lateralizing** features of brain shift and herniation
4. **epilepsy**

   new onset epilepsy in adult specially above age of 30 should warn the physician for possibility of tumor . because this occur in 30% of patients with tumors

Clinical presentation

5. **subtle changes in personality and behavior**
6. **progressive neurological deficit**

   depend on site

Clinical presentation

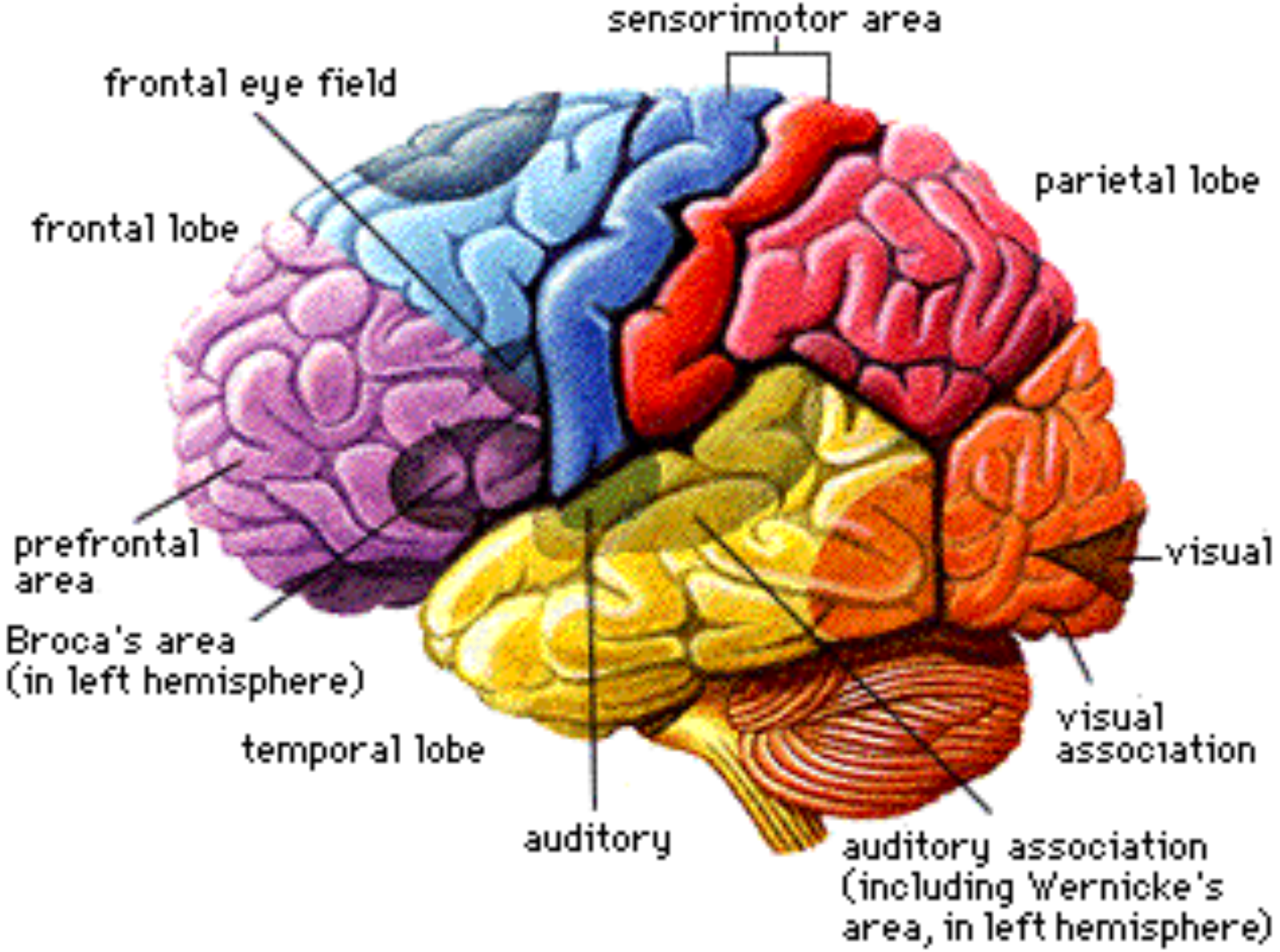
- signs and symptoms are divided according to tentorium cerebelli

Supratentorial

- frontal lobe
- parietal lobe
- temporal lobe
- occipital lobe
- hypothalamus and pituitary
- cranial nerves I II , cavernous sinus cranial nerves

Infratentorial

- increased ICP and hydrocephalus
- cerebellum sings
- brain stem signs : cranial nerve palsy III – XII . alternation in consciousness , long tract sings


sensorimotor area
frontal eye field
parietal lobe
frontal lobe
prefrontal area
visual
Broca's area (in left hemisphere)
visual association
temporal lobe
auditory
auditory association (including Wernicke's area, in left hemisphere)

Investigation

- Aim is :
  - to diagnose presence of brain tumor .
  - To find the source if you suspect the tumor to be a mets

Investigation

- **Skull X-RAY**
  - **calcification** : Oligodendroglioma , meningioma craniopharyngioma and ependymoma
  - **hyperostosis** of skull
  - **bone destruction** : mets , chordoma , craniopharyngioma
  - **erosion** of sella tursica
  - **sings of ICP**
  - **midline shift** of pineal gland if calcified

Investigation

- **brain CT**
  - site , mass effect , bone destruction , enhancement , multiplicity
  - **enhanced tumors**
    - high grade gliomas
    - meningioma
    - mets
    - acoustic neuroma
    - large pituitary tumors

Investigation

- **MRI** : Goldstandard
- **Angiography or MRA**
- **PET scan**
- **CSF cytology** : remember the contraindications

Investigation

- **Biopsy :**
  - needle biopsy thru burr hole ,
  - or stereo tactic biopsy image guided o
  - or at time of treatment
- **Tumor markers**

Differential diagnosis

- vascular : hematoma , aneurysm AVM
- infection : abscess , tubercloma , hydatid cyst
- arachnoid cyst , dermoid and epidermoid cyst

Treatment

- **medical therapy**
  - medical treatment doesn't affect tumor it self
  - this used only to reduce edema surrounding the tumor
  - steroid are used specially with mets , meningioma and GBM

Surgical Treatment

- aim of surgery
  - to take a biopsy
  - removal of tumor either completely or partially (cytoreduction)
  - to treat complication as hydrocephalus
- Surgical removal is recommended for most types of brain tumors

Surgical Treatment

- craniotomy
- cranioctomy
- tras-sphenoidal
- trans-oral

Radiotherapy

- differentiate between *radiation therapy* and *radiosurgery*.
- Conventional radiotherapy used as **adjuvent** therapy
- most radiosensitive are germinoma and medulloblastoma

Radiotherapy

- **complication** :
  - increase edema
  - demylenation
  - radionecrosis
  - affect cognitive functions
  - may induce other kind of tumors as meningioma

Chemotherapy

- problems facing conventional chemotherapy
  - presence of intact BBB.
  - small proportion of cells in active growth

Examples:

1. Alkylatingagents i.e.temozolomide(GBM)
2. Combination of drugs: Procarbazine, lomustine and vincristine (PCV)

New Treatment

- hyperthermia treatment
- immunotherapy : LAK
- gene therapy

Posterior Fossa Tumors

- May need shunting or EVD prior to definitive surgery .
- risk are :
  - possible peritoneal seeding
  - prolonged hospitalization
  - risk of shunt complications

GLIOMA

- Tumors that arise from cells derived from neuroectoderm , the glial cells
- Most common brain tumors **52%**
- Four different types

Astrocytoma

- tumor that arise from astrocyte
- function in
  - support neurons
  - absorb neurotransmitter
  - release neuroactive molecules
  - aid in formation of BBB

Astrocytoma

- most common primary tumors of brain , 45%
- peak age : 40 – 60 years
- astrocytoma ranges in aggressiveness
- site : equal incidence in frontal , temporal parietal and thalamic . less common in occipital

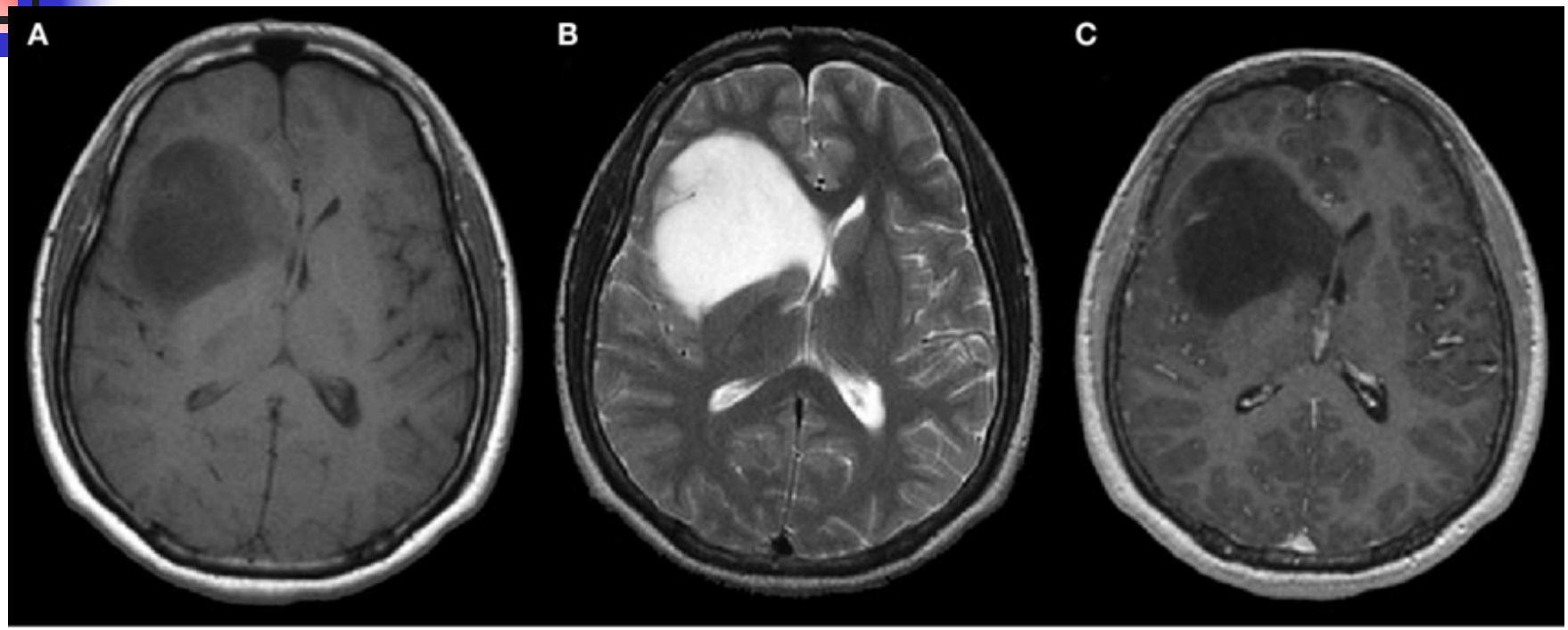
Astrocytoma

- multiple classification systems
- WHO :
  - **Grade 1** : pilocytic astrocytoma
  - **Grade 2** : diffuse astrocytoma
  - **Grade 3** : anaplastic astocytoma
  - **Grade 4** : glioblastoma multiforme

Low grade

- **Site** :
  - In adults usually in cerebral hemispheres
  - In children : in cerebellum
- **Macroscopic features :**
  - Not capsulated , no distinct margins
  - Relatively Avascular
  - Firm fibrous consistency
  - 15% show fine calcium deposit
  - Occasionally may invade diffusely
- **Microscopically:**

WHO Grade 1 and 2: well-differentiated and demonstrate hypercellular glia with nuclear atypia and rare mitotic activity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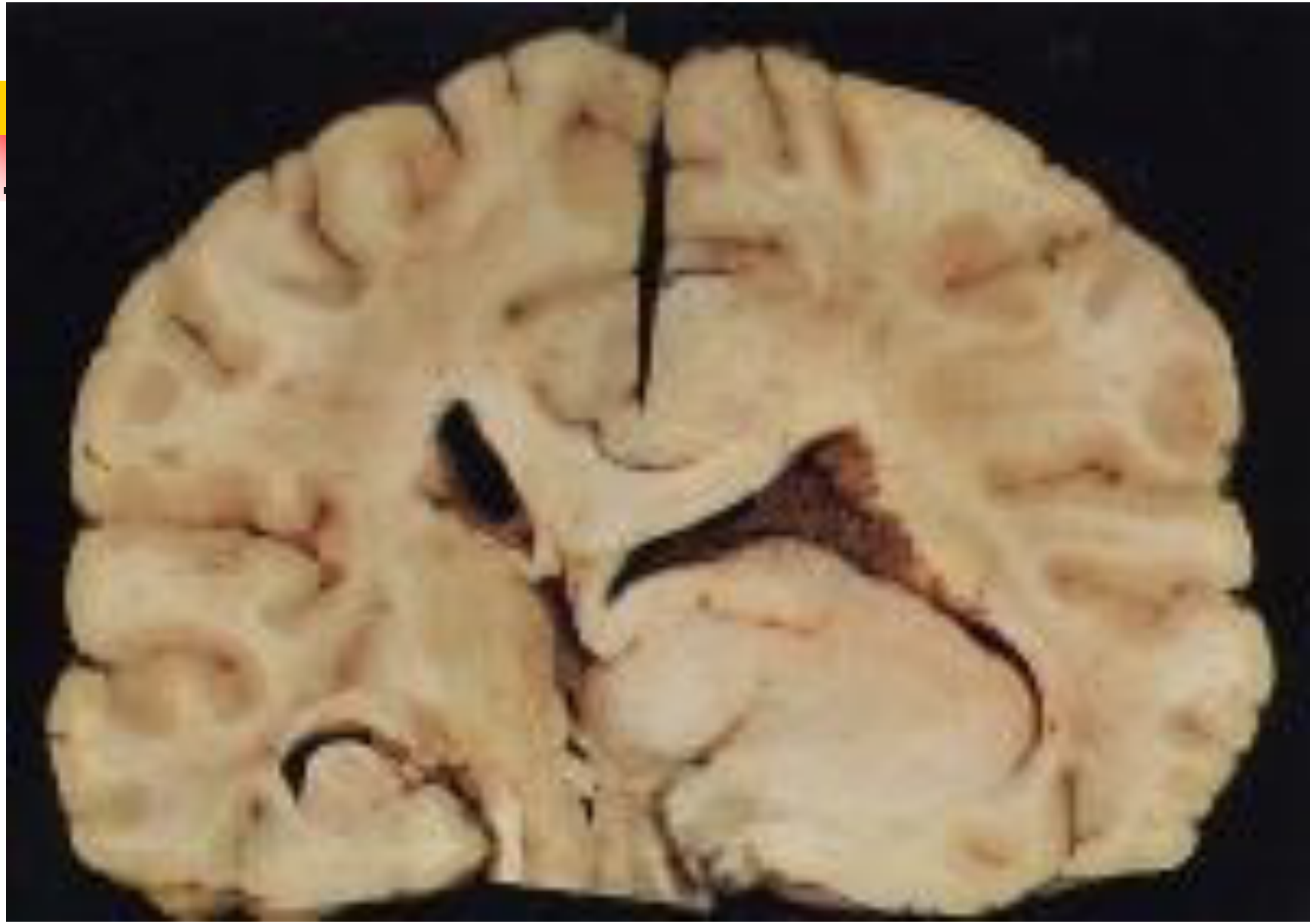
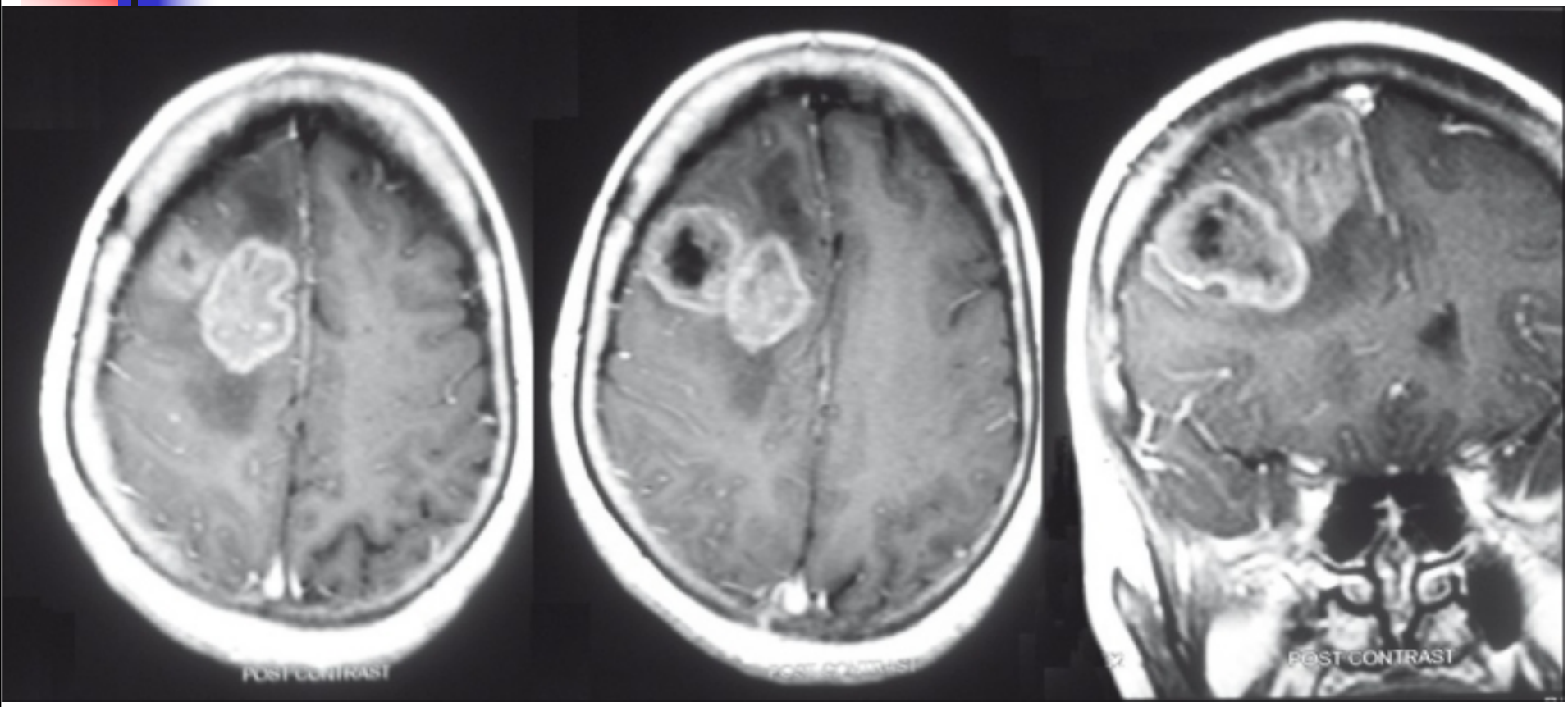


High grade

- **Site** :
  - cerebral hemisphere
- **Macroscopic features**:
  - Highly vascular margin ,necrosis
  - Butterfly glioma
- **Microscopic features**
  - Grade 3
  - Grade 4
- Rapidly growing and widely infiltrating


POST CONTRAST

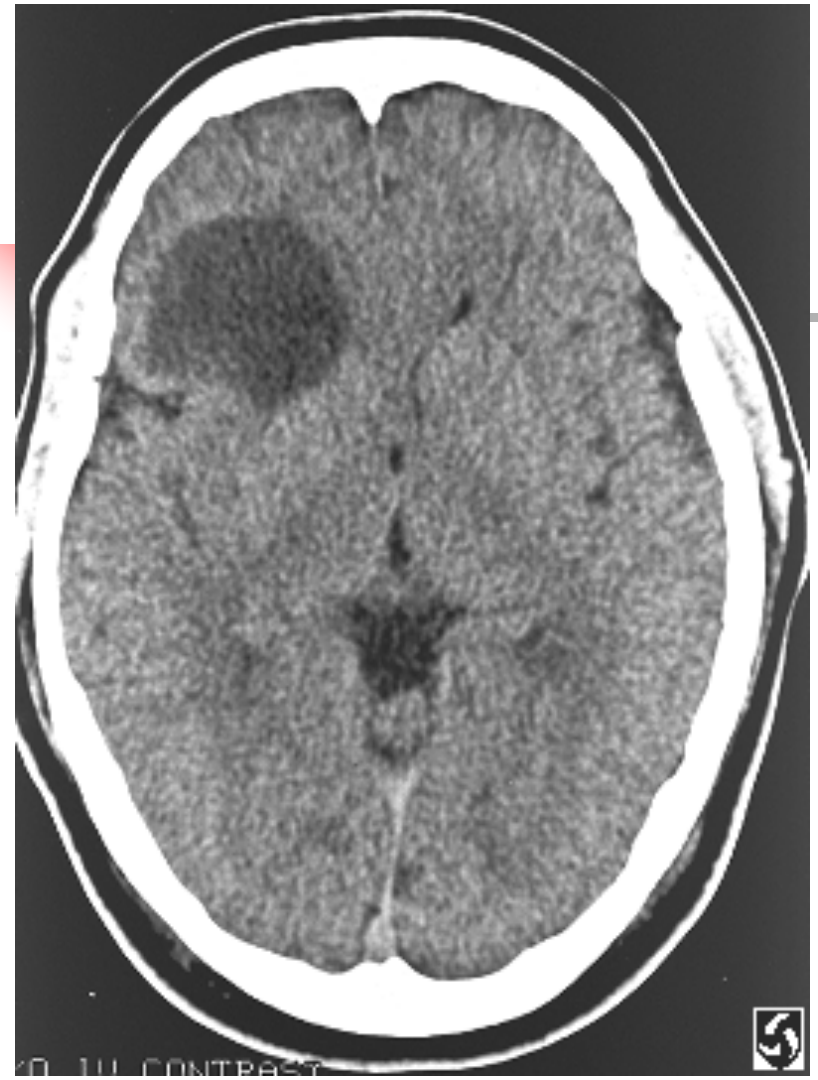
Clinical features

- Duration and progression of symptoms will depend on the grade

1. epilepsy
2. feature if increase ICP
3. focal neurological deficit

investigations

- **CT**
  - **Low grade** :
    - small hypodense mass
    - little surrounding edema
    - no enhancement
    - calcification may present
  - **high grade**
    - large mass
    - marked edema
    - enhance in non uniform manner ,



investigations

- MRI
- More sensitive than CT specially :
  - posterior fossa , brain stem and skull base tumor and for small tumor mass
  - usually both low and high appear decrease t1 signal increase t2 signal
- Angiograph
- Skull X-RAY

Astrocytoma

- spread :
  - systemic : rare
  - CSF seeding : 10 -25% of high grades
  - tracing thru white matter

Management

- surgical :

  aim is to
  - take biopsy
  - decrease tumor size
  - reduce tumor mass prior to adjuvant therapy

- radiotherapy

  as adjuvant therapy

- other therapy :

  chemotherapy , immunotherapy , hyperthermia

Prognosis

- at present there is no satisfactory treatment for grade 3 and 4
  - surgery alone is 17 weeks
  - adjuvant radiotherapy is 37 weeks
- low grades is approximately 8 years .

	Typical CT/MRI Findings	Survival
I – Pilocytic astrocytoma	± mass effect, ± enhancement	>10 yr, cure if gross total resection
II – Low grade/diffuse*	Mass effect, no enhancement	5 yr
III – Anaplastic*	Complex enhancement	1.5-2 yr
IV – Glioblastoma multiforme (GBM)	Necrosis (ring enhancement)	12 mo, 10% at 2 yr

*IDH mutant WHO Gr II/III tumours have a better overall prognosis than IDH wild-type; following IDH stratification, the chromosomal 1p/19q codeletion has prognostic value in IDH mutated grade II–III gliomas after adjustment for tumour proliferation, age, and adjuvant treatment

Oligodendroglioma

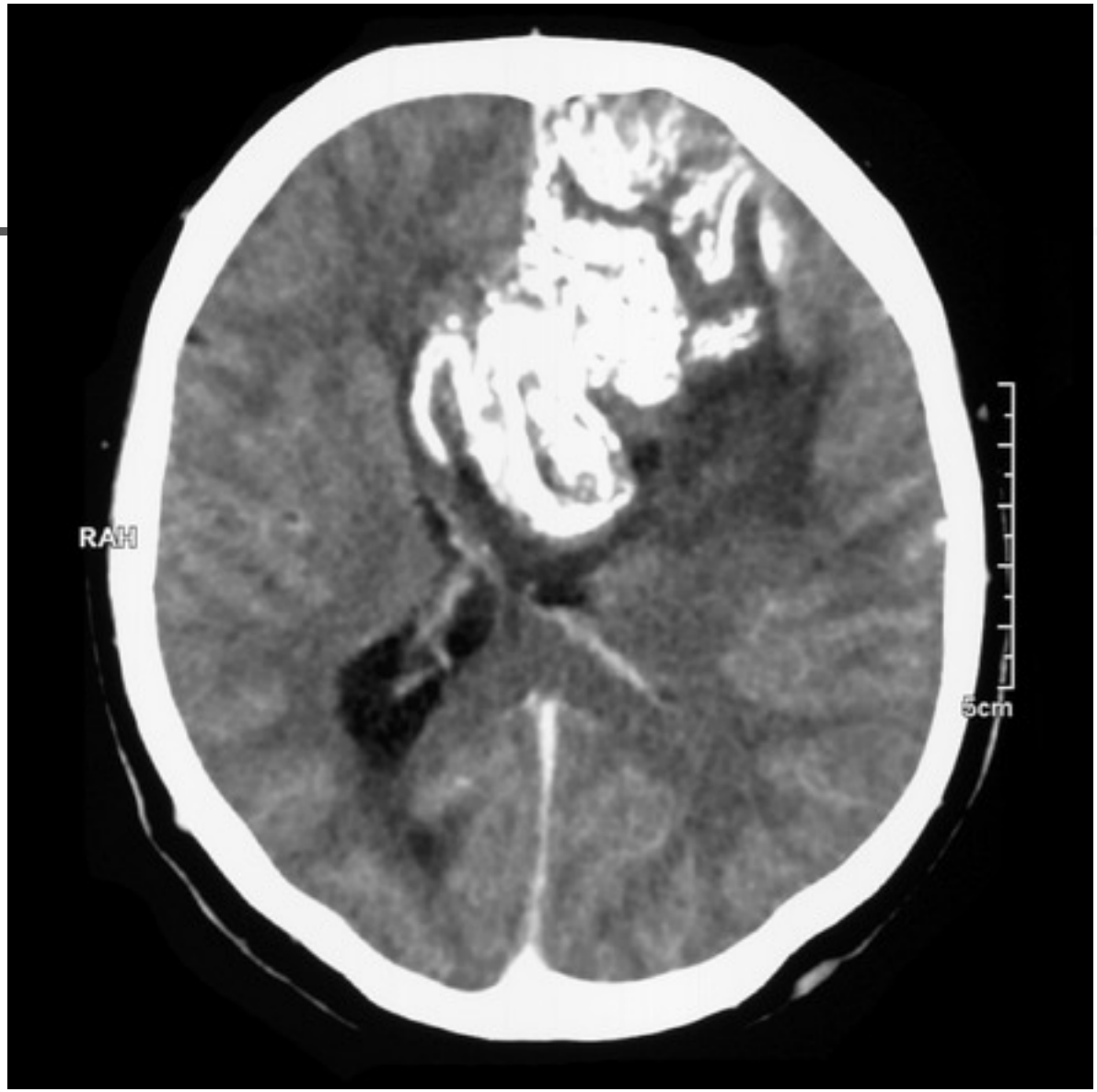
- Origin
- 5% of all gliomas
- peak age : maximal incidence in 5th decade
- site : supratentorial
- Presented as range
- most are well differentiated
- 40 % are mixed glioma with astrocytoma or ependymoma

Clinical features

- as astrocytoma

Investigations

- CT
- MRI
  - Calcification in 90%
  - Enhancement in 50%
  - Well demarcated edges


RAH
5cm

Treatment

- Standard treatment is aggressive resection followed by radiotherapy
- Prognosis : 5 year survival is 30 – 505

Ependymoma

- Origin
- 5% of all glioma
- Age : most are in children and adolescents
- Site :
  - 30% of cases are supratentorial , mainly in adults
  - 70% are infratentorial , mainly in children

classification

- **non-anaplastic tumors** :
  - **papillary** : occur in 2 patterns (rosette and psudorosette
  - **myxopapillary**
  - **subependymoma** : usually heavily calcified, may be found incidentally at autopsy or present clinically
- **anaplastic**
- anaplastic and pappilary are most common symptomatic ependymoma

clinically

- supratentorial :
  - presented with increased ICP
  - focal neurological deficit
- infratentorial :
  - increased ICP due to hydrocephalus
  - ataxia due to cerebellum involvement

Investigation

- **CT**
- **MRI**
  - Tumor arise in ventricle and enhance
  - calcification in 90% specially supratentorial
- Spread by:
  - seeding thru CSF
  - systemic spread is rare

Treatment

- Surgical resection
- Radiation of whole neuroaxis
  - Second most radio sensitive tumor after medulloblastoma
- Prognosis : 5 years survival 20 -50%

  Adults and supratentorial tumors have better prognosis

Medulloblastoma

- Peak age is 5 years
- It is most common midline posterior fossa tumor
- All are highly malignant
- Spread by
  - CSF seeding
  - hematogenous spread

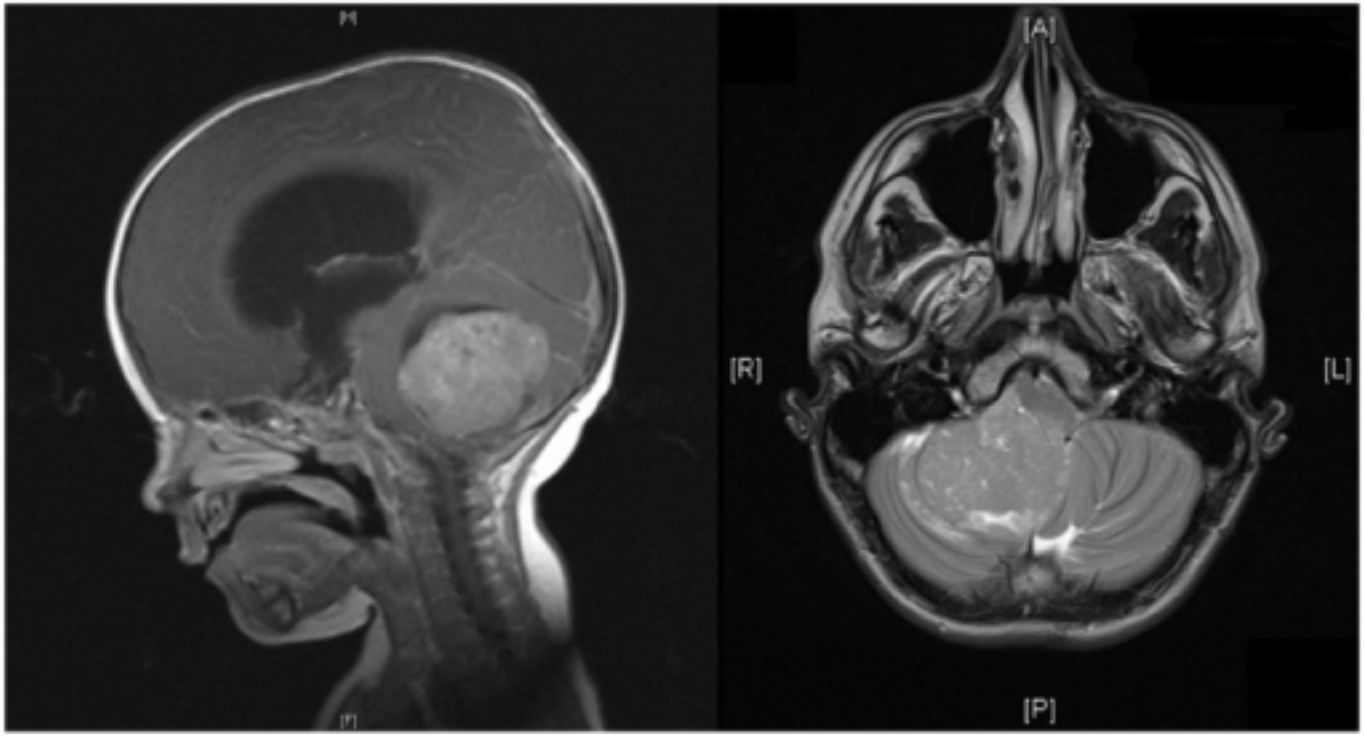
Medulloblastoma

- **CT**
  - Isodense midline lesion compressing 4th ventricle , with strong enhancement
- **MRI**

Treatment

- Treat hydrocephalus
- Surgery
- Neuraxis radiation

- Prognosis
  - 5 years survival is 40 – 60 %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Meningioma

- Tumor arise from arachnoids layer of meninges
- Most common benign brain tumors , 15% of all tumors
- Occur at any age , peak in middle age
- More in females

Etiology

- Possible risk factors
  - head trauma
  - Low levels of radiation
  - Nf2
  - Sex hormones are important

Meningioma

- **Site** :
  - Most common is parasagital region
  - Less frequently from convexity
  - sphenoidal wing
  - Olfactory groove
  - suprasellar
- **Classification**

  Depend on position of origin rather than histology

Histological types

- syncytial or meningiotheliomatous
- transitional type
- fibroblastic
- angiomatous
- malignant infrequent

Clinically

- **parasagital tumors**
  - patient present with epilepsy , contalateral lower limb paresis
  - may present with ICP in bilateral tumors
  - urinary incontinence especially if bilateral
  - if arise from posterior falx : hemianopia
- **convexity tumors**
  - ICP
- **Sphenoid ridge**
  - May compress optic nerve
  - May cause ICP
  - **foster kennedy syndrome** : contraleteral papilledema and optic atrophy in the other

Clinically

- **Olfactory groove**
  - Anosmia initially unilateral
  - Increased ICP
  - Foster kennedy
- **Suprasellar**
  - Bitemporal hemianopia but without endocrine disturbances
- **Ventricular tumors**
  - Increased ICP

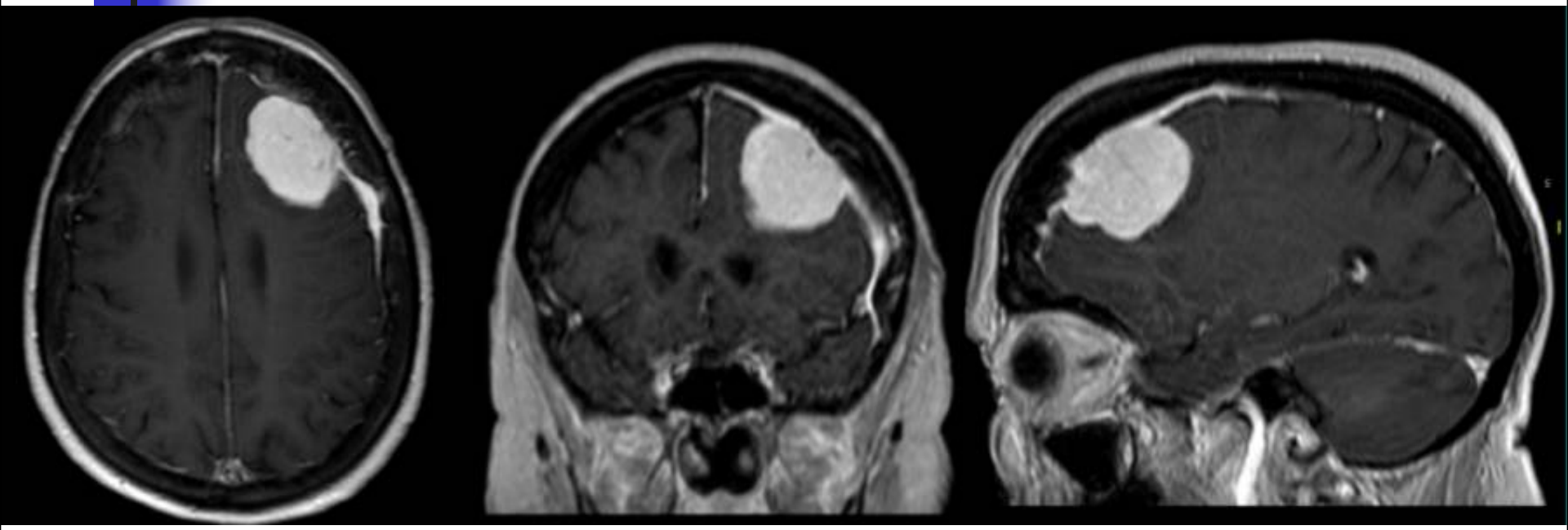
Investigations

- **CT**
  - Hyperdense
  - Enhance uniformly
  - Hyperostosis of cranial vault
- **MRI**
  - Isointense in t1

Treatment

- Total surgical excision
- Radiation may be used to treat residual tumors

- Risk of recurrence
  - Most common source tumor invaded dural sinus and not removed by surgery
  - And in malignant variant



Pituitary adenoma:

- Primarily from anterior pituitary, 3rd - 4th decades, M=F, associated with MEN-1 syndrome
- Incidence in autopsy studies approximately 20%

classification

- microadenoma <1 cm; macroadenoma ≥1 cm
- endocrine active (functional/secretory) vs. inactive (non-functional)
- most common functional: prolactinomas, adrenocorticotropic, growth-hormone (GH) producing
- differential diagnosis: parasellar tumours (e.g. craniopharyngioma, tuberculum sellae meningioma), carotid aneurysm

Clinical Features

- masseffects
- H/A
- Bitemporal hemianopsia (compression of optic chiasm) ; hydrocephalus (3rd ventricle compression)
- Invasive adenomas: CNIII,IV,V1,V2,VI palsy (cavernoussinuscompression) ; proptosis and chemosis
- (cavernous sinus occlusion)

- Endocrine effects:

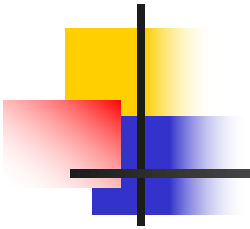
■ hyperprolactinemia (prolactinoma): infertility, amenorrhea, galactorrhea, decreased libido.

■ ACTH production: Cushing's disease, hyperpigmentation

■ GH production: acromegaly/gigantism

■ panhypopituitarism: due to compression of pituitary (hypothyroidism, hypoadrenalism, hypogonadism)

■ DI – rare, except in apoplexy



- Pituitary apoplexy (sudden expansion of mass due to hemorrhage or necrosis)
- abrupt onset H/A, visual disturbances, ophthalmoplegia, reduced mental status, panhypopituitarism and DI
- CSF rhinorrhea and seizures (rare)
- signs and symptoms of SAH (rare)

Investigations

- formal visual fields , CN testing
- endocrine tests (prolactinlevel , TSH , 8 AM cortisol , fasting glucose , FSH/LH , IGF-1) , electrolytes , urine electrolytes, and osmolarity
- imaging (MRI with and without contrast)

Treatment

- **medical**

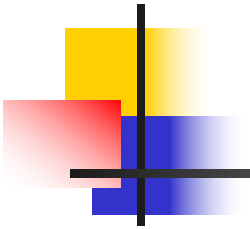
■ for apoplexy: rapid corticosteroid administration ± surgical decompression

■ for prolactinoma: dopamine agonists (e.g. bromocriptine)

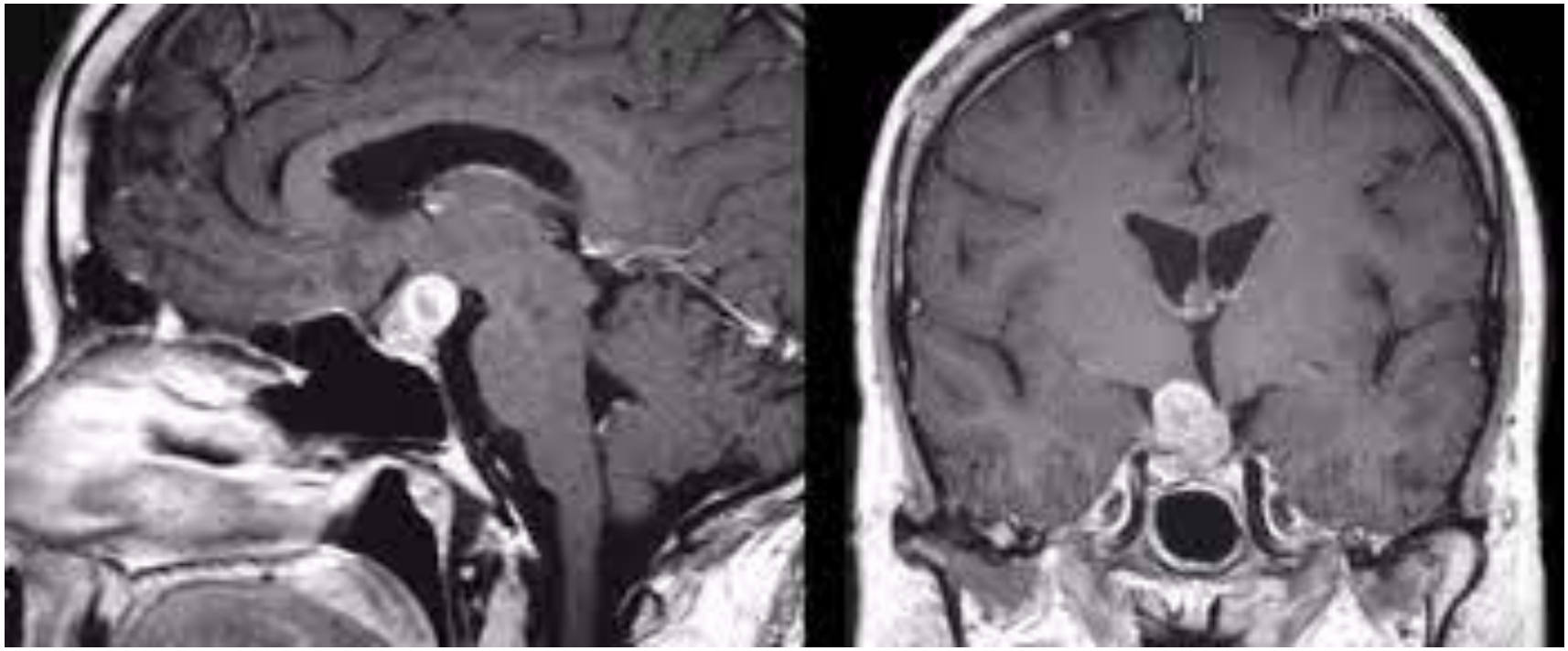
■ for Cushing's: serotonin antagonist (cyproheptadine), inhibition of cortisol production (ketoconazole)

■ for acromegaly: somatostatin analogue (octreotide) ± bromocriptine

■ endocrine replacement therapy



- surgical
- endoscopic trans-sphenoidal, trans-ethmoidal, and less commonly trans-cranial approaches (i.e. for significant suprasellar extension)



Vestibular Schwannoma (Acoustic Neuroma)

- slow-growing (60% show no growth over 1 yr; average rate for growing tumors 1-2 mm/yr), benign posterior fossa tumour (8-10% of tumours)

- arises from vestibular nerve of CNVIII in internal auditory canal , expanding into bony canal and cerebello-pontine angle (CPA)

- if bilateral ,diagnostic of NF2

- epidemiology : 1.5/100,000 ; all age groups affected , peaks at 4th-6th decades

Clinical Features

- Early clinical triad: (tumour<2cm) unilateral progressive hearingloss 98% , tinnitus , and disequilibrium (compression of CN VIII)
- Later clinical features:

■ tumour usually >2 cm: otalgia, facial numbness + weakness, changes to taste (due to CN V and VII compression, respectively)

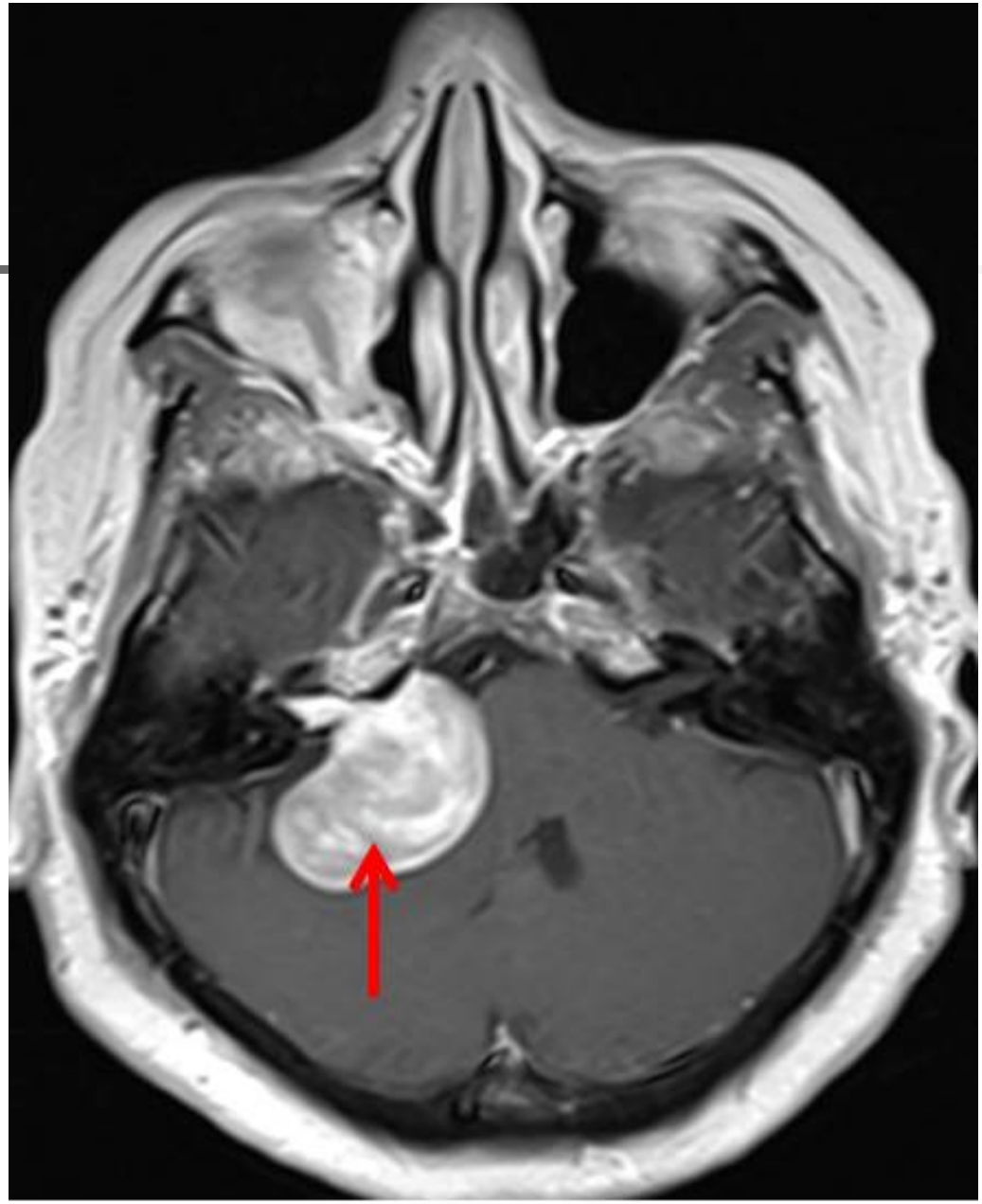
■ tumour usually >4 cm: ataxia, H/A, N/V, diplopia, cerebellar signs (due to brainstem compression; ± obstructive hydrocephalus)

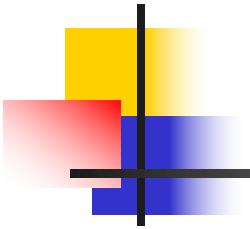
Investigations

- MRI with gadolinium or T2 FIESTA sequence (>98%sensitive/specific) ; CT with contrast 2nd choice
- audiogram , brain stem auditory evoked potentials , caloric tests.

Treatment

- expectant : serial imaging (CT/MRI q6mo) and audiometry if tumor is small , hearing is still preserved, high perioperative risk, or elderly patient
- radiation: Stereotactic Radiosurgery (Gamma Knife) SRS or XRT
- surgery: if lesion>3cm , brain stem compression , edema , hydrocephalus
- Curable if complete resection (almost always possible)
- Operative complications: CSF leak , meningitis , required shunt ; CNV,VII,VIII dysfunction
- (proportional to tumour size; only significant CNVIII disability if bilateral)
- Implications for testing of family members of NF2 mutation carrier





- Questions??