

Meningioma

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EPIDEMIOLOGY..... 1
ETIOLOGY 1
PATHOLOGY..... 1
 Multiple meningiomas..... 2
 Location..... 2
 Histology 4
CLINICAL FEATURES 6
DIAGNOSIS..... 7
 DIFFERENTIAL DIAGNOSIS 10
TREATMENT 10
 SURGERY 11
 RADIOTHERAPY 11
 CHEMOTHERAPY 12
PROGNOSIS, FOLLOW-UP 12
PEDIATRIC MENINGIOMAS..... 13
MENINGIOMAS OF SPINAL CANAL → see p. Onc54 >>

EPIDEMIOLOGY

- 13-30% of all primary intracranial neoplasms (only 1-5% in children); 30% in Africa!
- at autopsy, 1.4-2.3% people have undiagnosed asymptomatic meningiomas.
- INCIDENCE increases with age (in general, 2 cases per 100,000 individuals):
 - 0-19 years - 0.12 per 100,000 individuals - occur in children (more aggressive forms) >>
 - 20-34 years - 0.74
 - 35-44 years - 2.62
 - 45-54 years - 4.89
 - 55-64 years - 7.89
 - 65-74 years - 12.79
 - 75-84 years - 17.04
 - ≥ 85 years - 18.86
- male-to-female ratio = 1:1.4-2.8 (peaks to 1:3.5: in patients 40–44 years);
 - ratio increased over time - use of hormonal medications (hypothesis has not been proven to date).
 - meningiomas associated with HEREDITARY tumor syndromes occur in younger patients, and more equally in men and women.
 - ATYPICAL and ANAPLASTIC meningiomas show male predominance.
 - SPINAL meningiomas – 90% women.
- in Scandinavia, incidence has increased between 1968 and 1997 from 2.6 to 4.5 per 100 000 in women, and from 1.4 to 1.9 in men.
- in one Italian study, numbers have remained stable for decades.

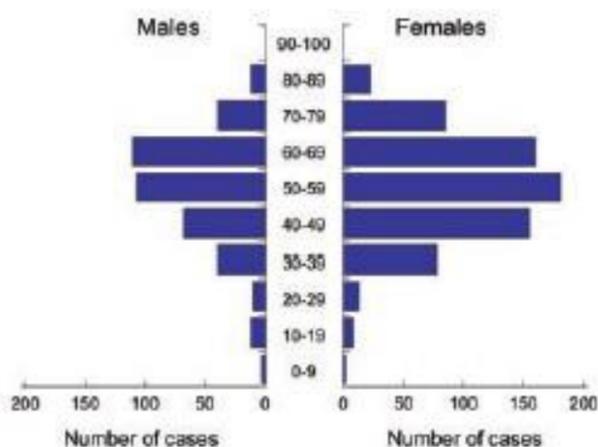


Fig. 10.01 Age and sex distribution of meningioma, based on 1078 cases treated at the University Hospital Zurich.

ETIOLOGY

- Radiation**
 - meningiomas are known to be induced by low-, moderate-, and high-dose radiation (average time interval to tumor appearance of 35, 26 and 19–24 years, respectively)
 - history of low-dose irradiation (800 rad) to scalp for tinea capitis → 4-fold increased risk for multiple meningiomas decades later.
 - high-dose irradiation (> 2000 rad) for primary brain tumors
- N.B. radiation-induced meningiomas tend to be more atypical or aggressive, multifocal, highly proliferative, and occur in younger age groups.

- Genetic causes**
 - familial meningiomas are rare (unless associated with neurofibromatosis-2).
 - most common (60% of sporadic meningiomas) - loss of NF-2 gene (22q12), meningioma locus is close to but probably different from gene responsible for NF-2.
 - others - chromosomal loss of 1p, 3p, 6q, 14q, 8p12 (Werner's syndrome).
 - chromosome 7 monosomy - frequent in radiation-induced meningiomas.
 - events associated with higher grades of meningioma:
 - loss of chromosome 10.
 - loss of tumor suppressor in lung cancer-1 gene (TSLC-1).
 - loss of progesterone receptors.
 - increased expression of cyclooxygenase-2 and ornithine decarboxylase.
 - 17q - associated with progression to anaplastic meningioma.
- association between sex hormones (estrogens, progesterone, androgens) and risk for meningiomas remains under investigation.

meningiomas may wax and wane with pregnancy, and they are positively associated with breast cancer

PATHOLOGY

Benign extra-axial neoplasm of arachnoidal (meningothelial) cells in arachnoidal cap (component of arachnoidal villi in dura), typically attached to inner surface of dura mater.

- globular, well-demarcated (MENINGIOMA EN MASSE).
- MENINGIOMA EN PLAQUE – sheet-like extension that covers dura (may not invaginate parenchyma); when biopsy is taken from macroscopically uninvolved dura, abnormal cells are found there.
- CAVERNOUS SINUS MENINGIOMA – infiltrates cavernous sinus and becomes interdigitated with its contents.
- firm to soft.
- wide dural attachment.
- cut surface is either translucent pale or homogeneously reddish brown (may be gritty on cutting).
- calcification (small punctate calcium deposits) within meningiomas is found in 10-20% cases.
- necrosis or extensive hemorrhage are not present.

- **grow** very slowly (≈ 0.24 cm in diameter per year).
- **invaginate into underlying brain without invading it** (i.e. well demarcated from surrounding brain);
 - degree of **edema** around tumor is variable (may be massive).
 - **true brain invasion** upgrades to grade II (even if histology is benign).
- can invade **skull bones** \rightarrow *hyperostosis* or bone *destruction!*; sometimes causes reactive *hyperostosis* without invasion!
 - bone invasion has been reported in 20-68% of studies with histopathologically confirmed data.
 - bone infiltration has been described in 10%–40% of cases with no hyperostosis (imaging is insufficient to predict bone invasion!!!)
- **blood supply** - from dura.
 - over long term, **parasitization (recruitment) of cortical vessels** by malignant tumors over cerebral convexity or of branches of ophthalmic artery by subfrontal masses is not rare – makes tumor resection much more difficult.
- **encased vessels**: if not circular, vessel is not invaded; if circular, vessel wall may be invaded (esp. if lumen is abnormal on MRI flow voids).
- **malignant** potential is extremely rare (features as clear signs of malignancy: **cortical invasion** by tumor and **distal metastasis**).
 - immunohistologic stains for mitotic activity used to predict malignant behavior of meningiomas:
 - a) **bromodeoxyuridine labeling** (IV injection before tumor removal) – tumors with indices $> 5\%$ have recurrence rate $\approx 100\%$.
 - b) **proliferating cell nuclear antigen PCNA** (can be performed on fixed specimens).
 - c) **Ki-67** (Ki-67 antigen is present in nuclei of cells in G1, S, G2 and M-phases, while, resting cells in G0 phase do not express it).

MULTIPLE MENINGIOMAS

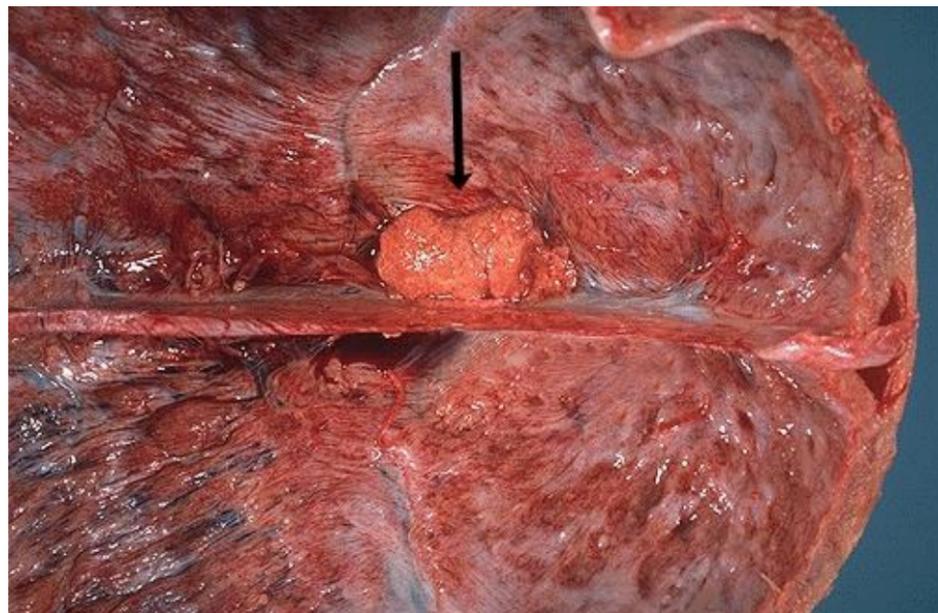
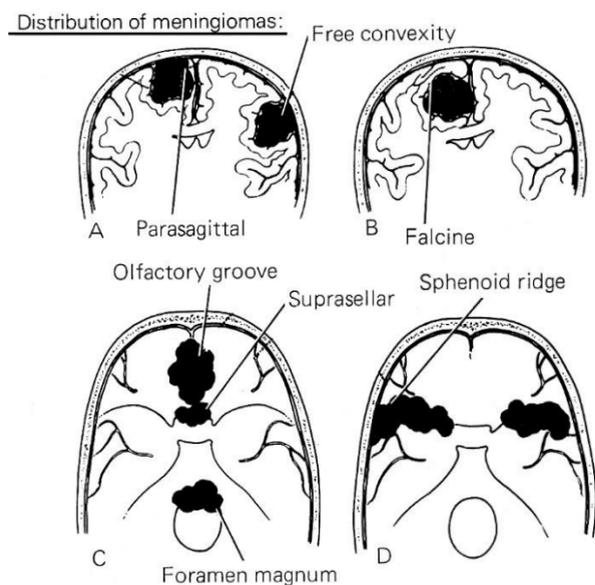
- 1) neurofibromatosis type 2 (NF2)
- 2) families with hereditary predisposition to meningioma
- 3) $< 10\%$ of cases of sporadic meningiomas

LOCATION

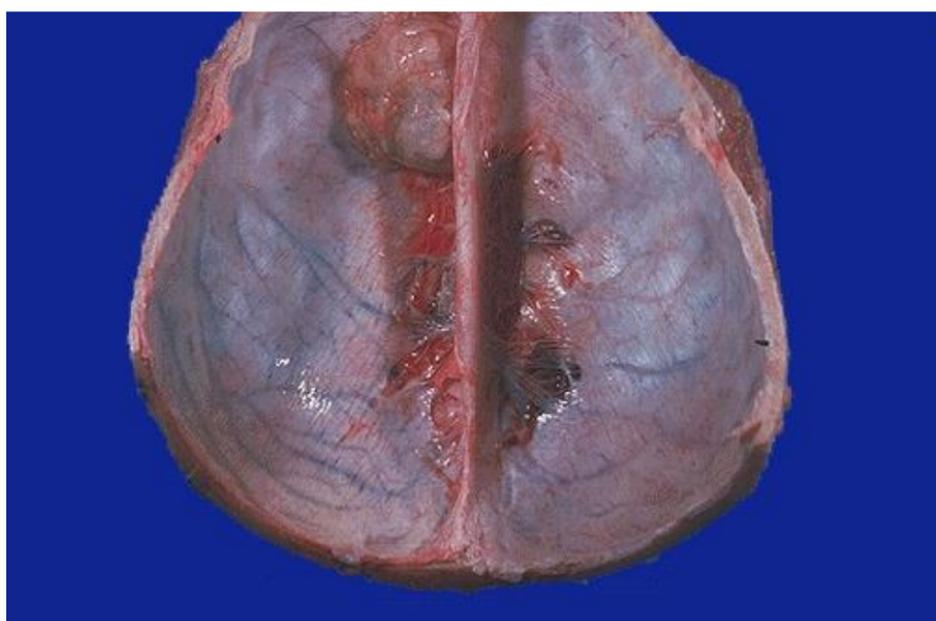
- **brain surface** wherever there is dura (over **convexity** or at **skull base**).
- 2% meningiomas occur in **intraventricular** location (presumably from cells migrating in with choroid plexus; 75% are located in left occipital horn).
- rarely in **intraosseous** location.
- meningiomas in **spine** are almost always found in **women** (10:1). see p. Onc54 >>

Site of Tumor	%
Parasagittal (arise from convexity or falx)	25
Convexity (usually around coronal suture)	20
Sphenoidal ridge	20
Olfactory groove (arise from lamina cribrosa)	10
Suprasellar (region of tuberculum sellae)	10
Posterior fossa (on clivus or foramen magnum)	10
Middle fossa	3
Intraventricular	2

N.B. 90% meningiomas are **supratentorial!**



Source of picture: "WebPath - The Internet Pathology Laboratory for Medical Education" (by Edward C. Klatt, MD) >>

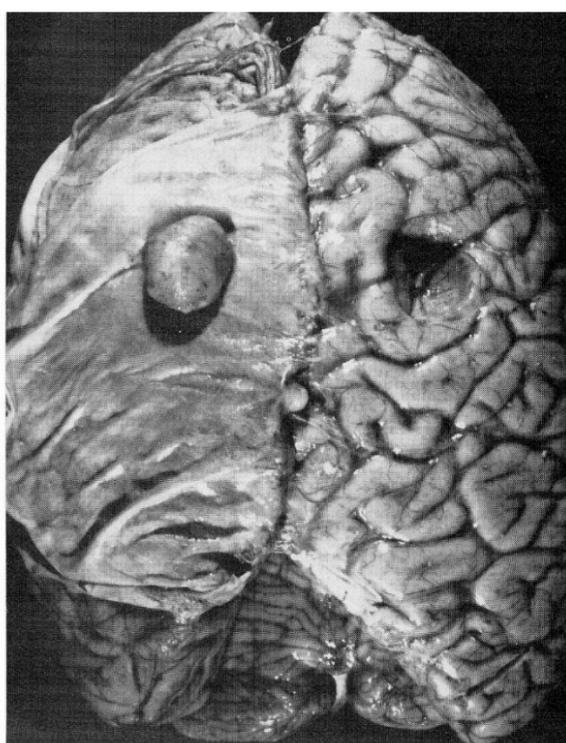


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Note how this meningioma beneath dura has compressed underlying cerebral hemisphere:



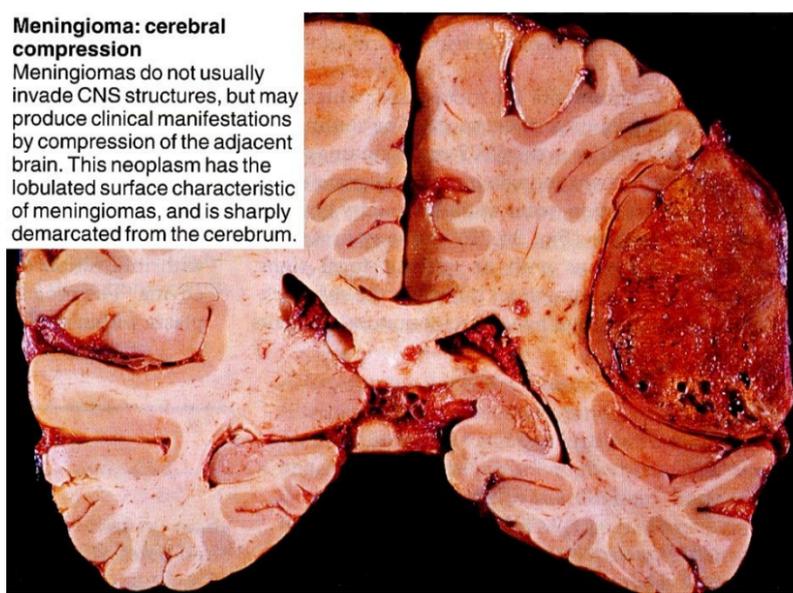
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Reflected dura (on left) showing one large and one small (in middle of illustration) meningioma. Note prominent indentation of right cerebral hemisphere by the larger tumor.

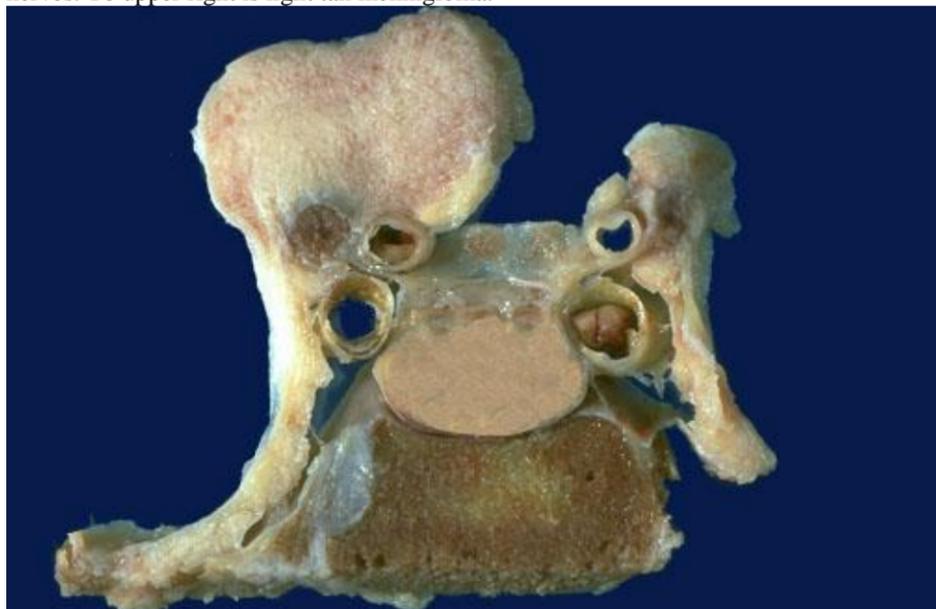
Meningioma: cerebral compression

Meningiomas do not usually invade CNS structures, but may produce clinical manifestations by compression of the adjacent brain. This neoplasm has the lobulated surface characteristic of meningiomas, and is sharply demarcated from the cerebrum.



Source of picture: James C.E. Underwood "General and Systematic Pathology" (1992); Churchill Livingstone; ISBN-13: 978-0443037122 >>

Incidental finding at autopsy - meningioma of **sphenoid ridge**; base of sella is at bottom center, above which is tan pituitary. Above and lateral to pituitary are common carotid and anterior cerebral arteries, above which slightly medially are optic nerves. To upper right is light tan meningioma:



Source of picture: "WebPath - The Internet Pathology Laboratory for Medical Education" (by Edward C. Klatt, MD) >>

Surgical view - dura is opened, and meningioma can be seen extending en plaque over brain surface:

Intraoperative view shows skull involvement:



Bone flap was removed. Note tumoral breach of dura:



Here is resected meningioma:



Source of picture: "WebPath - The Internet Pathology Laboratory for Medical Education" (by Edward C. Klatt, MD) >>

HISTOLOGY

WHO 2007 Classification of Meningiomas:

Grade	Subtypes
Grade I - (benign) meningioma (90-94%)	Meningothelial, fibrous, transitional, psammomatous, angiomatous, microcystic, secretory, lymphoplasmacyte-rich, metaplastic
Grade II - atypical meningioma (5-20%)* 4-19 mitoses per 10 high-power fields or brain invasion	Atypical, clear cell (intracranial), chordoid II
Grade III - anaplastic meningioma (1-5%) ≥ 20 mitoses per 10 high-power fields	Rhabdoid, papillary

Many previously called 'angioblastic' meningiomas have now been reclassified as intracranial *HEMANGIOPERICYTOMAS*

N.B. tumor type that closely resembles meningioma is *HEMANGIOPERICYTOMA*

*Full WHO 2007 criteria for atypical meningioma - 1 or more of the following:

- 4-19 mitoses per 10 high-power fields
- At least 3 of the following 5 atypical features: spontaneous necrosis, macronucleoli, loss of architecture (sheeting), hypercellularity, small-cell change.
- Brain invasion
- Predominant (> 50% of tumor volume) clear-cell or chordoid morphology

- certain histological subtypes or meningiomas with specific combinations of morphologic parameters are associated with less favorable clinical outcomes and correspond to WHO grades II (atypical) and III (anaplastic or malignant).
- can have nuclear polymorphism.

Most common histologic subtypes:

- meningothelial (syncytial) - densely packed polygonal cells with *no clearly visible cell membranes* arranged in solid sheets and whorled nests; characteristic calcified foci (*psammoma bodies*).
- fibroblastic (fibrous) - sheets of interlacing *long spindle cells*; intercellular stroma is composed of reticulin and *abundant collagen*.
- transitional (mixed) - features common to both meningothelial and fibroblastic varieties.

Meningiomas grouped by likelihood of recurrence and grade:

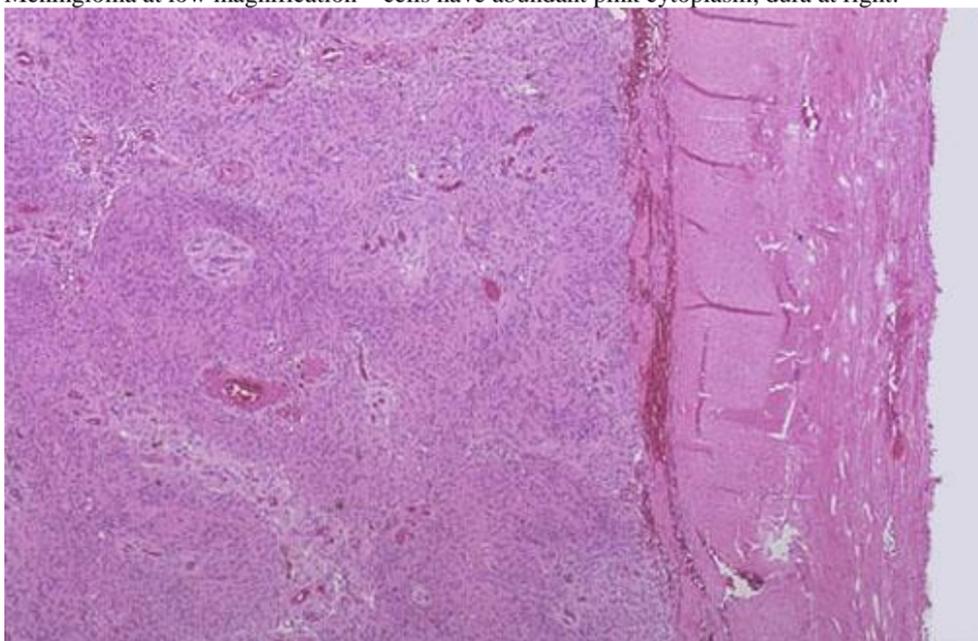
Meningiomas with low risk of recurrence and aggressive growth:		
Meningothelial meningioma	WHO grade I	ICD-O code 9531/0
Fibrous (fibroblastic) meningioma	WHO grade I	9532/0
Transitional (mixed) meningioma	WHO grade I	9537/0
Psammomatous meningioma	WHO grade I	9533/0
Angiomatous meningioma	WHO grade I	9534/0
Microcystic meningioma	WHO grade I	9530/0
Secretory meningioma	WHO grade I	9530/0
Lymphoplasmacyte-rich meningioma	WHO grade I	9530/0
Metaplastic meningioma	WHO grade I	9530/0
Meningiomas with greater likelihood of recurrence and/or aggressive behaviour:		
Chordoid meningioma	WHO grade II	9538/1
Clear cell meningioma (intracranial)	WHO grade II	9538/1
Atypical meningioma	WHO grade II	9539/1
Papillary meningioma	WHO grade III	9538/3
Rhabdoid meningioma	WHO grade III	9538/3
Anaplastic (malignant) meningioma	WHO grade III	9530/3
Meningiomas of any subtype or grade with high proliferation index and/or brain invasion		

Immunohistochemistry:

- 80% stain positive for **epithelial membrane antigen (EMA)**.
- stain **negative** for **anti-Leu 7 antibodies** (positive in *SCHWANNOMAS*) and for **glial fibrillary acidic protein (GFAP)**.
- PROGESTERONE receptors** present consistently in cytosol of meningiomas; presence of other sex hormone (estrogen, androgen) receptors is much less consistent.

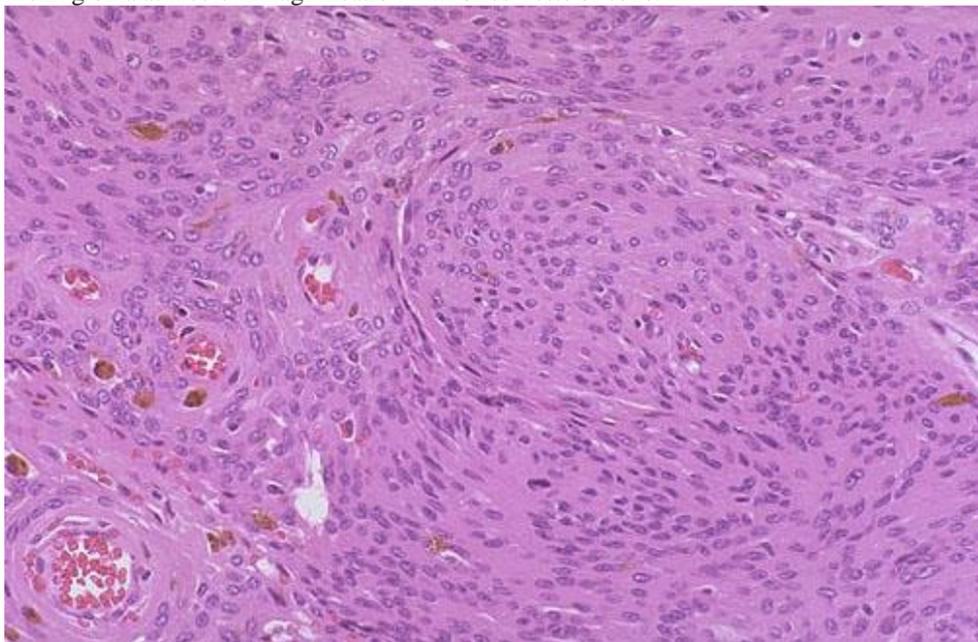
- 88% of meningiomas have progesterone, 40% have estrogen and 39% have androgen receptors.
- with worsening grade, meningiomas lose **progesterone receptors** and start expressing **estrogen receptors**.
- **SOMATOSTATIN receptors** present 100% (esp. SSTR2).

Meningioma at low magnification – cells have abundant pink cytoplasm; dura at right:



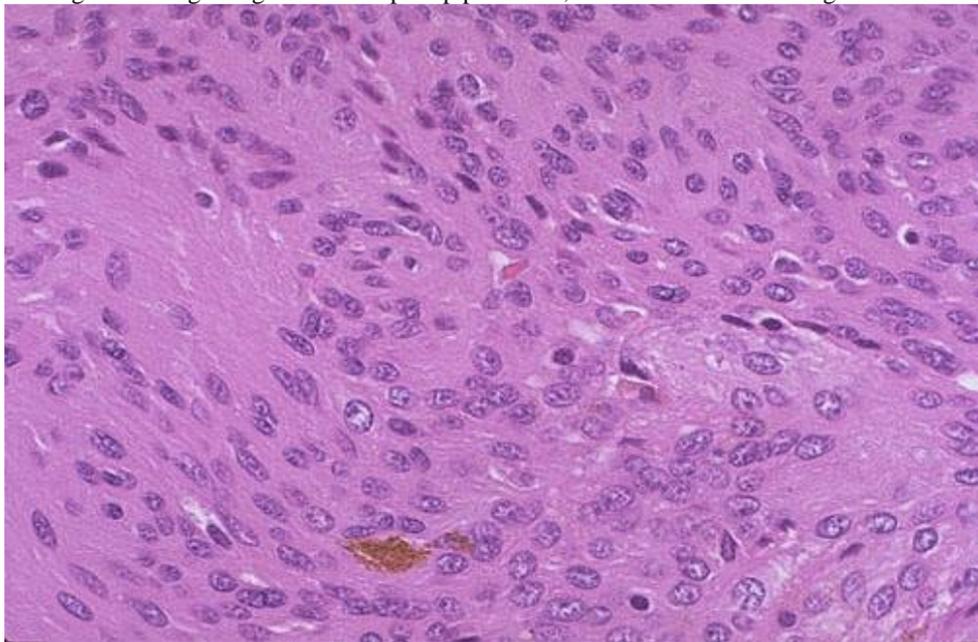
Source of picture: “WebPath - The Internet Pathology Laboratory for Medical Education” (by Edward C. Klatt, MD) >>

Meningioma at medium magnification – whorled nests of cells:

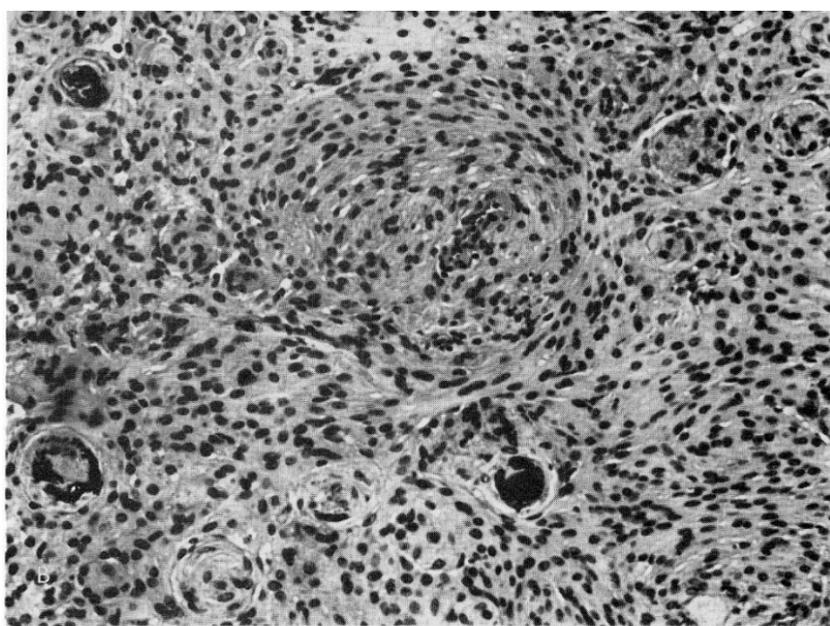


Source of picture: “WebPath - The Internet Pathology Laboratory for Medical Education” (by Edward C. Klatt, MD) >>

Meningioma at high magnification – plump pink cells; small amount of brown granular hemosiderin:



Source of picture: “WebPath - The Internet Pathology Laboratory for Medical Education” (by Edward C. Klatt, MD) >>



Transitional meningioma with hypercellularity, whorled pattern of cells, and psammoma bodies (H and E stain).

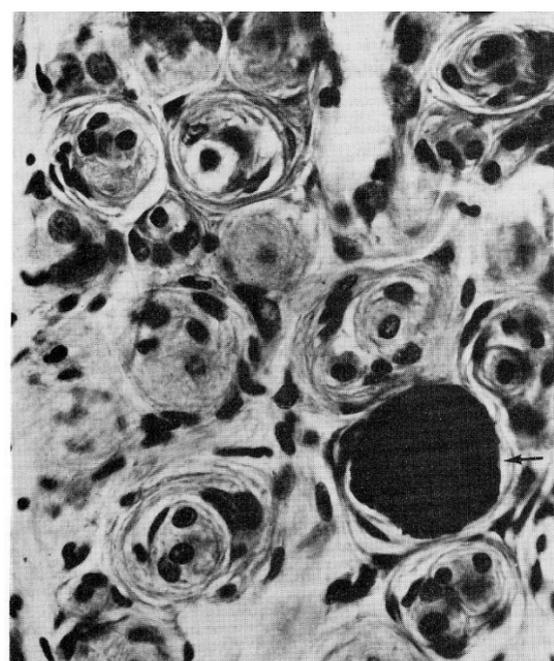
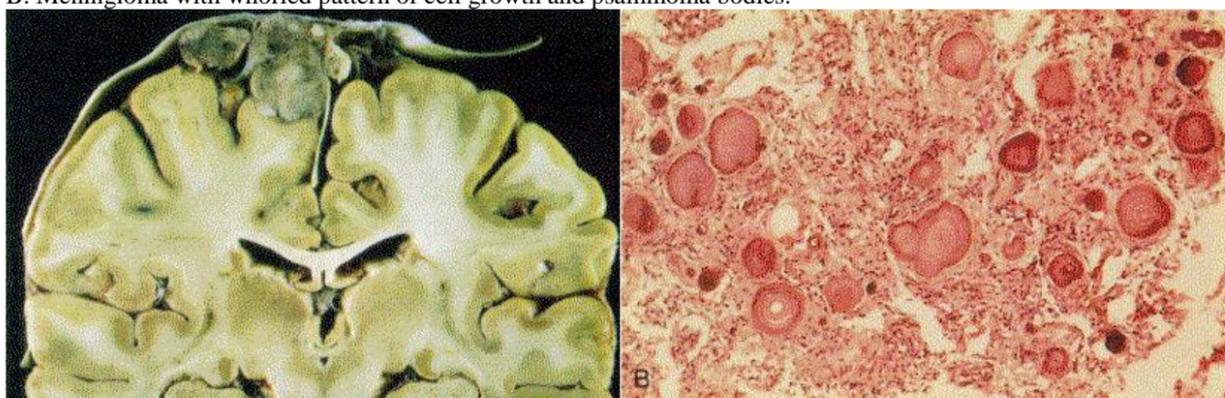


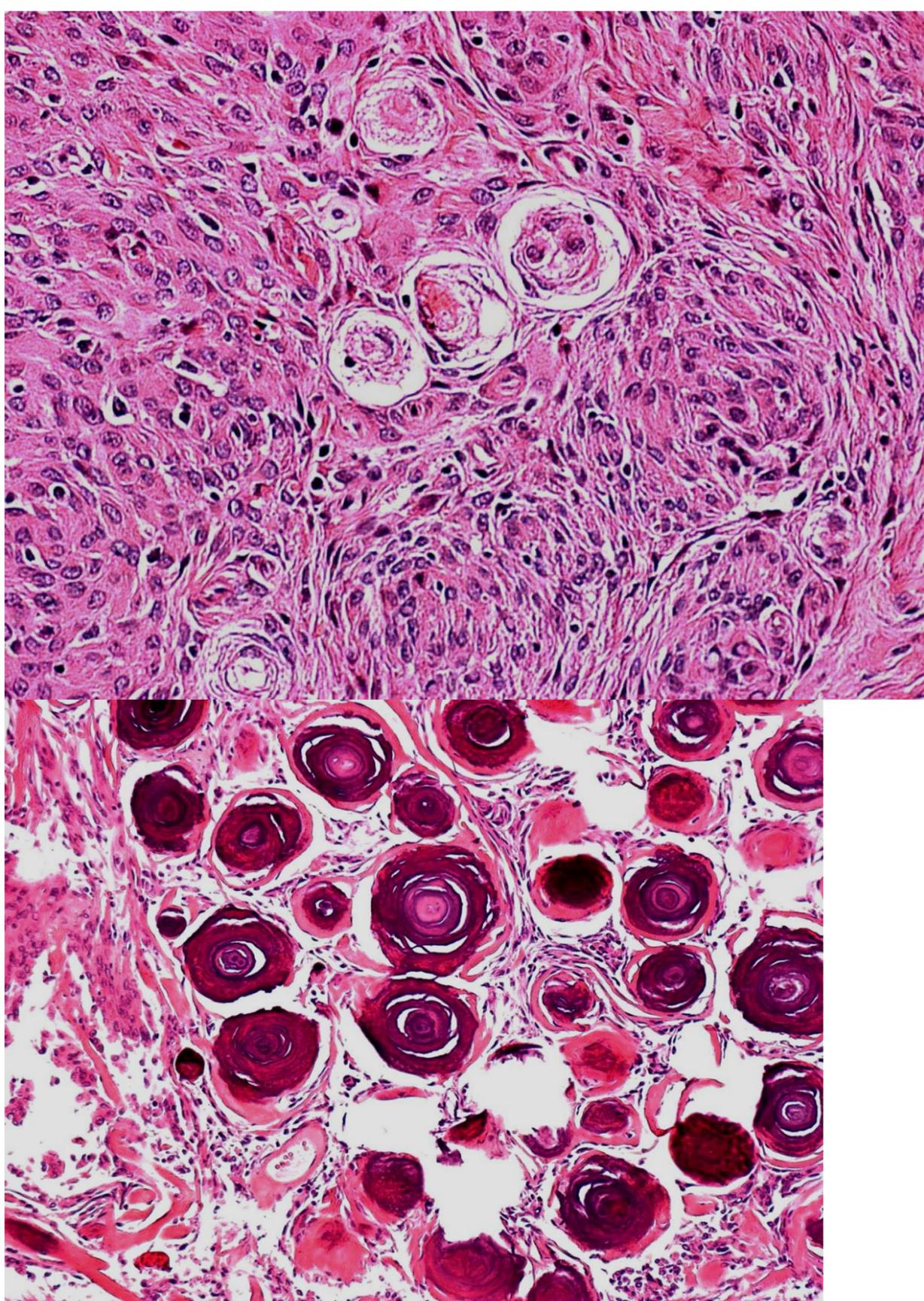
Figure 21-13. Microscopic detail of a meningioma, showing numerous concentric whorls and a large psammoma body (arrow).

A. Parasagittal multilobular meningioma attached to dura with compression of underlying brain.

B. Meningioma with whorled pattern of cell growth and psammoma bodies.



Source of picture: Ramzi S. Cotran "Robbins Pathologic Basis of Disease", 6th ed. (1999); W. B. Saunders Company; ISBN-13: 978-0721673356 >>



CLINICAL FEATURES

- may be *asymptomatic* (very slow growth sometimes permits brain to accommodate tumors even when they reach large size).
 - signs & symptoms become exacerbated during pregnancy (but usually improve postpartum).
1. **Irritation of underlying cortex** (*CONVEXITY MENINGIOMAS*) → **seizures** (risk of recurrent seizures [after surgery] increases from low after one seizure to high with every repeat seizure – indication for early surgery even for small meningiomas that cause seizures)
 2. **Compression of brain / cranial nerves**: **focal or more generalized cerebral dysfunction, cranial nerve palsies**, ultimately **ICP↑** (headache → herniation).

Location	Symptoms
Parasagittal	Contralateral leg monoparesis/numbness or paraparesis, dementia-like loss of cognition
Subfrontal	Change in mentation, apathy, disinhibited behavior, urinary incontinence
Olfactory groove	Anosmia with possible Kennedy-Foster syndrome; frontal syndrome (late)
Cavernous sinus	Multiple cranial nerve deficits (II, III, IV, V, VI)
Optic nerve sheath	Exophthalmos, monocular vision loss with optic nerve swelling & opto-ciliary shunt vessels (optic atrophy occurs before loss of vision is complete!!!)
Sphenoid wing:	
medial	Grow into cavernous sinus, carotid artery, optic nerve
middle	Grow anteriorly into orbit (proptosis)
lateral	Grow into temporal bone
Parasellar	Panhypopituitarism, visual field defects
Tentorial	May protrude within supratentorial and infratentorial compartments; hydrocephalus
Occipital lobe	Contralateral hemianopsia
Cerebellopontine angle	Decreased hearing, facial weakness and numbness
Foramen magnum	Ipsilateral cervical-occipital pain, Lhermitte's sign, spastic weakness in all 4 limbs (begins in ipsilateral arm, progresses to ipsilateral leg, and then moves to opposite leg and arm), posterior column deficits (arms > legs), sphincteric troubles, lower CN palsy (tongue atrophy & fasciculation, dysphagia)
Intraventricular	Obstructive hydrocephalus
Spinal cord	Localized spinal pain, Brown-Sequard syndrome → quadriplegia or paraparesis

3. **Vascular injuries**:
 - *PARASAGITTAL MENINGIOMAS* frequently involve **sagittal sinus** and important cortical veins that drain into this sinus (middle and posterior thirds of sagittal sinus, if involved but patent, cannot be sacrificed without severe neurologic sequelae; therefore, total resection of these tumors is often impossible!)
 - *SKULL BASE MENINGIOMAS* may narrow cerebral arteries → **TIAs, stroke**.
4. **Involvement of bone & subcutaneous* tissues** → **hyperostosis**.

*i.e. tumor may breach sanctity of dura and bone, thus appearing subcutaneously.

DIAGNOSIS

Imaging is mainstay of diagnosis (typical features and location do offer reasonable amount of certainty in diagnosis).

Plain skull radiograph – hyperostosis, bone invasion, calcifications within tumor (10-20%), enlarged vascular channels over skull vault (convexity meningiomas are heavily supplied by meningeal arteries).

- ‘blistering’ (expansion of sphenoid sinus, with elevation of its roof) is extremely suggestive of meningioma of planum sphenoidale.

CT – dural-based extraaxial tumor with well-defined borders; compresses brain without invading it (white matter buckling!!!)

- isodense or hyperdense (60%).
- enhance homogeneously and intensely (multiple meningiomas may be difficult to differentiate from metastasis).
- perilesional edema may be extensive.

MRI – isointense on all MRI sequences to cortex.

- enhance homogeneously and intensely.
- **"dural tail"** (streak of dural enhancement flanking main tumor mass) may be apparent; not pathognomonic for meningioma!
- **fat suppression** images are used for tumors adjacent to orbit or infratemporal fossa or after previous skull base approach.
- **image fusion with bone-window CT scan** may be helpful for meningiomas in cranial base locations.
- look at **T2** – if edema in surrounding brain – higher risk of seizures.

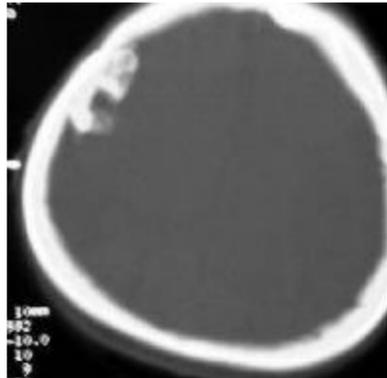
Angiography (preoperatively* - tumor vascularization [characteristically extracerebral] and encroachment on vital vascular structures) - both internal (or vertebral) and external carotid arteries should be selectively injected!

*better than MRA / MRV

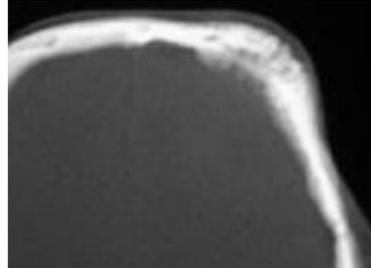
- *supply from external circulation* (sunburst or radial appearance of feeding arteries).
- cortical vessels are displaced away from tumor.
- **“mother-in-law” blush** (prolonged homogeneous vascular stain that comes early and leaves late).
- late venous images are important to determine patency of involved dural sinuses (esp. sagittal).
- tumor embolization is possible.

Somatostatin receptor **scintigraphy** with ¹¹¹In octreotide can confirm diagnosis + detect residual or recurrent tumor.

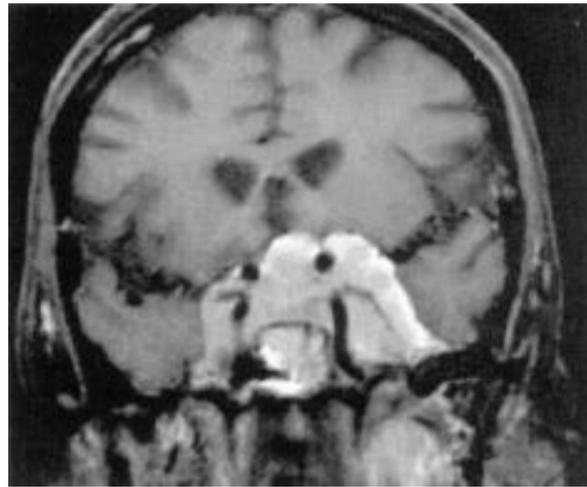
Bone-window CT reveals **calcification** of meningioma:



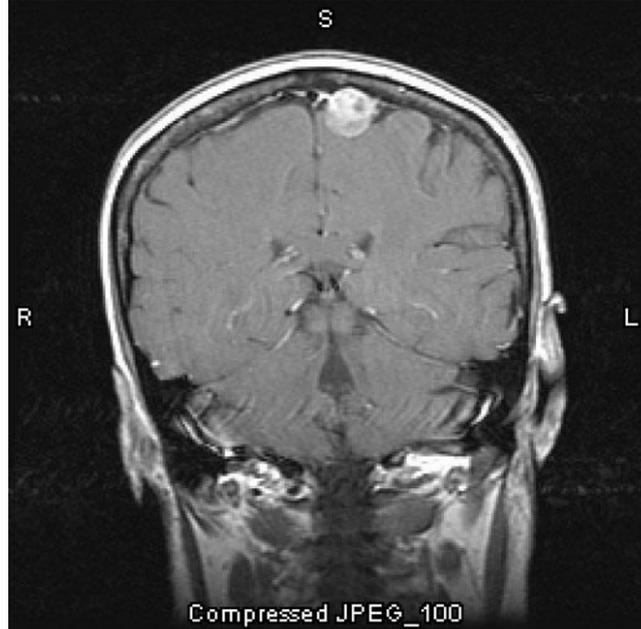
Bone-window CT scan reveals **skull involvement**; absence of tumoral calcification:



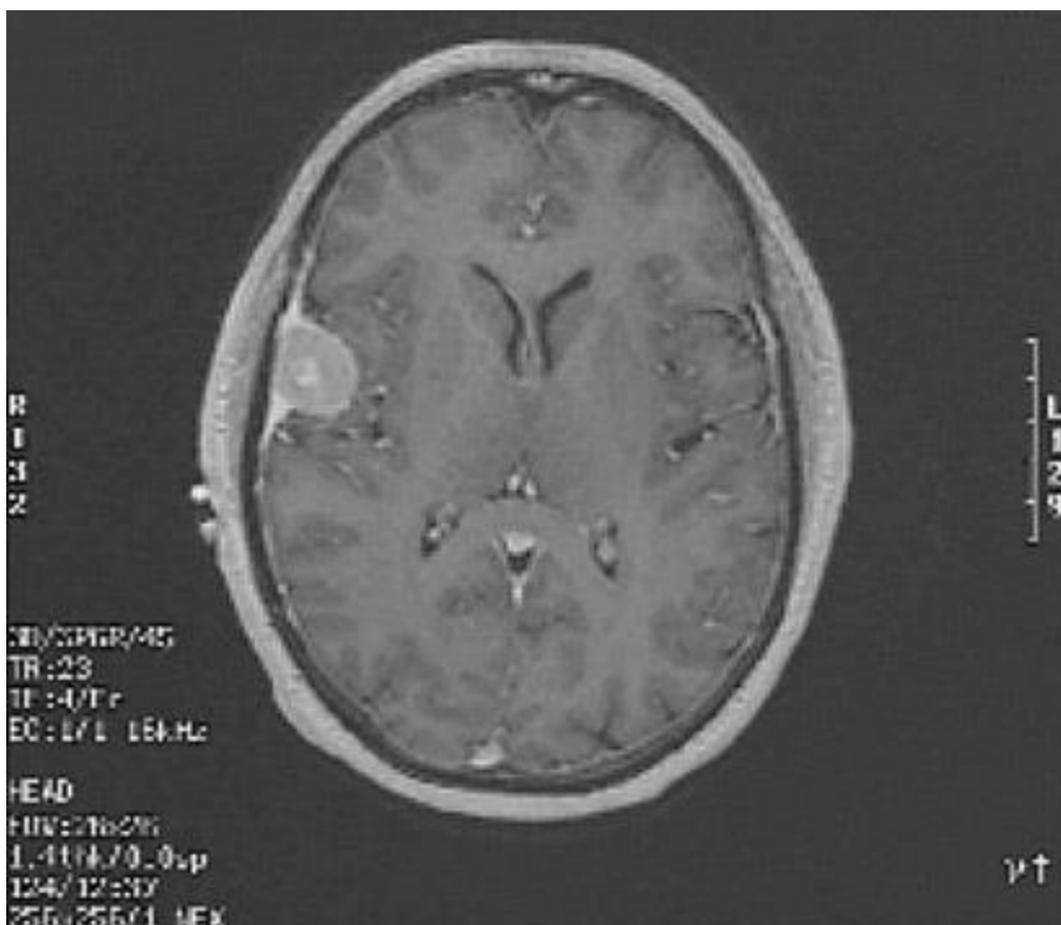
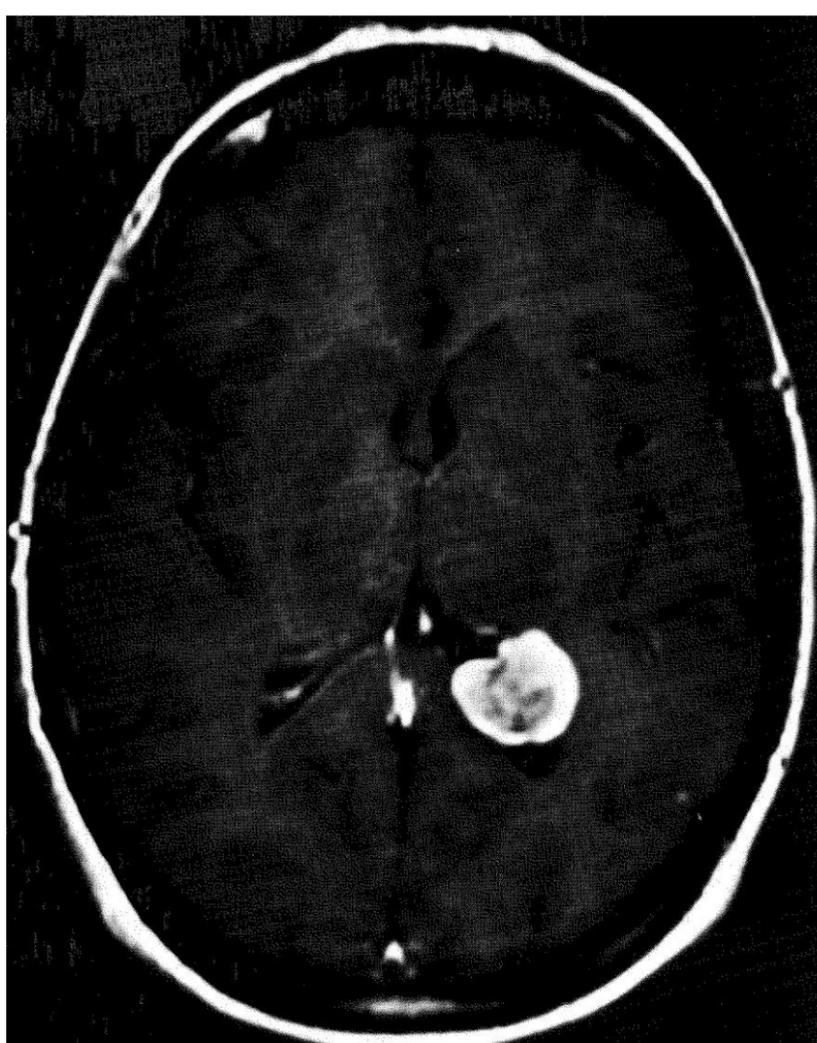
Sphenoid ridge meningioma (contrast T1-MRI): extensive tumor with bilateral cavernous sinus invasion and encasement of both carotid arteries:



Parasagittal meningioma (contrast MRI):

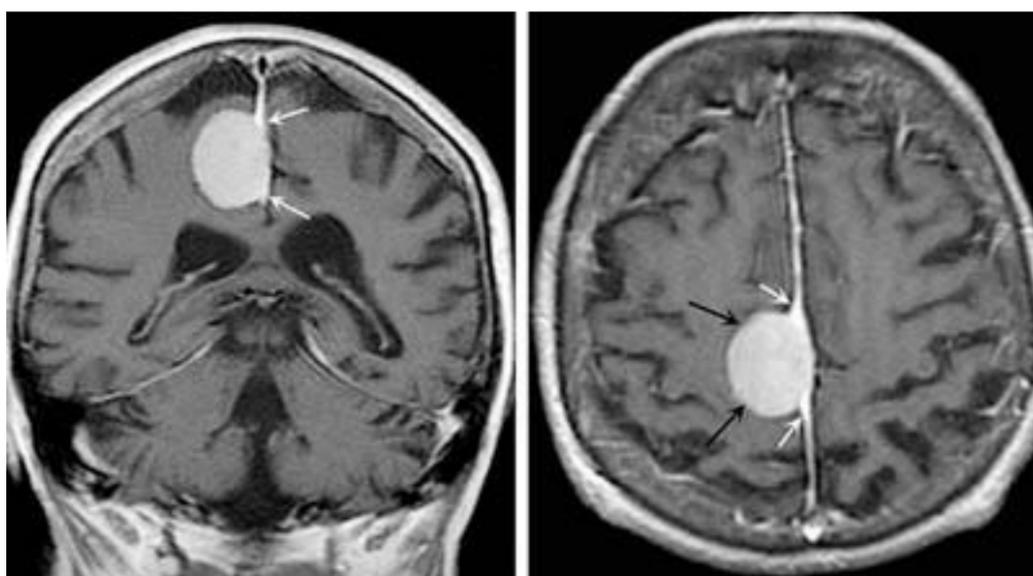


Intraventricular meningioma (MRI and angiogram):

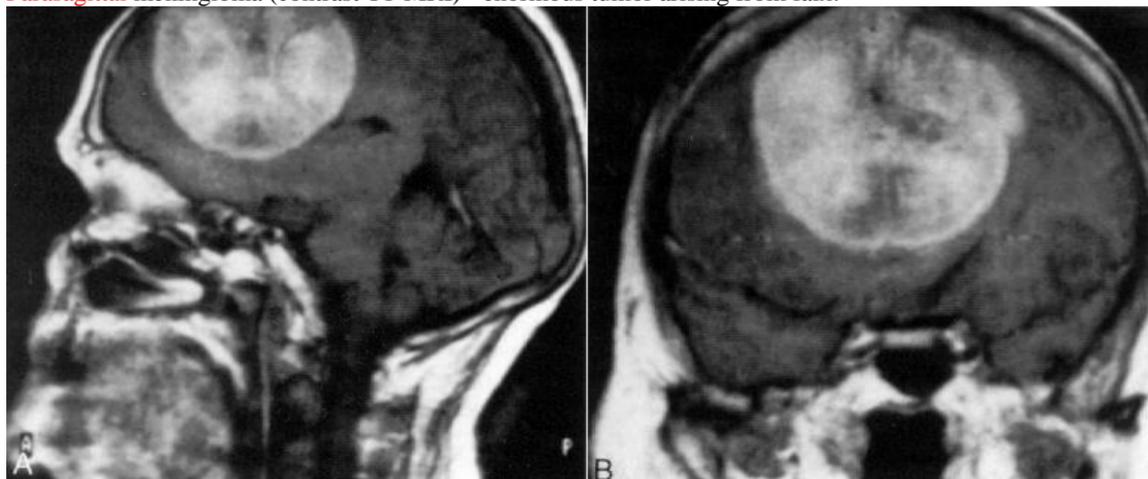


Source of picture: "WebPath - The Internet Pathology Laboratory for Medical Education" (by Edward C. Klatt, MD) >>

Falx meningioma (contrast T1-MRI) - enhancing extraaxial mass arising from falx (*arrows*); note "dural tail" that extends along falx (*white arrows*):



Parasagittal meningioma (contrast T1-MRI) - enormous tumor arising from falx:



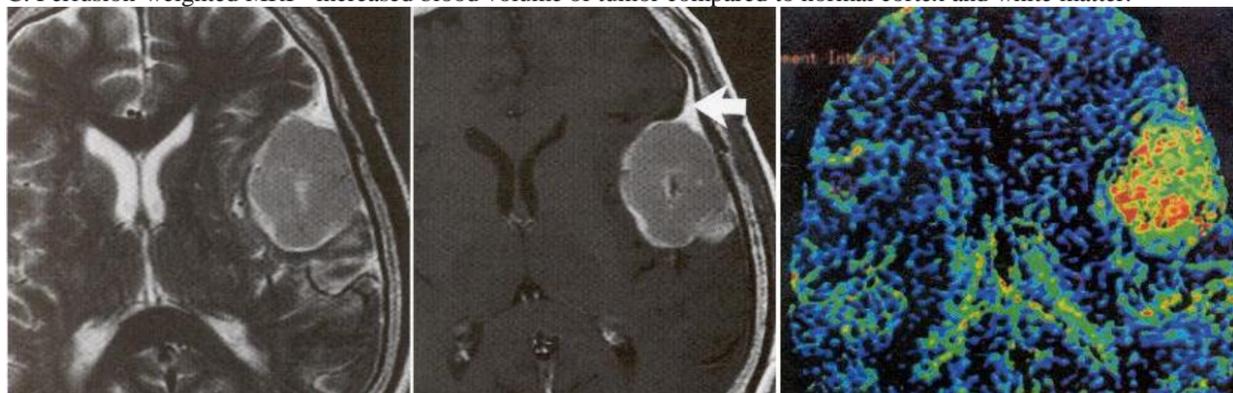
Clival / foramen magnum meningioma (contrast T1-MRI) - marked compression of medulla:



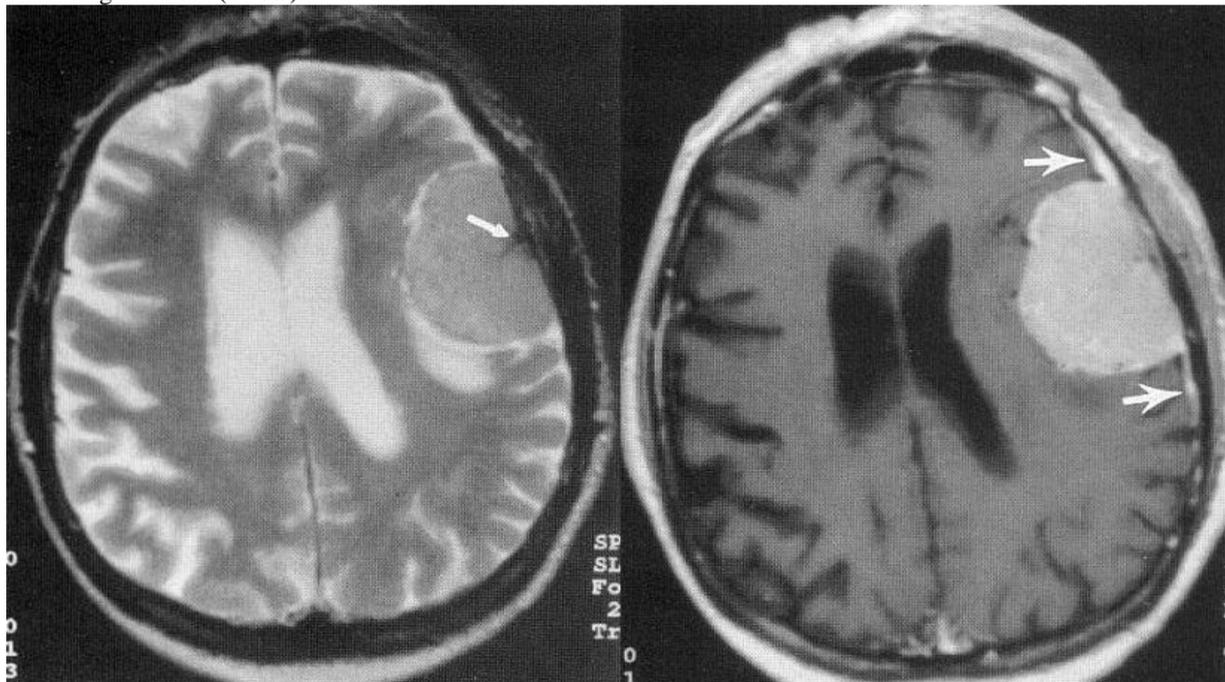
Subfrontal meningioma (A – noncontrast CT; B - contrast CT; C - lateral projection of common carotid arteriogram) - large isodense circumscribed mass in anterior cranial fossa; foci of calcification centrally; enhances homogeneously; edema in white matter of both frontal lobes and posterior displacement and splaying of frontal horns of lateral ventricles. On arteriogram mass is delineated by tumor blush and there is posterior displacement of anterior cerebral arteries (arrowhead), mirroring mass effect seen on CT; ophthalmic artery is enlarged as its ethmoidal branches supply tumor (arrow):



A. T2-MRI - grey-matter isointense mass deeply indents left cerebral convexity; broad dural base, surrounding displaced cerebral sulci and small pial vessel between tumor and brain surface (arrowhead) are all features of extra-axial lesion.
 B. Contrast T1-MRI - tumor enhances and there is 'dural tail' (arrow).
 C. Perfusion-weighted MRI - increased blood volume of tumor compared to normal cortex and white matter.



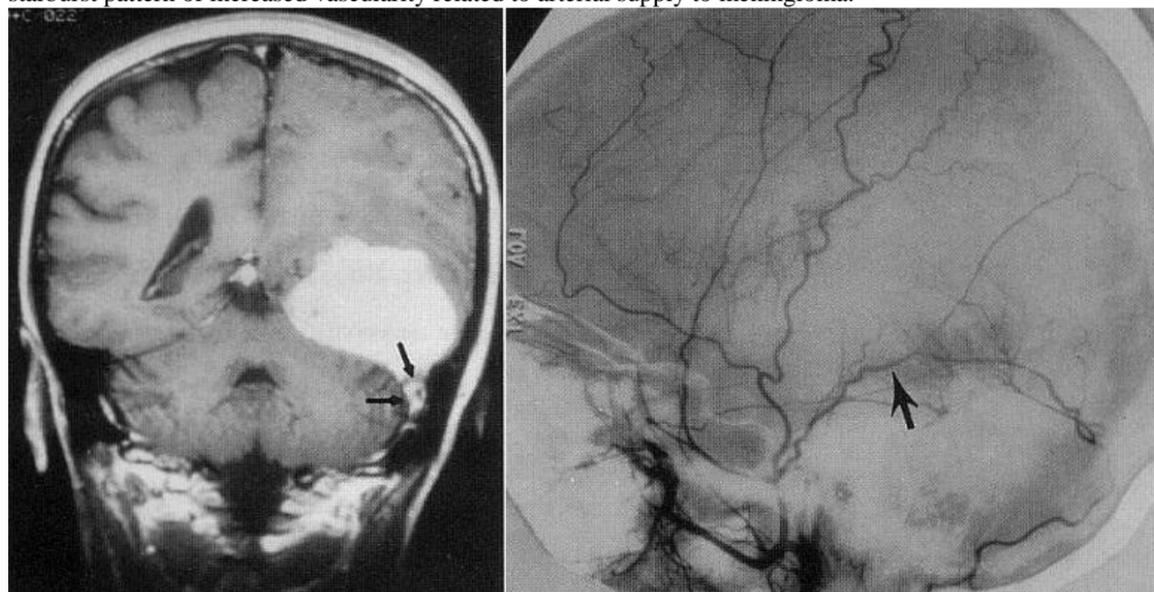
A. T2-MRI - isointense tumor; central low-signal-intensity structures (arrow) are hypertrophied meningeal vessels supplying meningioma.
 B. Contrast T1-MRI - homogeneously enhancing dural-based neoplasm; note thickened dura adjacent to meningioma; enhancing dural tail (arrow).



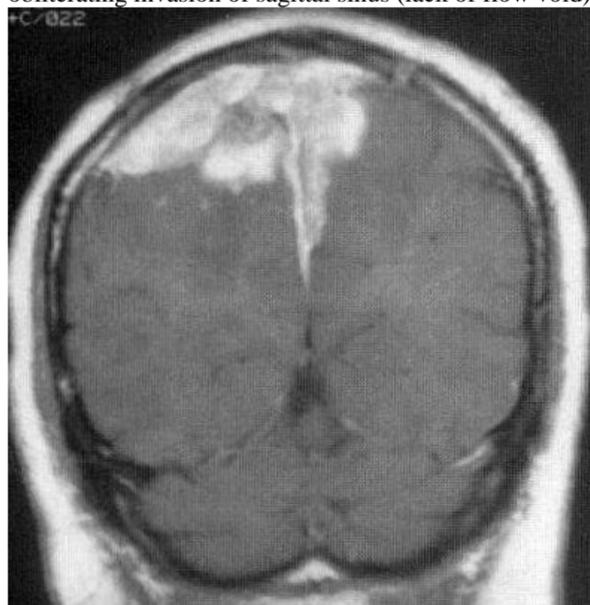
Tentorial meningioma:

A. Contrast T1-MRI - large, dural-based, homogeneously enhancing meningioma; right transverse sinus also enhances, suggesting that flow may be altered within dural sinus (*arrows*).

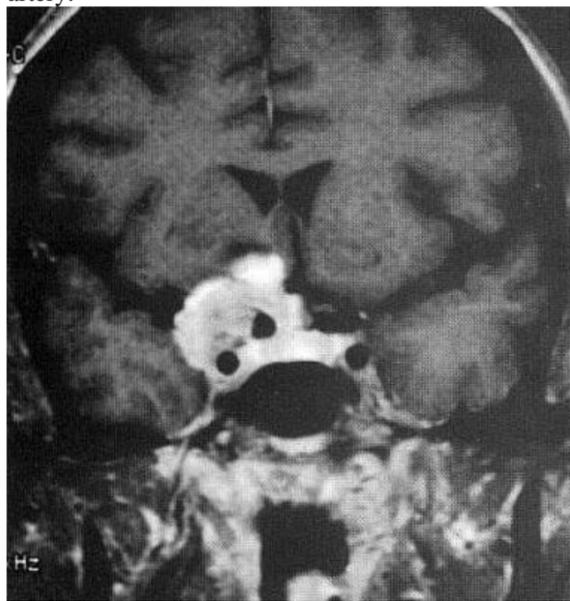
B. Lateral view of left external carotid arteriogram - hypertrophy of posterior branch of middle artery (*arrow*); note starburst pattern of increased vascularity related to arterial supply to meningioma.



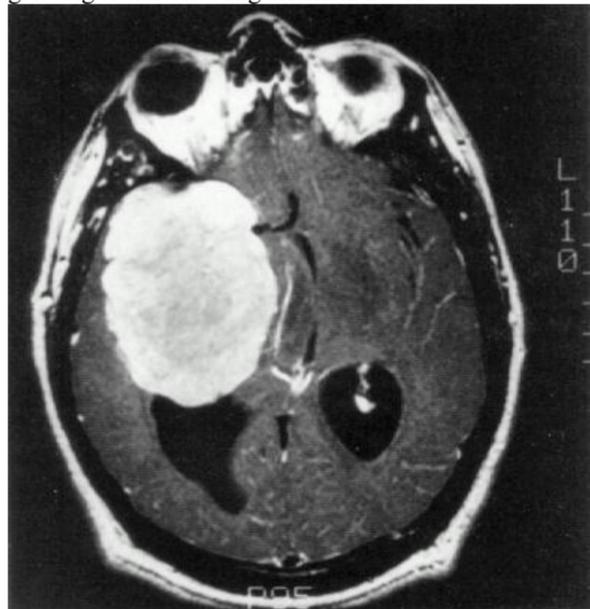
Parasagittal meningioma (contrast T1-MRI): en plaque meningioma extending along right parietal convexity; obliterating invasion of sagittal sinus (lack of flow void):



Juxtaseellar meningioma has encased supraclinoid carotid artery:



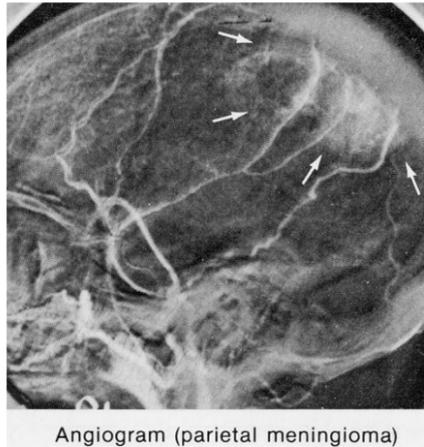
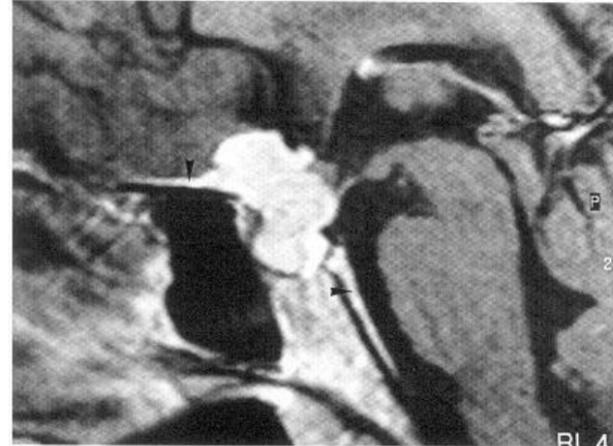
Temporal meningioma (contrast MRI) - large, slowly growing tumor affecting "silent area" of brain:



Contrast CT - meningioma in patient who presented with only mild cognitive deficits:



Suprasellar meningioma (contrast T1-MRI): lobulated, enhancing suprasellar mass arises from region of tuberculum sellae and extends down into pituitary fossa displacing pituitary stalk posteriorly; dural 'tails' (*arrowheads*) extend over planum sphenoidale and clivus:



Angiogram (parietal meningioma)

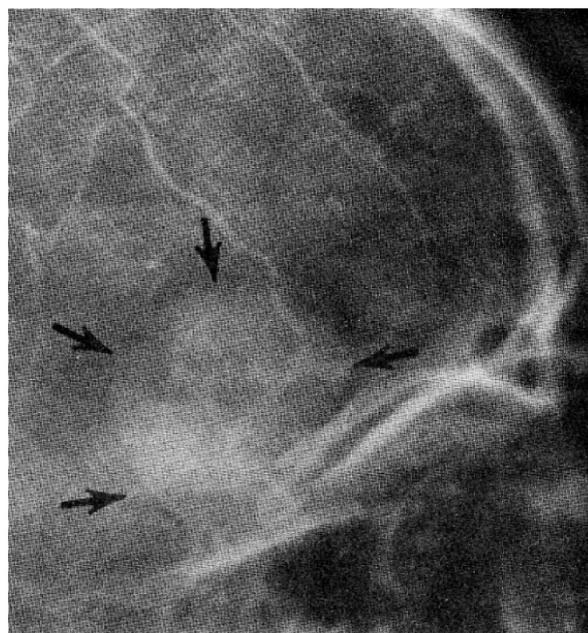


FIGURE 115. A subfrontal meningioma showing typical "blush" (arrows) in the late arterial phase.

DIFFERENTIAL DIAGNOSIS

(of meningioma-like dural-based tumors)

1. Dural metastasis
2. Dural lymphoma
3. Dural histiocytoma

TREATMENT

- *small asymptomatic tumors* are best left for **observation** (esp. for elderly patients) – repeat MR in 3-6 months – to establish growth pattern (growth only few mm excludes major mimickers – metastasis, lymphomas).
- growth > 2 mm / year – indication for surgery (unless patient is old and tumor unlikely will reach the size to become symptomatic).

SURGERY

See p. Op340 >>

RADIOTHERAPY

Meningiomas are not very radiosensitive! – but this is not relevant for SRS

Indications for SRS (clinical benefit in many case series):

- a) **ADJUVANT therapy** - for incompletely resected (residual)* / high grade** / recurrent tumors.
 - **subtotal resection* – wait 1.5-3 mos, then SRS (some experts prescribe SRS only if residual tumor demonstrates growth).
 - **after *gross total resection* of ATYPICAL meningiomas, EBRT appears not to affect progression-free survival and overall survival - observation rather than EBRT may be indicated! vs. After *subtotal resection* of ATYPICAL meningiomas, EBRT or SRS improves tumor control and delays progression, but this effect may be diminished in tumors with spontaneous necrosis.
- b) **PRIMARY treatment** – elderly patients, skull base, parasagittal, some unresectable tumors; used less frequently in convexity or optic nerve sheath tumors – meningiomas tend to swell a lot after SRS.

Benign tumor as a target for SRS – see p. Onc26 >>

Stereotactic radiosurgery (13-16 Gy to 50 % isodose line covering entire meningioma) - excellent local tumor control used mainly for:

- 1) small (< 3 cm) residual or recurrent lesions when surgery is significantly risky.
 - 2) meningiomas involving skull base or cavernous sinus
- primary SRS gives 86-97% long-term local control for benign small- and medium-sized (≤ 3.5 cm) meningiomas (durability of this response is beyond 10 years) - **equivalent to a Simpson grade I resection**.
Pollock, 2003 (Mayo clinic) – local control (tumor shrinkage or no further growth) at median f/u 43 months (2-138): benign meningiomas – 98%, atypical/malignant meningiomas – 60% (vs. 20% with surgery)
 - SRS for atypical meningioma - include up to 1 cm of brain margin to kill brain invading cells.
 - **radiation-induced edema** is the main cause of post-treatment morbidity (esp. with ≥ 16 Gy – up to brain herniation; other risk factors: **preexisting edema, large tumor-brain contact interface area**).

Large published SRS outcome series for meningiomas:

Author	Year	No. pts	Med. f/u (months)	Median Dose (Gy)	5-yr PFS
DiBiase	2004	162	54	14	86%
Kreil	2005	200	94.8	12	98.5%
Malik	2005	309	44	20	87%
Kollova	2007	325	60	12.6	97.9%

Meningioma of cavernous sinus – concern for **CN3-6 injury, carotid injury**. see p. Rx11 >>

- a) tumor is small enough and sufficiently far from optic pathways → **radiosurgery**
- b) lesion is too big or too close to optic pathway → **combined approach** (resection of portion of lesion out of cavernous sinus + radiosurgery) or **conventional radiotherapy**

Surgery vs. SRS for Cavernous Sinus Meningiomas:

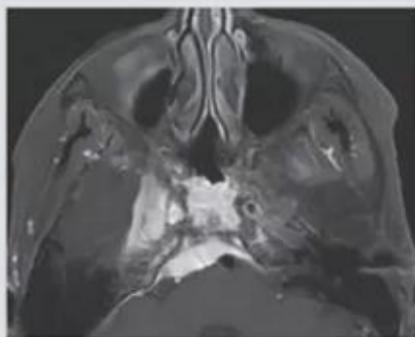
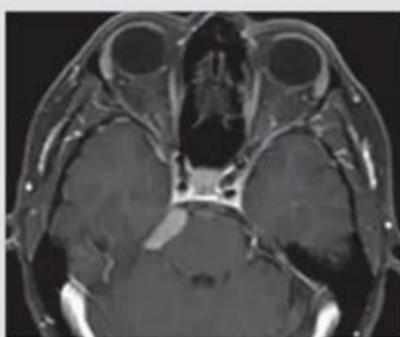
- Complete resection in 76 % of cavernous sinus meningiomas¹
- Mortality : 2.4 %
- Morbidity : 4.8 %
- Preoperative cranial nerve deficits:
 - Improved – 14 %
 - Unchanged – 80 %
 - Worse 6 %
- Incomplete resection
 - 40 % 5 yr tumor progression²
 - 89 % 15 year tumor progression³
- Complications post GK 8.7%, tumor control 94 %⁴
- Cranial nerve deficits affected 17 pts (5.7 %); 4 pts (1.3 %) with multiple cranial neuropathies
- Symptomatic brain edema 5 pts (1.7 %)
- ICA injury 2 pts (0.7 %)
- Cyst adjacent to treated tumor 2 pts (0.7 %)

1) DeMonte F, et al 1994 2) Jung H, et al , 2000 3) Klink DF, et al, 2000 4) Pollock, 2003

Meningioma involving optic pathways (sellar, parasellar meningiomas) - concern for **radiation-induced optic neuropathy**. see p. Rx11 >>

Marchetti, Marcello. Multisession Radiosurgery for Sellar and Parasellar Benign Meningiomas: Long-term Tumor Growth Control and Visual Outcome. Neurosurgery: May 2016 - Volume 78 - Issue 5 - p 638–646

multisession radiosurgery (mRS) → progression-free survival at 3, 5, and 8 years was 100%, 93%, and 90%, respectively. Compared with baseline, visual function improved in 36% of patients, whereas 7.4% experienced a worsening in visual function (5.1% excluding the patients with progressive disease).

	External beam radiation therapy	Stereotactic radiosurgery
Example		
Tumor features	<ul style="list-style-type: none"> Large (> 3–4 cm) Contacting optic apparatus 	<ul style="list-style-type: none"> Small ≥ 2–3 mm from optic apparatus
Example prescription for WHO grade I	<ul style="list-style-type: none"> 54 Gy at 1.8 Gy per fraction 	<ul style="list-style-type: none"> 15 Gy in a single fraction
Additional technical considerations	<ul style="list-style-type: none"> Increase conformality with IMRT or VMAT Prescribe to high isodose line to minimize hot spots to adjacent critical structures 	<ul style="list-style-type: none"> No margin added to GTV Gamma knife SRS commonly prescribes to 50% isodose line for steep dose gradients; linear accelerator SRS typically treats at the 80% isodose line
Follow-up expectations	<ul style="list-style-type: none"> EBRT and SRS generally prevent the growth of benign meningiomas on long-term follow-up; transient swelling after RT has been observed Little to no tumor reduction Symptomatic improvement is common despite minimal tumor reduction 	

CHEMOTHERAPY

- disappointing!

- reserved for malignant cases after failure of surgery and radiotherapy.
- drugs that had no effect in studies - TEMOZOLOMIDE, HYDROXYUREA, MIFEPRISTONE (RU-486), INTERFERON- α , IRINOTECAN.

SUNITINIB (Sutent®) - small-molecule tyrosine kinase inhibitor.

- targets vascular *endothelial growth-factor receptors (VEGFR)* and *platelet-derived growth-factor receptors*, both of which are highly expressed in meningiomas.
- might be the first effective medical treatment for recurrent atypical/malignant meningioma.
- 60% rate of grade 3/4 **toxicity!!!!**

PROGNOSIS, FOLLOW-UP

Meningiomas can be cured surgically!

- 5-year survival 73-94%
- average survival – 9 years.

Follow-up schedule (Dr. JD Day):

- annually for 5 years, then q2yrs for 3 yrs, then q3-5 yrs indefinitely.
- atypical meningiomas - q6mos for 5 yrs, then annually indefinitely.
- skull base meningiomas - annually indefinitely (to detect the recurrence while still small and good for SRS or else repeat surgery complication rate is much higher).

RECURRENCE AFTER SRS – see above >>

RECURRENCE AFTER SURGERY (by 5 years*):

*average interval for recurrence is 5 years.

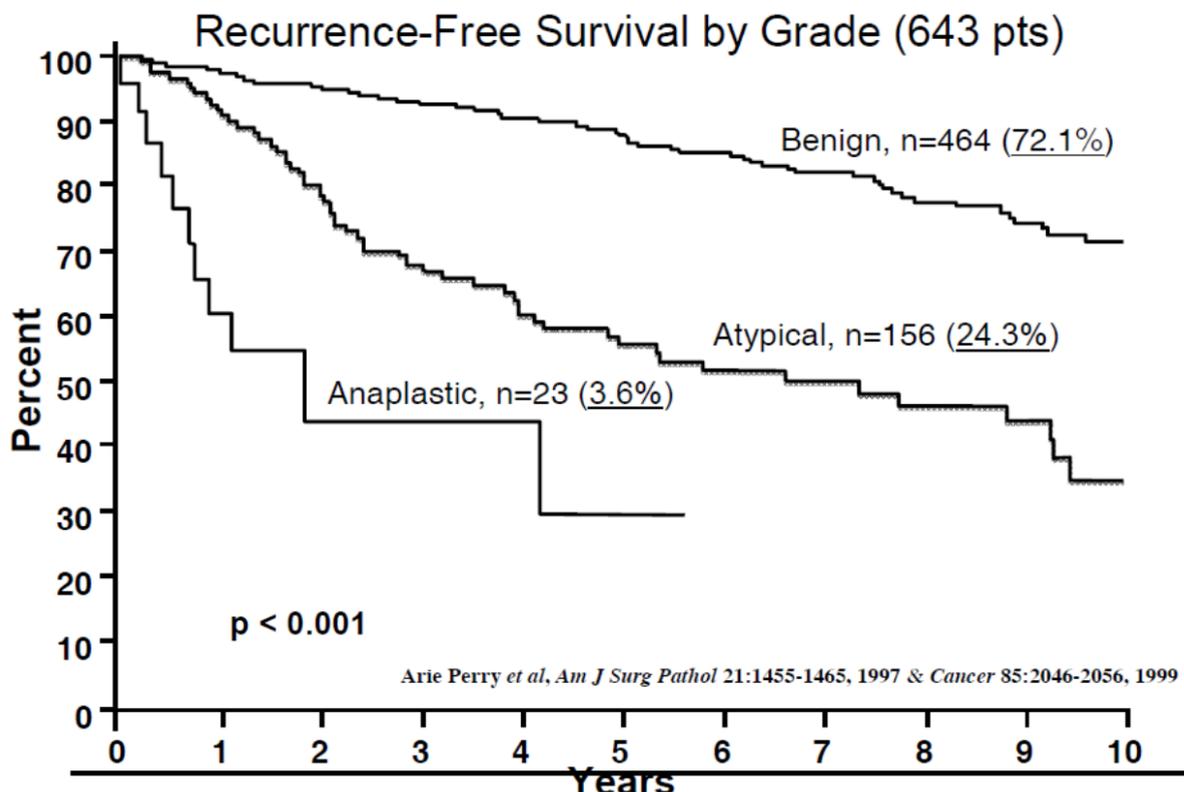
presumably removed (GTR) tumors (Simpson I) - 10% (20% at 20 years);
 when dural attachment is cauterized but not removed (Simpson II) – 15-20%;
 when definite portion of tumor remains (Simpson IV) - 39%.

see also Simpson Grades (prognosis) p. Op340 >>

- routine follow-up MRI* is best means of detecting recurrence.
- recurrent meningiomas ordinarily represent focal benign neoplasms - **can again be treated by surgical resection.**
- major clinical factor in recurrence is **extent of resection**; less powerful predictors of recurrence: **young age** and **male gender**.

Significant predictors of poor outcome:

- mitotic index > 6**
 - malignant (**WHO III**) tumor grade
benign meningiomas have recurrence rates 7–25%, **atypical meningiomas** 29–52%, **anaplastic meningiomas** 50–94%
 - progesterone receptor score of 0 (i.e. **absence of progesterone receptors**)
 N.B. significant subset of histologically and clinically benign meningiomas also lacks progesterone receptor expression.
- brain invasion** and **bone invasion** are independent predictors of tumor recurrence!



PEDIATRIC MENINGIOMAS

- behave very differently from their adult counterparts - have **more malignant** histological subtypes and **recur more frequently!**

BIBLIOGRAPHY for ch. "Neuro-Oncology" → follow this [LINK >>](#)