#### BRAIN TUMORS

Dr. Mahmoud Abdallat Neurosurgery Department

#### 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 dropmetastases to spinal cord from a primary CNS tumour (rare)

# Epidemiology

#### Table 8. Tumour Location: Etiology and Clinical Feature

	Supratentorial	Infratentorial (Posterior Fossa)
Epidemiology		
<b>Age &lt;15 yr</b> 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
<b>Age &gt;15 yr</b> 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	<ul> <li>Seizure: commonly the first symptom</li> <li>Progressive neurological deficits (70%)</li> <li>Frontal lobe: hemiparesis, dysphasia, personality changes, cognitive changes</li> <li>Temporal lobe: auditory/olfactory hallucinations, memory deficits, contralateral superior quadrantanopsia</li> <li>Mental Status Change: depression, apathy, confusion, lethargy</li> <li>"Tumour TIA" (transient ischemic attack) stroke like symptoms caused by <ul> <li>a) occlusion of vessel by tumour cells</li> <li>b) hemorrhage</li> <li>c) 2° to "steal phenomenon" - blood is shunted from ischemic regions to non-ischemic regions</li> </ul> </li> <li>Endocrine disturbance - with pituitary tumours (see Endocrinology, E20)</li> </ul>	<ul> <li>Brainstem involvement: cranial nerve deficits and long tract signs</li> <li>N/V: compression on vagal nucleus/area postrema</li> <li>Diplopia: direct compression CN VI Vertigo</li> <li>Nystagmus</li> <li>Truncal ataxia + titubation: cerebellar vermis lesions</li> <li>Limb ataxia, dysmetria, intention tremor: cerebellar hemisphere lesions</li> <li>Obstructive hydrocephalus more common than supratentorial lesions</li> </ul>	

#### 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



- 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<sup>th</sup> 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 .

- Gradual vs acute onset
- 1. headache
  - result of :
  - increase in ICP
  - invasion or compression of pain sensitive
  - secondary to vision difficulties

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

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

- 5. subtle changes in personality and behavior Frontal lobe
- progressive neurological deficit
   depend on site

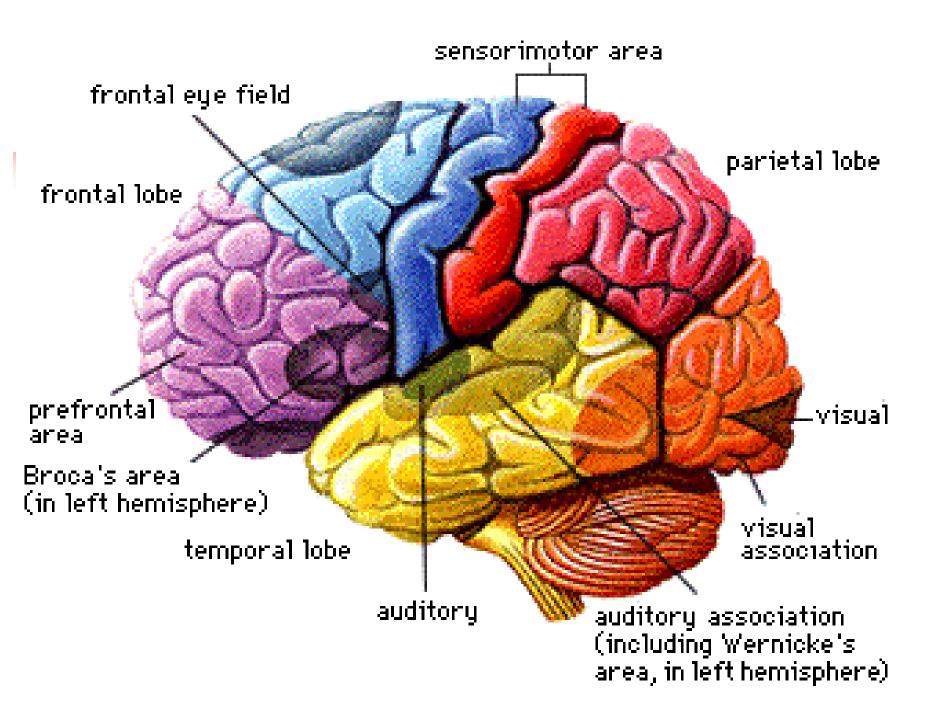
signs and symptoms are divided according to tentorium cerebelli

# 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



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

#### 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

#### brain CT

 site , mass effect , bone destruction , enhancement , multiplicity

#### enhanced tumors

- high grade gliomas
- meningioma
- mets
- acoustic neuroma
- large pituitary tumors

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

#### 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 Can be confused with glioblastoma
- 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

Vasogenic edema

 steroid are used specially with mets, meningioma and GBM

### **Surgical Treatment**

#### aim of surgery

to take a biopsy

#### We aim for total resection but when it's not possible to resect the entire tumor we go for subtotal resection & radiotherapy

- 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

To target the tumor itself rather than exposing the whole brain to radiation we go for stereotactic radiotherapy (navigational MRI / Frame based)

# Radiotherapy

#### complication :

- increase edema
- demylenation
- radionecrosis
- affect cognitive functions
   Especially in kids <3 y.o (developing brain)
- 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: We choose ones that cross the BBB

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



- 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

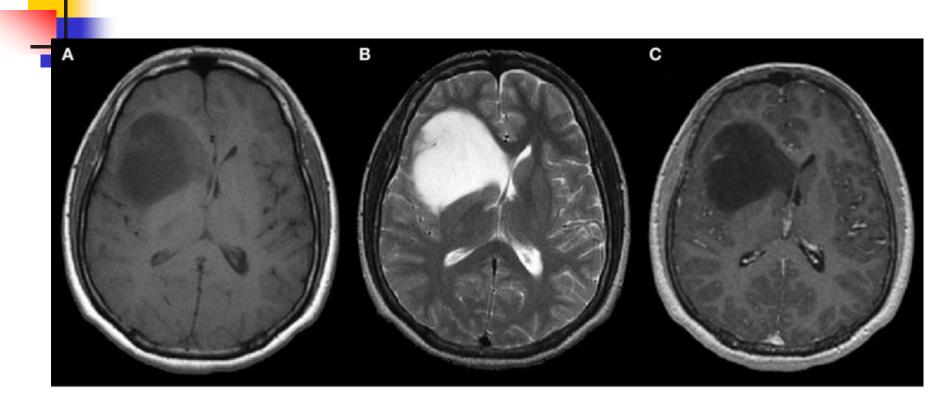
- multiple classification systems
- WHO :
  - Grade 1 : pilocytic astrocytoma
  - **Grade 2** : diffuse astrocytoma
  - **Grade 3** : anaplastic astocytoma
  - Grade 4 : glioblastoma multiforme

# LOW grade No enhancement (intact BBB) Site :

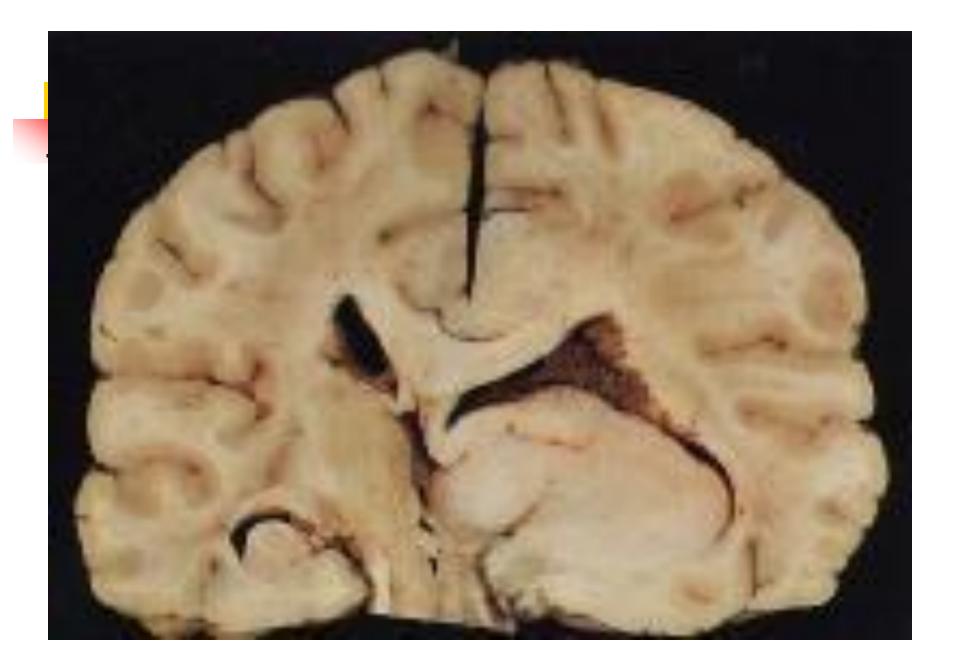
- In adults usually in cerebral hemispheres
- In children : in cerebellum
- Macroscopic features :
  - Not capsulated , no distinct margins
  - Relatively Avascular
  - Firm fibrous consistency
  - 15% show fine calcium deposit
  - Occasionally may invade diffusely

#### Microscopically:

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



T1 with contrast



## High grade

- Site :
  - cerebral hemisphere

#### Macroscopic features:

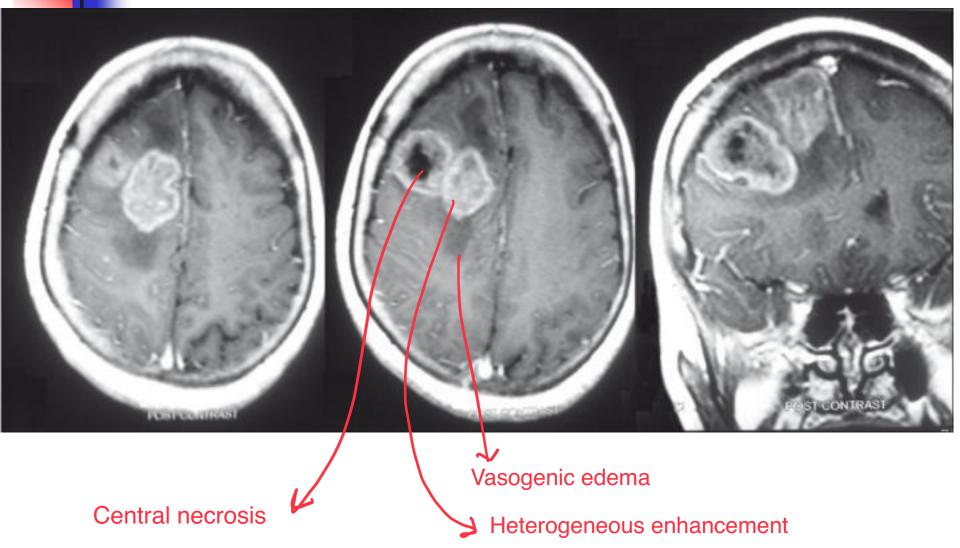
- Highly vascular margin ,necrosis
- Butterfly glioma

#### Microscopic features

- Grade 3
- Grade 4

Rapidly growing and widely infiltrating

#### Subfalcine herniation



## **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

- Iarge 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 Vascularity of the tumor (if highly vascular >> embolization prior to surgery)

### 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

The dr said that in high grade tumors Survival without treatment >> 6 months Survival following surgery alone >> 1 year Survival following surgery + adjuvant therapy >> 1.5-2 years However the numbers shown below are different

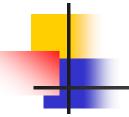
at present there is no satisfactory treatment for grade 3 and 4

surgery alone is 17 weeks

Prognosis

adjuvant radiotherapy is 37 weeks

Iow 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



as astrocytoma

### Investigations

- CTMRI
  - Calcification in 90%
  - Enhancement in 50%
  - Well demarcated edges





### 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

- CTMRI
  - Tumor arise in ventricle and enhance
  - calcification in 90% specially supratentorial

### Spread by:

- Seeding thru CSF Investigated through a CSF sample
- 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 All are grade 4

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

In most of the countries medulloblastoma is considered the most common brain tumor in children. However, in some other countries pilocytic astrocytoma is considered the commonest.

## Medulloblastoma

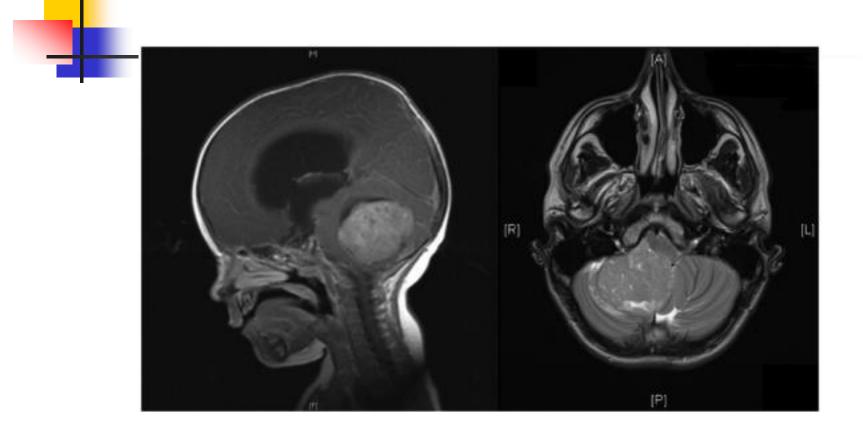
CT

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

### Treatment

- Treat hydrocephalus
- Surgery
- Neuraxis radiation Brain + spinal cord

- Prognosis
  - 5 years survival is 40 60 %



## 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**

We don't care about the histological classification that much

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

Grade 1-2: Benign (grade 2 is atypical so it's neither malignant nor benign but may become malignant at some point) Grade 3: Malignant

## 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

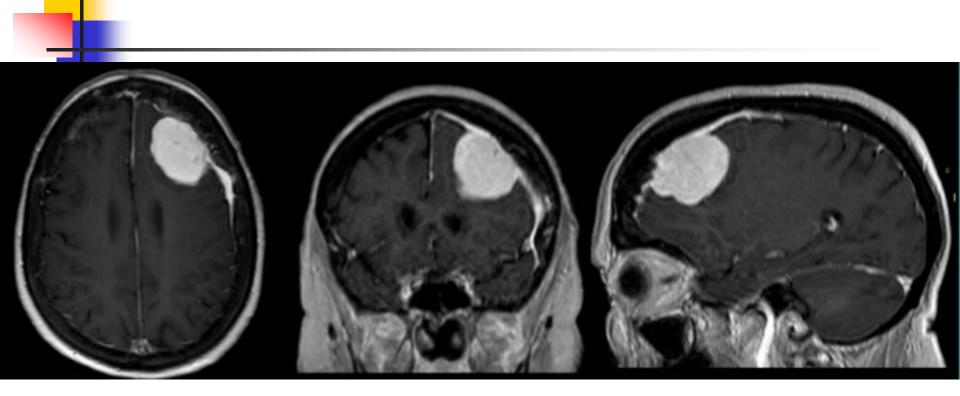
## Investigations

### 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



Homogeneous enhancement

### Pituitary adenoma:

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

## classification

Most likely functional Most likely nonfunctional/ mass effect ■ 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

- $\rightarrow$  The most common is prolactinoma
- All are microadenomas except for prolactinoma

The 1st line of treatment in all of them is surgical except for prolactinoma

# **Clinical Features**

- masseffects
- H/A
- Bitemporal hemianopsia (compression of optic chiasm); hydrocephalus (3<sup>rd</sup> 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

Presents with the symptoms of subarachnoid hemorrhage

- 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. <sup>Only if surgery is</sup> bromocriptine)

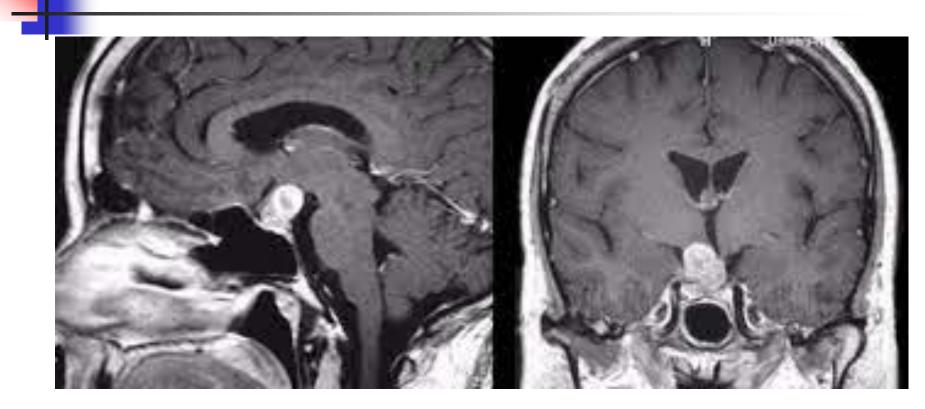
> for Cushing's: serotonin antagonist (cyproheptadine), inhibition of cortisol production (ketoconazole)

> for acromegaly: somatostatin analogue (octreotide) ± bromocriptine

endocrine replacement therapy Panhypopituitarism

### surgical

endoscopic trans-sphenoidal, transethmoidal, and less commonly transcranial approaches (i.e. for significant suprasellar extension)



### Vestibular Schwannoma (Acoustic

**Neuroma**) It could affect any nerve but its most common site is CN8

 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
- Rare epidemiology : 1.5/100,000 ; all age groups affected , peaks at 4th-6<sup>th</sup> 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 numbress + 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 2<sup>nd</sup> choice

Judiogram , brain stem auditory evoked potentials , caloric tests.

Baseline readings to assess improvement

### Treatment

If small or if in a

location that

makes it

difficult on us to

remove it surgically

or if there's an

- 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

Cerebellopontine angle

Large mass >> surgery

