### Clinical Application of Pathology

#### Brain Tumours III – Meningioma – ICD-O 9530/0

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<th>Sub-type</th>
<th>WHO grade I</th>
<th>WHO grade II</th>
<th>WHO grade III</th>
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*These subtypes are almost always WHO Grade I, but very uncommonly, can be WHO Grade II i.e. demonstrate atypical features.

Thursday, November 17, 2016
Introduction: Meningioma is the most common primary adult intracranial tumour (13-20%).

The diagnosis of many meningiomas is relatively straightforward but there are areas of diagnostic difficulty and concepts related to grading and identification of microscopic features, associated with aggressive behaviour, continue to evolve.

A large number of microscopic subtypes are recognized. Some subtypes tend to occur in ‘pure’ form, whilst others may be mixed, or become so during the process of recurrence and anaplastic transformation.

The recognition of many of these meningioma subtypes is of little clinical significance, as they share similar biological potential and behaviours. However, the identification of certain other subtypes is critical, either because they are specifically associated with aggressive behaviour, or because their distinctive histological patterns, although of no particular clinical significance, may lead to misdiagnosis as other neoplasms, which may lead to inappropriate treatment.

The World Health Organization has recognized 3 grades of Meningioma.

**WHO grade I** – this has a low risk of recurrence and of aggressive growth. It is a ‘benign’ meningioma. There are 9 variants of grade I - Includes meningothelial, fibrous, microcystic, secretory, lymphoplasmacyte-rich, psammomatous, angiomatosus, metaplastic and transitional (mixed).

WHO grade I meningiomas constitute approximately 80% of meningiomas, are well differentiated, lack brain invasion and macronucleoli, have only scant mitoses, and a MIB1 labelling index of less than 1%. Necrosis is absent (provided pre-operative embolization has not been performed). WHO grade I benign meningiomas have recurrence rates of about 7 – 20% compared with atypical meningiomas which recur in 29 – 40% of cases, and anaplastic meningiomas which have recurrence rates of 50 – 78%.

**WHO grade II** – this has some likelihood of recurrence and aggressive growth. It is the ‘low grade’ meningioma. It includes atypical, clear cell and chordoid meningioma. Atypical meningiomas (WHO grade II) are not uncommon and account for 7 – 10% of all meningiomas in various series. Atypical meningiomas recur in 29 – 40% of cases.

**WHO grade III** – this has a considerable likelihood of recurrence and aggressive growth. These are meningiomas of any subtype or grade showing a microscopically high proliferation index. This is the ‘high grade’ meningioma. It includes rhabdoid, papillary and anaplastic meningioma. Anaplastic meningioma (WHO grade III) are rare, and amount to no more than approximately 1 – 5% of all meningiomas. Clinically they recur in 50 – 78% of cases, are usually fatal, with median survivals of the order of 18 months and a five year mortality rate of almost 70%.

Genetic: Loss of one copy of chromosome 22 is the most prevalent chromosomal change in meningioma.

Genetic changes associated with meningioma progression: Mutations in the neurofibromatosis 2 (NF2) gene have been detected in up to 60% of sporadic meningiomas. Fibroblastic and transitional meningiomas carry such mutations in 80% of cases but in meningothelial this occurs in only 25%.

Atypical and Anaplastic meningiomas carry NF2 mutations in 70%, so one cannot conclude the NF2 gene is involved in progression of a benign meningioma to a higher grade. However, when a Meningioma (grade I) progresses to Atypical Meningioma (grade II), there is a change in the genetic profile.
Locations of Meningiomas: primary intradural and rarely primary extradural.
**Macroscopic appearance:** image courtesy of Dharam Ramnani, Radiopaedia.org. rID: 29626

![Image](https://example.com/image)

**Incidence of meningiomas:** Meningioma is the most common primary CNS tumour of non-glial origin and accounts for 25% of all primary brain tumours.

**Peak age** incidence is in the 5th decade.

**Gender:** more common in women and a meningioma may undergo increased rate of growth during pregnancy. Female : male = 2 : 1 when intracranially and 4 : 1 if spinal.

However, atypical and anaplastic meningiomas are slightly more common in males.

**Groups:**
- 80 – 90% are typical “benign” meningiomas
- 7 – 10% are atypical meningioma – low grade
- 1 - 5% are anaplastic meningioma – high grade
- 5% of cases have multiple meningiomas.

**Sites:** Meningiomas develop from arachnoidal cells and 90% are supratentorial and 10% infratentorial.

The tumours occur along dural venous sinuses, along sutures and arise from arachnoid granulations. 25% are parasagittal, 20% convexity, 20% sphenoid ridge, 10% olfactory groove and 10% parasellar, 10% cerebello-pontine angle and the foramen magnum, 2% intraventricular, pineal region, optic nerve sheath, 1% extracranial e.g. nose, sinuses, skull and 2% other.

**Reference:** Osborn AG. Diagnostic Neuroradiology, Mosby-Year Book, Inc., 2004 2nd printing of 1st ed

Most meningiomas grow inward toward the brain as discrete well-defined, dural-based masses and are spherical or lobulated in contour. Flat tumours, termed en plaque, infiltrate the dura and grow as a thin carpet or sheet of tumour along the convexity dura, falx, or tentorium. Dural attachment of meningiomas can be pedunculated or broad-based (sessile). Because the pia and arachnoid form a membranous barrier between brain and tumour, some meningiomas grow into the subarachnoid space, but invasion of the brain is infrequent.

**Imaging information** about the dural attachment site, the location and severity of oedema and the displacement of critical neurovascular structures is useful for planning the operative approach and has an effect on the outcome.

**CT scan** - approximately 75% of meningiomas are hyperattenuating to surrounding brain parenchyma, while roughly 25% are isodense. A rare group of meningiomas (the lipoblastic subtype) contain fat and are thus hypoattenuating.

Calcification is seen in 25% of cases. The CT nature of the calcification may be nodular, fine and punctate, or dense. Surrounding vasogenic oedema is common as hypodense brain tissue.
Occasionally, the oedema is extensive and, as it predominantly affects white matter, can resemble fingers of low attenuation. Oedema, however, is absent in 50% of cases because of the neoplasm’s slow growth.

An advantage of CT over MRI is the evaluation of underlying bone which demonstrates hyperostosis in 20% of patients. Other bony findings include an increase in vascular markings and cortical irregularity. Less common meningioma findings include haemorrhage, cyst formation, and necrosis. Cystic components of meningiomas may be present inside the tumour or between the tumour and the adjacent brain (so-called trapped CSF).

More than 90% of cases will demonstrate intense homogeneous enhancement. Inhomogeneous enhancement can result because of necrosis or rare haemorrhage.

The plain skull radiograph below shows localised calcification – arrow. The middle image is a non-contrast CT scan and the right image is post contrast. Courtesy of Islam O. Medscape Mar 20 2016.

The calcification is so dense that any enhancement would be hidden.

MRI MRI can demonstrate tumour vascularity, arterial encasement, venous sinus invasion, and the relationship between the tumour and surrounding structures. MRI is valuable in depicting the juxtasellar area and the posterior fossa and in demonstrating the rare presence of disseminated disease via the CSF. The multi-planar capability is often the best means to visualize the broad contact of tumours to the meninges, tumour capsules, and meningeal contrast enhancement adjacent to the tumour.

MRI T1W Gd contrast shows a meningioma of the clivus – arrow. Courtesy of Assoc. Professor Frank Gaillard, Radiopaedia.org, rID : 3288.
**MRI** T1W Gd contrast shows a meningioma arising in the right cerebello-pontine angle – see arrow. The bony roof and floor of the internal auditory canals show as black. Image courtesy of Dr Ahmed Abd Rabou, Radiopaedia.org, rID : 36505.

**MRI** is best for the meningioma at the cranio-vertebral junction – see arrows below on T1W Gd with a fat saturation sequence. Image courtesy of Dr Paresh K Desai, Radiopaedia.org, rID : 3142

**MRI** – Meningioma in a suprasellar location - T1W Gd sagittal – courtesy of Assoc. Professor Frank Gaillard, Radiopaedia.org, r ID : 15824 - see arrow.
The mimic from which this suprasellar meningioma has to be distinguished is a pituitary macroadenoma which – see image below – has grown down into and filled the sphenoid sinus and also extended superiorly above the pituitary fossa.

Image courtesy of Assoc. Professor Frank Gaillard, Radiopaedia.org, rID 2648.

**Angiography:** Prior to surgery, cerebral angiography is often performed to assist the surgeon with suitable operative approaches. The images below are (a) a post contrast CT scan showing a tumour in the right posterior parietal region and (b) and (c) the right side angiogram from a bilateral selective internal carotid angiogram. No contribution was found to the tumour. The arrows in (c) indicate the junction of the extra-axial tumour with compressed vessels in the underlying brain.
However, a bilateral external carotid angiogram – prepared as a composite in image (d) shows the right sided tumour has its major blood supply from the branches of the left external carotid artery. These findings caused the surgeon to clip the left-sided major feeder before opening the cranium.

**Differential diagnosis:** The differential diagnosis for brain meningioma includes dural metastasis (with breast and prostate cancer being the most common primary malignancies), solitary fibrous tumour/ hemangiopericytoma, granulomatous disease (including sarcoidosis and tuberculosis), idiopathic hypertrophic pachymeningitis, extramedullary hematopoiesis, haemangioma, and dura/venous sinuses. With certain anatomic locations, other differential diagnoses should be considered, including **vestibular schwannoma** for cerebellopontine angle tumors, **pituitary macroadenoma** and craniopharyngioma for parasellar tumours, and chordoma/chondrosarcoma for masses around the clivus.

**Treatment** for benign meningiomas is complete surgical resection of the tumour. Nevertheless, interventional neuroradiologists commonly contribute in performing preoperative embolization to reduce the blood supply to the tumour. Treatment of meningiomas is benefited by embolization, and especially those with a complex presentation, giant meningiomas, meningiomas exhibiting
malignant or angioblastic characteristics, or meningiomas involving the skull base, scalp, or critical vascular structures.

The embolization of meningiomas is commonly used in surgically inaccessible locations such as the apex of the orbit and the cavernous sinus. In image (a) the CT scan shows a tumour at the apex of the left orbit - arrow and (b) is post contrast on bone windows and shows the tumour also involves the left cavernous sinus. Image (c) shows the angiogram pre and post-embolisation.
Meningioma subtypes which usually pose little difficulty in diagnosis.

**Meningothelial, fibrous, and transitional meningiomas** are the most common of the meningioma subtypes. Their stereotypic meningothelial patterns (whorls and syncytial cellular arrangements, nuclear pseudoinclusions, psammoma bodies and stromal calcification) are common to most meningioma subtypes. The identification of these features may assist greatly in the evaluation of difficult biopsies and in the recognition of uncommon meningioma subtypes.

**Immunohistochemical** and ultrastructural studies also have a role to play in some diagnostic settings. The vast majority of meningiomas are characterized by membranous positivity for epithelial membrane antigen (EMA) and strong, diffuse vimentin positivity.

**Ultrastructural** features of meningioma include the presence of complex interdigitating cell processes, desmosomal junctions and abundant cytoplasmic intermediate filaments.

**MENINGOTHELIAL MENINGIOMA** - 9531/0: is the most common histological type and found in 60% of meningiomas. It is a pure single type in 18% and combined with the fibrous type in 40%. Combined patterns are referred to as “transitional meningioma” – see below. Meningioma most closely resemble arachnoid cap cells and are characterised by sheets, whorls or syncytia of neoplastic cells which have round or oval centrally located nuclei with dispersed chromatin, smooth nuclear profiles and small indistinct nucleoli. Whorls and psammoma bodies, if present, tend to be less well formed than in other meningioma subtypes. They also sometimes demonstrate eosinophilic cytoplasmic invaginations (intranuclear pseudo-inclusions) and central nuclear clearing. Lobules of tumour are separated from each other with collagen sheets.

**Imaging:** a left parafalcine frontal meningothelial meningioma with severe oedema (left T2W image) and right frontal convexity (right T2W image) shown on a MRI scan -courtesy of Assoc Prof Frank Gaillard, Radiology.org.rID : 39336 and rID 42309.
FIBROUS or Fibroblastic meningioma – 9532/0

**Macroscopic:** A hard consistency, as encountered in fibroblastic subtypes, makes the removal of the tumour difficult, especially if it is located at the skull base. Therefore, preoperative information about the histologic grade and subtype of a meningioma is crucial because it aids in surgical planning. Results suggest that histogram analysis of diffusion tensor imaging metrics can help determine the grades and subtypes of meningiomas, which can better assist in surgical planning.

**Microscopic:** is typically composed of elongated spindle cells, separated by a fibrous matrix and contains few, if any, meningothelial whorls or psammoma bodies.

Storiform cellular arrangements (denoting a matted, irregularly whorled pattern, somewhat resembling that of a straw mat) and thick collagen bundles, which sometimes may be calcified, may also occur – see image below.

Microscopic appearance of fibroblastic meningioma: - there is a relative paucity of cytoplasmic intermediate filaments and desmosomes. The fibroblastic meningioma contains glycogen, exhibits at least focal EMA positivity, is often S-100 positive and is either CD34 negative or lacks the diffuse CD34 positivity characteristic of solitary fibrous tumour. Only patchy mild to moderate CD34 staining is observed in approximately 50% of fibroblastic meningiomas.

**Imaging:** MRI images below, T1W on the left and T2W on the right, courtesy of Dr Hani El Salam, Radiopaedia.org, rID : 12305
TRANSITIONAL meningiomas – 9537/0 - demonstrate combined meningotheelial features (whorls and syncytial arrangements) and fibroblastic elements (spindle cells and fibrous stroma). Psammoma bodies, lamellated calcified structures often arising within meningotheelial whorls, are often conspicuous.

MENINGIOMA and NEUROFIBROMATOSIS 2

Meningiomas are known to be associated with Neurofibromatosis 2. The latter condition is also known to be associated with intracranial schwannoma. The CT scan below is a 46 year old patient who had multiple peripheral neurofibromata proven on biopsy. The scan was undertaken to document acoustic neuromas if present and also the patient had been complaining of headaches. A pre and post contrast CT scan was undertaken – the PC illustrates a hyperdense mass in the left lateral ventricle which had enhanced uniformly – horizontal arrow. There is also some entrapment of part of the left lateral ventricle – oblique arrow.

The intracranial mass is believed to be arising from the ependyma of the left lateral ventricle, so judging from its point of origin, it was thought more likely to be an intraventricular meningioma rather than a schwannoma. It was not considered to be of current clinical significance, so was not biopsied but follow-up in one year was arranged.

Distinctive histological patterns of meningioma, which are of no particular clinical significance but which may be misinterpreted.

MICROCYSTIC meningioma – 9530/0 although it is WHO grade I, it is very different in appearance from the transitional meningioma. It is characterized by a microscopic pattern in which spindle and stellate cells with long slender cytoplasmic processes surround variably sized intercellular spaces, resulting in a loose ‘bubbly’ and cystic appearance. In pure forms, meningotheelial characteristics may be inconspicuous or absent. Hyaline thickening of stromal tissues and blood vessel walls is often a feature and tumour cells may show xanthomatous change. The microcystic pattern may be associated with a large cyst adherent to, or displacing the brain, but is otherwise of no particular clinical significance.

Pronounced nuclear enlargement and hyperchromasia are not uncommon but mitoses are rare and care must be taken that this pleomorphism does not result in an erroneous diagnosis of atypical meningioma (WHO grade II).

On occasion, xanthomatous change may be confused with haemangioblastoma (WHO grade I), which is EMA negative.

Another potential mimic is clear cell meningioma (WHO grade II), especially in areas with pronounced vascular hyalinization but it is characterized by abundant PAS positive cytoplasmic glycogen.
**Microscopy:** note the variably sized intercellular spaces. The cell processes appear elongated and result in the loose bubbly cystic appearance.

**Microcystic meningioma** may be confused with microcystic areas of schwannoma and on rare occasion with superficial astrocytomas of pilocytic, fibrillary or protoplasmic type.

EMA, S-100 and GFAP immunostaining usually resolve any uncertainty.

**Imaging:** The tumour is hypodense but not quite as low attenuation as C.S.F.

In the example - CT non contrast – see below, the picture is due to the tumour having a mucinous background and being comprised of multiple small cysts. The tumour also has a smooth edge and displaces the grey-white junction internally, confirming its extra-axial location. The post contrast CT – image (b), shows enhancement only occurring at the perimeter of the mass. This feature would raise the possibility of the appearance being due to an abscess, a metastasis or a necrotic glioma.

Although 60% of meningiomas are associated with brain oedema, this is not evident in this case.

**SECRETORY Meningioma – 9530/0**

It is characterized by the presence of epithelial differentiation. ‘Pseudo-psammoma’ bodies, which represent the expression of the epithelial phenotype, are rounded, non-calcifying, intracytoplasmic
eosinophilic inclusions, which contain PAS (Periodic acid–Schiff)-positive protein secretions and measure 3 - 100µm. Pseudo-psammoma bodies may be single or multiple within a given cell, are CEA (carcinoembryonic antigen) positive and often surround cytokeratin-positive tumour cells.

May be associated with peritumoural oedema and show elevated levels of CEA.

**Mimics:** can be confused with metastatic mucinous adenocarcinoma.

**Microscopy:**

![](image)

**Imaging:** secretory meningiomas very frequently have prominent adjacent parenchymal oedema.

The typical MRI signal intensity of secretory meningiomas:

- **T1:** iso- to hypointense to grey matter
- **T2 / FLAIR:** hyperintense to grey matter
- **T1 C+:** vivid homogeneous enhancement

![](images)

MRI Images above are from 2 patients: A – heterogeneous strong enhancement of a mass in the right frontal area, with low signal oedema associated, causing compression of the right lateral ventricle and midline shift. B. – homogeneous strong enhancement of bifrontal masses, with the associated oedema displacing the frontal horn of the left lateral ventricle considerably posteriorly and the right frontal horn shows some compression.

Treatment

Disproportionate oedema associated with this type of meningioma can result in unexpected postoperative complications so extended sedation, aggressive treatment of peritumoural cerebral oedema, and a lower threshold for postoperative imaging are required for this type of meningioma.

It is very important to recognise the imaging pattern and warn clinicians before operation so intra-operative frozen sections can be performed and subtype of the tumour determined prior to the transfer of the patient to the ICU for early and more aggressive initiation of the post-op treatment.

Prognosis: of secretory meningiomas is related with operation completeness and surgical risks, rather than the extent of peritumoural brain oedema. Residual secretory meningioma grows slowly and reacts well to gamma-knife therapy.

LYMPHOPLASMACYTE-RICH MENINGIOMA – 9530/0

Incidence: a rare variant of WHO grade I meningioma

Age: younger patients.

Gender: no gender predilection.

Sites: The most common locations are convexity, skull base, para-sagittal and cervical canal, while some of them are multiple or diffuse lesions. More than 20% patients have peripheral blood abnormalities, and one-third of the cases have moderate to severe peritumoural brain oedema.

Clinical presentation: Although the presenting symptom is similar to other intracranial masses (headache - most common, hemiparesis, seizure, dizziness, visual deficits), the course is more acute mimicking an intracranial inflammatory disease. The natural history is often over one year, while a few might present suddenly, due to the location of lesions or inflammatory cell infiltration and oedema.

Peripheral blood abnormalities are also detectable, including iron deficiency anaemia and hyperglobulinaemia, which normalize following resection.

Imaging: often solitary, resembling other variants of meningioma, but multiple masses have been reported, including involving the spine. They can have extensive relatively flat growth, similar to en plaque meningioma, and may have indistinct margins and vasogenic oedema in the adjacent brain parenchyma.

The CT – image (a) shows a high density mass in the left temporal lobe and middle cranial fossa.

Image (b) is MRI and shows a lobulated tumour. Image (c) T2W image. Image (d) is a contrast enhanced T1W coronal view and shows the lobule and slightly irregular enhanced mass with a relatively sharp boundary.

**Microscopy:**

Is characterized by pronounced lymphoplasmacytic infiltrates, (lymphocytes and plasma cells) which may be so dense as to obscure the underlying neoplastic meningothelial cells. The plasma cells are polyclonal and amyloid may be deposited.
This subtype of meningioma may prove diagnostically challenging. Other dural masses with prominent lymphoid and/or plasmacytic infiltrates, such as inflammatory myofibroblastic tumour (‘inflammatory pseudotumour’), lymphoma, plasmacytoma and other lymphoproliferative disorders may enter the differential diagnosis if the underlying meningioma is not recognized. To increase the difficulty in diagnosis, a small number of lymphoplasmacytic meningiomas are associated with haematological abnormalities.

Importantly, and supporting the contention that these are actually meningiomas with inflammatory infiltrates is that the inflammatory cells are not monoclonal/neoplastic.

Images again courtesy of Zhu Hong-Da, Xie Q, Gong Y et al.

A: H&E showed the chronic inflammatory cells infiltrated in the lobules of meningothe1ial cells.

A repeated in the group of 6 slides.

B: Epithelial Membrane Antigen staining (EMA, ×400): Both the tumor cells and the reactive plasma cells were positive for EMA.

C: Vimentin staining (Vim, ×400): The meningothe1ial components were Vim positive.

D: Leukocyte common antigen staining (LCA, ×400): Lymphocytes and plasma cells were positive for LCA.

E: MIB-1 index: 3%. F: Progesterone receptor staining (PR, ×400):

F: Progesterone receptor staining (PR, ×400):
The meningothelial components were PR positive. Scale bar = 200 μm.

**Treatment:** surgical resection

**Prognosis:** Incidence of tumour related recurrence or death is rather low although total resection was achieved only in about 60% cases, and MIB-1 in a third of cases was higher than 3%.

**ANGIOMATOUS MENINGIOMA – 9534/0**

Refers to meningiomas with a prominent vasculature which may account for 50% of the whole tumour. There is meningothelial differentiation. Angiomatous patterns of meningioma are important only in so far as they must not be confused with solitary fibrous tumour / meningeal haemangiopericytoma, or haemangioblastoma.

**Incidence:** rare – account for only 2% of all meningiomas.

**Clinical:** present as for any other meningioma.

Meningiomas with fibroblastic and angiomatous patterns must be distinguished not only from solitary fibrous tumour /meningeal haemangiopericytoma and haemangioblastoma but also primary meningeal sarcomas with rich vascularity or a pericytoma-like pattern (e.g. mesenchymal chondrosarcoma).

**Solitary fibrous tumour / Meningeal ‘haemangiopericytoma’ - 8815/0/1/3** is an aggressive malignancy, which is often complicated by repeated episodes of local recurrence and late metastatic dissemination.

Meningeal Solitary fibrous tumour /haemangiopericytoma demonstrates a range of histological appearances. The neoplastic cells characteristically form closely packed aggregates, punctuated by thin walled vascular spaces, which may be of capillary size or form large gaping structures with an
antler or stag-horn outline. The nuclei of the neoplastic cells are spindle or spherical in outline and demonstrate variable degrees of hyperchromasia and pleomorphism. Mitotic activity is variable. Features of meningioma such as tight concentric cellular whorls and psammoma bodies are absent. The neoplastic cells of Solitary fibrous tumour / haemangiopericytoma are vimentin positive but EMA negative and demonstrate only weak and patchy CD34 positivity in 30% of cases.

**Imaging:** On CT - similar to more typical meningothelial and fibrous subtypes. It appears slightly hyperdense to adjacent brain and shows vivid contrast enhancement.

**MRI** - it can look very like microcystic meningiomas and chordoid meningiomas. However, there are often prominent flow voids and frequently there are dural tails and some cystic change.

- **T1:** hypointense and T2 hypertense compared to grey matter
- **T2:** peritumoural oedema very common (75-100%)

The axial T2 (left image) shows marked peritumoural oedema and sagittal T1Gd right image shows vivid enhancement and a few flow voids - courtesy of Assoc. Professor Frank Gaillard, Radiopaedia.org, rID : 4313. This tumour was a mixture of microcystic and angiomatous meningioma.

- **MRA:** - in some cases feeding vessels may be visible.

**Differential diagnosis** : 1. Other entities to be considered on MRI are extra-axial masses with high T2 signal and masses with prominent blood supply.

These include: Solitary fibrous tumour / Haemangiopericytoma - can appear very similar but brain and bone invasion is more common. Also affects males more than females. Less likely to have a dural tail and more likely to enhance heterogeneously and show micro-lobulation.

2. other meningioma variants which usually do not have as prominent flow voids

- microcystic meningioma
- chordoid meningioma
- secretory meningioma
o angiomatous meningioma
o cartilaginous metaplastic meningioma

3. haemangioblastoma

- intra-axial (albeit peripheral) usually in the posterior fossa
- typically cyst with an enhancing mural nodule.

**Microscopic:** characteristic is a prominent vasculature.

**Treatment:** surgery is the treatment of choice but the presence of such abundant blood supply can make surgery more difficult. Pre-operative embolisation may be of benefit.

**PSAMMOMATOUS MENINGIOMA - 9533/0**

Characterized by abundant psammoma bodies which causes the tumour to be densely calcified. These represent lamillated calcified structures often arising within meningothelial whorls.

**Imaging:** courtesy of Dr Saeed Soltany Hosn, Radiopaedia.org, rID : 33441, CT non contrast on soft tissue and bone windows. Can sometimes just be hyperdense on CT without obvious calcification.
**MRI** - findings depend on amount of calcification. With heavy calcification, the mass will have low signal on all sequences, with almost no visible contrast enhancement. If less calcification, the mass is hypo or isointense on T1 and T2 and post contrast T1 will show enhancement.

The MRI images below – T1, T2 and T1 post contrast – show a partly calcified mass (low signal on T2) attached to the falx cerebri in the left frontal region. It has displaced the frontal horns of the lateral ventricles in a posterior direction. Courtesy of Assoc. Professor Frank Gaillard, Radiopaedia.org, rID : 14221.

![MRI images](image)

**Microscopy:** the arrow in the image below indicates a psammoma body.

![Microscopy image](image)

**Treatment:** Surgical treatment could provide a partial or complete resection of the tumour.

**Prognosis:** depend on the extent of resection.

Recurrence rates after surgery is also related to a young age (<50 years), multiple lesions, calcification extension, and ossification.

**METAPLASTIC MENINGIOMA – 9530/0**

**Definition:** uncommon histological variant of benign WHO grade I meningiomas, characterized by tumour cells sharing the characteristics of tissues from other parts of the body. There are 6 subtypes.

**Imaging:** appearances depend on the type of tissue they contain e.g. osseous meningiomas resemble mature bone, with bone marrow and lipomatous meningiomas contain areas of fat.
**Nomenclature:** named according to the cell type that they resemble and include:

Cartilaginous meningioma, lipomatous meningioma, melanotic meningioma, myxoid meningioma, osseous meningioma and xanthomatous meningioma.

**CARTILAGINOUS MENINGIOMA** - there is essentially a pure and regular cartilaginous tumour proliferation with focal clusters of meningeal cells with rounded nuclei containing intranuclear inclusions and clear scanty cytoplasm.

**Imaging:** images courtesy of Onen J, Coulibaly O, Derraz S, Harmouch A, Sefiani S, El Ouahabi A and El Khamlichi A. Internet J Neurosurgery 2013, 9(2)

A non contrast CT scan shows a meningioma in the left pre-rolandic area as a hyperdense lesion and there is evidence of hyperostosis on bone windows.

**Microscopic:**

The chondroid tissue is surrounding arachnoid proliferation (black arrow extreme left image). Arachnoid cells with pseudo inclusions are wound in clusters (black arrows centre image) and extreme right shows regular chondroid tissue.

**Treatment:** is radical resection.

**Prognosis:** is good with low or delayed rate of recurrence.

**LIPOMATOUS MENINGIOMA**

**Incidence:** 0.3% of all meningiomas.

**Pathology:** represent accumulation of lipids within meningothelial cells. When fat is abundant, then they deviate from the normal conventional appearance of meningiomas in line with the presence of fat.

**Clinical:** rapid progression of symptoms in reported cases is probably related to development of the surrounding oedema, which is unrelated to fatty degeneration.
**Imaging:** CT - Lipid rich lipomatous meningiomas are of lower density than conventional meningiomas. Have density measurements as low as -50 to -100HU. However usually have some enhancing components and share some of the morphological features of meningiomas such as a dural tail.

**MRI** Lipomatous meningiomas with abundant fat will have fat like signal:

- T1: hyperintense
- T2: hyperintense
- **Fat saturated sequences:** will demonstrate signal loss
- T1 C+: heterogeneous enhancement

Image courtesy of Jaiswal AK et al. (see below). Contrast MRI coronal section showing enhancement of dural mass in the frontal region along with dural tail.

**Microscopic:** numerous thin-walled capillaries; most of them are hyalinized with a few adipocyte-like cells. Courtesy of Jaiswal AK, Mehrotra A, Kumar B, Jaiswal S, Mukul V, BehanS, Pal L. Neurology India 2011, 59 (1) : 87-91.

The cytoplasm is filled with a large fat droplet, and the nucleus is placed peripherally. See arrow on image below. The second type of fat deposition is seen in the xanthomatous variant. There are cells containing numerous fine vacuoles of fat, with a centrally located nucleus. It has also been suggested that lipomatous and lipoblastic features are the result of metaplastic change and that xanthomatous change is simply due to lipid storage.
**Differential diagnosis**

Lipomatous meningiomas with little lipid accumulation will be indistinguishable from typical meningiomas and thus share their differential diagnosis. Those with abundant fatty material will have a different differential diagnosis consisting of: intracranial lipoma, intracranial dermoid cyst, xanthomatous meningioma, osseous meningioma and intra-axial tumours such as glioblastoma, pleomorphic xanthoastrocytoma and metastatic mucinous carcinoma.

**Treatment:** surgical removal.

**Prognosis:** The prognosis is good provided that removal is complete.

**MELANOTIC MELANOMA – also known as meningeal melanocytoma.**

**Pathology:** This is a very rare variant of metaplastic meningioma which arises from leptomeningeal melanocytes; small pigment cells found mostly in the meninges covering the ventrolateral surfaces of the medulla oblongata, posterior fossa or Meckel’s cave.

**Imaging:** On CT these are commonly isodense to grey matter, with variable enhancement. – see tumour in the cerebello-pontine angle below.

**MRI** – appearances vary with the amount of melanin in the pigment cells.

- **T1 and T2:** iso- or hyperintense and **T1 C+**: homogenous enhancement - see below a further tumour on the convexity.

![Images courtesy of Jaiswal S, Mukul V, Tungria A, Jaiswal AK, Srivastava AK, Behan S. Neurology India 2011, 59 (3) : 413-419.](image)

**Treatment and prognosis:**

Similarly to other meningiomas the treatment of melanotic meningiomas is usually surgical excision, with complete tumour removal being the best therapeutic option.
MYXOID MENINGIOMA

Is a rare histological tumour and one of the subtypes of metaplastic meningiomas. They are characterised by a marked myxoid transformation, containing endothelial cells, pericytes, and stromal cells. Myxoid meningiomas cells have a stellate appearance, an oval nucleus, scant eosinophilic cytoplasm, and a characteristic nuclear pseudo-inclusion (invagination of the cytoplasm into the nucleus).

Immunohistochemistry plays an important role in the diagnosis of these tumours, differentiating them from a more aggressive tumour, such as chordoid meningioma, which also demonstrates a myxoid stroma.


Axial head CT scan (A) revealing a left middle cranial fossa, extraaxial low-density mass with areas of hyperdensity which could be haemorrhage within tumour. There is significant mass effect, midline shift, uncal herniation, and pending entrapment of the right lateral ventricle.

MRI – axial and coronal T1 Gd contrast shows avid enhancement. (B–C) It demonstrates a broad-based dural margin along the tentorium and the floor of the left middle cranial fossa, especially in the coronal series. Magnetic resonance image (D) obtained after gross total removal, shows improvement in midline shift and mass effect.

Microscopic: see next page
Panels A – C show a myxoid, spindle cell neoplasm of moderate cellularity. The neoplastic cells show oval to irregularly shaped nuclei with occasional nuclear pseudo-inclusions. No significant mitotic figures or tumour necrosis were seen.

Panel D – Alcian blue – pH 2.5 The myxoid appearance in the myxoid type is attributable to the excessive presence of hyaluronic acid and chondroitin sulphate, which impart strong aqua blue staining when stained with Alcian blue at an acidic pH of 2.5. Hyaluronidase reduces the stain and therefore indirectly confirms the presence of hyaluronic acid within the matrix of these cells.

**Immunohistochemistry**: shows reactivity for epithelial membrane antigen and vimentin with little nonspecific S100 reactivity.

**Differential diagnosis**: it is important to differentiate “myxoid” metaplastic meningioma from higher-grade meningiomas with similar histological characteristics that may be associated with a worse prognosis, especially the chordoid meningioma that also has a myxoid stroma but differs in cellular appearance and immunohistochemical reactivity. Unlike the myxoid metaplastic meningioma cells, chordoid cells are polygonal in shape with round nucleoli and abundant vacuolated cytoplasm. The cells are often arranged in a cord-like fashion rather than in tandem. Moreover, with myxoid meningioma almost never see lymphocytic cell involvement. In rare instances, however, and mostly in the paediatric age group in association with Castleman disease, one may come across some lymphocytic cells with the chordoid type. All these points are important in differentiating low-grade myxoid (metaplastic) meningioma from the higher-grade chordoid meningioma.

**Prognosis**: this lesion is believed to carry a good prognosis with little chance for recurrence.
OSSEOUS MENINGIOMA - account for most of the metaplastic meningiomas. Frequently spinal in location. Rare - less than 25 cases of ossified meningioma had been reported from 1977 to 2005.

Microscopy:
Specimen A - has areas of calcification and ossification. B – tumour cells were positive for EMA (epithelial membrane antigen).


Figure 1: A) The CT scan – left image - reveals the presence of a subcortical tumour (arrow) located in the posterior frontal lobe of the right side. There is heavy calcification within the tumour (indicated by star).

B) MRI T1W – middle image - The extra-axial well-defined lobulated tumour with relative mixed hypo- and iso-signal intensity occupies the right temporal region. Increased signal density is in the periphery of the tumour (T-weighted MRI) – arrows.

C) MRI T2W Decreased signal density in the central portion of tumour corresponding to the calcification – arrows.

Treatment: surgical excision.
Prognosis: excellent

XANTHOMATOUS MENINGIOMA

Extremely rare variant of metaplastic meningioma characterised by cells with a lipid-filled vacuolated cytoplasm. Only 5 cases reported by 2013.
**Age:** all age groups affected

**Pathology:** In the case of xanthomatous meningiomas, they show an extensive xanthomatous change in their cells together with the characteristic features of meningotheial meningiomas. As these cells are positive for the epithelial membrane antigen (EMA), they can be differentiated from macrophages.


They tend to be hypodense on non-contrasted CT images due to the lipid content. MRI - with contrast showing a well-circumscribed tumour with attachment to the dura mater in the parasagittal to frontal region.

**Histopathological features.**

A: left panel of upper row - The tumor comprises two components. The conventional meningioma component (upper right in that image) is composed of polygonal cells with eosinophilic cytoplasm and bland round to oval nuclei. The xanthomatous component (lower left in that image) comprises vacuolated clear cytoplasm with bland round nuclei. HE, x 200.

B: Xanthomatous component – right panel of upper row. The tumor cells have rich clear vacuolated cytoplasm. HE, x 400.

C: - lower row - A transition between the conventional meningioma and the xanthomatous area is present. Psammomas are present. HE, x 100.
Immunohistochemical features. A: Epithelial membrane antigen is expressed in the xanthomatous area, x 200. B: Adipophilin is expressed in the xanthomatous area as well as in the conventional meningioma, x 200. Adipophilin is an antibody that recognizes protein associated with lipid droplets, and is used as a useful immunohistochemical marker.

**Treatment:** total resection

**Prognosis:** satisfactory in the 5 cases described.

**Specific meningioma subtypes associated with recurrence and aggressive behavior.**

This includes as WHO grade II- chordoid, clear cell and atypical

And WHO grade III – rhabdoid, papillary and anaplastic

**WHO grade II**

**CHORDOID – 9538/1**

Chordoid meningioma is characterized by nests and aggregates of neoplastic meningoepithelial cells separated by abundant extracellular myxoid matrix.

**Age:** occurs at all ages.

**Sites:** adult examples form large supratentorial masses, frequently lack lymphoplasmacytic infiltrates and are not associated with systemic manifestations.

**Imaging:** courtesy of Dr Mahomed A Osman, Radiopaedia.org, rID: 23037. T1W post contrast sagittal on the left and an axial T2W image on the right.
T1 and T2 signal characteristics are generally similar to other meningiomas, and no morphological features are particularly helpful in distinguishing chordoid meningiomas from other variants. They are more heterogeneous and perhaps more likely to involve adjacent bone.

**T1** - typically iso-intense to grey matter (same as typical grade 1 meningiomas)

**T2** - typically mildly hyper-intense to grey matter (grade 1 tumours are typically isointense)

- peritumoural oedema is variable (absent to pronounced)

**T1 C+** - most are vividly enhancing but occasional areas of non enhancement due to necrosis may be seen.

**Microscopy:** The epithelioid tumour cells demonstrate cytoplasmic vacuolization, and are embedded in a mucoid matrix which has abundant hyaluronic acid and chondroitin sulphate.

The mitotic index of these tumours has been variably reported (0.4-11.4%) and it is likely that this is not the underlying cause of higher reported recurrence rate.

Chordoid tumours are usually vimentin positive and at least focally EMA positive, and GFAP negative. Focal positivity for S-100 protein and Cam 5.2 is occasionally observed.

Chordoid meningioma has areas that look like chordoma and clinically there is a high rate of local recurrence following subtotal resection. The microscopic features associated with recurrence and aggressive behaviour in ordinary meningiomas are often lacking in chordoid meningioma. Despite this chordoid meningioma almost always recur when subtotally excised, at a rate higher than that for subtotally resected atypical meningiomas. It is suggested that the mucoid quality of the stroma may facilitate local tumour spill and spread during surgical manipulation.

The chordoid appearance corresponds to the presence at least focally within the meningioma of clusters and cords of epithelioid cells, often with vacuolated cytoplasm, set amidst a pale basophilic myxoid matrix. Areas of conventional meningioma are usually present, but classical meningotheelial patterns may be very limited and focal in distribution.
Differential diagnosis: has to be distinguished from microcystic meningioma, chordoma, chondrosarcoma and myxoid soft tissue tumours.

In suprasellar locations chordoid glioma enters the differential diagnosis. This demonstrates strong GFAP and vimentin positivity in the clusters and cords of epithelioid cells but only weak or negative EMA staining.

Treatment: surgical excision.

Prognosis: may live for a few years before recurrence.

CLEAR CELL MENINGIOMA – 9538/1

Incidence: rare variant was first described in 1995 and by 2009, 50 cases only had been reported.

Age: mean age 30 years.

Gender: no sex predilection.

Sites: often arises in the spinal canal, especially the lumbar region, or the posterior fossa (in particular the cerebello-pontine angle).

Pathology: microscopic appearances may be quite bland but the tumour has the capacity to behave aggressively, particularly when arising in intracranial sites.

Microscopic: generally lack typical meningothelial characteristics such as whorls and psammoma bodies. The clear cells are polygonal with abundant clear, PAS-positive (glycogen-rich) cytoplasm, separated by extensive collagenous bands and hyalinised vessels. The clear cell appearance results from the accumulation of glycogen. The nuclei lack pseudo-inclusions and are uniform and rounded.
**Immunohistochemistry:** In keeping with their meningothelial character, all clear cell meningiomas demonstrate strong and diffuse vimentin positivity and EMA (epithelial membrane antigen) positivity. The tumours are generally cytokeratin and S 100 protein negative, and often demonstrate a progesterone receptor positive, oestrogen receptor negative phenotype.

**Differential diagnosis**

Clear-cell meningioma is histologically unique but should be differentiated from other similar clear cell tumors of the central nervous system, such as metastatic renal cell carcinoma, haemangioblastoma, oligodendroglioma, germinoma, pleomorphic xanthoastrocytoma, lipid-rich glioblastoma, and clear-cell ependymoma.

Some metastatic clear cell carcinomas e.g. renal cell carcinoma – may be glycogen-rich, EMA and vimentin positive, like clear cell meningioma but have a strong and widespread cytokeratin positivity, unlike clear cell meningioma.


**Clinical example:** MR imaging findings of clear-cell meningioma with diffuse leptomeningeal seeding in 17-year-old man.

A. Initial contrast-enhanced T1-weighted axial MR image shows 1 × 3-cm, strongly enhancing mass at left parietal convexity (arrow) associated with localized leptomeningeal enhancement in ipsilateral Sylvian fissure (small arrows). Mild hydrocephalus is present. Mass was isointense on T1-weighted image and slightly hyperintense on T2-weighted image (not shown).

B. Microscopy: Tumour is composed of back-to-back monotonous round cells with clear cytoplasm and fine nuclear chromatin.

C. Contrast-enhanced T1-weighted axial MR image obtained 7 months later shows extension of leptomeningeal enhancement into subarachnoid space around anterior portions of left frontal and parietal lobes and perimesencephalic cistern (small arrows). Hydrocephalus was greater. Round low intensity in left posterior temporal calvarial region is owing to susceptibility artifact secondary to previous surgery (arrow).

D. Contrast-enhanced T1-weighted sagittal MR image obtained another 7 months later shows more diffuse enhancement of almost entire subarachnoid space. Hydrocephalus disappeared after placement of ventriculoperitoneal shunt (not shown).

E. Contrast-enhanced T1-weighted sagittal MR image of whole spine taken at same time as D shows diffuse leptomeningeal enhancement along surface of whole spinal cord and nerve roots (small arrows).

F. Contrast-enhanced T1-weighted sagittal MR image 2 months after radiation therapy shows marked decrease of diffuse enhancement of subarachnoid space compared with figure D.
Treatment: surgery followed by radiation therapy to the brain and entire spine in view of the leptomeningeal seeding from the cranium.

Prognosis: Tend to recur in 60% of cases. Histologic parameters do not predict recurrence, because cellular anaplasia is lacking and growth fraction is low in most clear-cell meningioma. Survival to 13 years is known in some cases.

ATYPICAL MENINGIOMA – 9539/1

Incidence: Account for 7 – 10% of all meningiomas.

The entity of atypical meningioma recognizes that the presence of certain morphological features, whilst not diagnostic of ‘malignant’/anaplastic meningioma, identifies a group of meningiomas at increased risk of local recurrence for whom more careful post-operative surveillance and/or post-operative adjuvant therapy might be appropriate. Atypical histological features may be evident de novo, or as a result of progressive transformation of a pre-existing meningioma.

In the latest WHO classification, the meningioma grading scheme was revised so that the microscopic variables are graded on the basis of their absence or presence, rather than their extent.

Atypical meningiomas recur in 29 – 40% of cases and anaplastic meningiomas recur in 50 – 78%.

Criteria: atypical meningioma is defined by any one of the following 3 criteria:-

1. 4 or more mitoses per ten high power fields (field area of 0.16 mm²)
2. Presence of at least 3 of the following 4 features:-
   - sheeting architecture (uninterrupted pattern-less or sheet-like growth)
   - hypercellularity
   - macronucleoli
   - small cells with high nucleus:cytoplasm ratios
   - foci of ‘spontaneous’ or ‘geographic necrosis.
In the example, there is an irregular interface between the meningioma and the underlying cortex. There is microscopic evidence of parenchymal invasion by the meningioma – see arrow. Irregular nests of the neoplastic meningotheelial cells infiltrate amongst gliotic and reactive cortical tissue.

- **mitotic activity, ‘sheeting’**
- **necrosis**
- **‘small cell’ change**
**Molecular pathology/genetics:** atypical meningioma is associated with the following changes –

*Atypical meningioma (WHO grade II)*

- -1p (40%-75%)
- -6q (30%)
- -10 (30%-40%)
- -14q (40%-60%)
- -18q (40%)
- +1q, 9q, 12q, 15q, 17q, 20q (30%-50% each)
- Loss of TSLC1 expression (70%)
- Loss of PR expression (60%-80%)
- Telomerase/hTERT activation (60%-90%)
- Notch, WNT, IGF, VEGF activation

**Imaging:** The post contrast CT scan below of an 82 year old female shows finger-like projections of tumour - (horizontal arrow) - extending beyond the main bulk of the tumour indicating infiltration of the underlying brain. The tumour was almost iso-dense with brain non-contrast and then enhanced considerably following the injection of I.V. contrast. At a few sites connection with the falx cerebri exists and the mass caused the falx to be bowed to the left of the midline.

The mass has amputated the tip of the frontal horn of the right lateral ventricle and attenuated and stretched the tip of the frontal horn of the left lateral ventricle (small arrow).

Some element of localized oedema is present contiguous with the lateral aspect of the mass – long thin oblique arrow.

The atypical meningioma can extend through the bone of the skull vault. The coronal post contrast CT image below, with bone windows, courtesy of Assoc. Professor Frank Gaillard, Radiopaedia.org, rID : 4729 shows the bilateral parafalcine mass has eroded the adjacent skull vault.
**Prognosis:** Survival at 5 and 10 years was recorded in 95% and 79%, respectively, of patients with atypical meningioma.

Recurrence-free survival and median time to recurrence were longer in patients with atypical malignant meningiomas than those with anaplastic meningioma: 11.9 versus 2 years.

**WHO grade III**

**ANAPLASTIC MENINGIOMA – (malignant) – 9530/3 (was called meningeal sarcoma)**

**Definition:** defined by either of the following criteria:

- A high mitotic index (20 or more mitoses per ten high-power fields -field area 0.16 mm²)
- Focal or diffuse loss of meningotheelial differentiation at light microscopic level, with obviously malignant cytology resulting in a sarcoma, carcinoma or melanoma-like appearance.

**Incidence:** are rare – account for no more than 1 – 5% of all meningiomas.

**Etiology:** like the atypical meningioma, it can arise *de novo*. Or it can be the result of progressive transformation of a pre-existing meningioma.

**Clinical:** the CT study below was a baby aged 4 months who had presented with a rapidly enlarging head.

**Imaging:** the CT shows a massive almost centrally placed tumour which had enhanced with contrast. The baby died soon after exploratory surgery.

**Microscopic:** spindle cell sarcoma
Molecular/genetic:

- -1p (100%)
- -6q (50%)
- -9p21 (60-80%)
- -10 (40-70%)
- -14q (60-100%)
- -18q (60-70%)
- NDRG2 hypermethylation (70%)
- Loss of TSLC1 expression (70%)
- Loss of PR receptor (80-90%)
- 17q23 amplification (40%)

**Prognosis:** They recur in 50 – 78% of cases, are usually fatal, with median survivals of the order of 18 months and a 5-year mortality rate of almost 70%.

A primary sarcoma is invasive from the start. It can arise in the first decade of life and have a short clinical history with rapid deterioration and swift recurrence post-op.

**PAPILLARY MENINGIOMA – 9538/3**

**Definition:** Is a rare form of meningioma.

**Age:** Often occurs in children and young adults.

**Clinical:** Symptoms depend on location. Headaches, seizures and neurological deficits may occur.

**Pathology:** Characterized by aggressive clinical behavior with frequent brain invasion and local recurrence and has significant capacity for metastatic spread. The morphological diagnosis rests upon the presence, at least focally, of a perivascular papillary pattern, with neoplastic cells radially arranged around blood vessels. In the image below, the arrow indicates a well formed papilla with a central fibro-vascular core.


The local image below is also a papillary meningioma. The papillary structures of this meningioma variant comprise central fibrovascular stromal cores lined by neoplastic meningothelial cells.
**Differential diagnosis:** other primary and metastatic CNS tumours with a papillary architecture. In certain sites and clinical settings choroidplexustumours,ependymomas,astroblastomas,and metastaticpapillary carcinomas may enter the differential.

**Imaging:** the MRI, T1W post contrast showed the mass in the frontal area with central necrosis. Marked contrast enhancement has occurred.

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**RHABDOID MENINGIOMA - 9538/3**

The term rhabdoid morphology is referring to the characteristic resemblance of the cells to arhabdomyoblast without true skeletal muscle differentiation.

**Age:** middle age and occurs about a decade earlier than conventional meningioma.

**Gender:** some predilection for females.
**Imaging:** Rhabdoid meningioma tends to have cystic and solid components with homogeneous enhancement of the solid component.

There is extensive peri-tumoural oedema.- see CT below.

Bone destruction, indistinct margins and central necrosis are known to correlate with aggressiveness

![CT Image](image)

**MRI:** Signal characteristics that correlate with aggressive behaviour of meningiomas include:

- **T1:** indistinct tumour border (saw teeth appearance of the margins) and marked mass effect
- **T2/FLAIR:** marked peritumoural oedema
- **DWI/ADC:** hyper-intense signals on DWI that show restricted diffusion on ADC correlate with hyper-cellularity and more aggressive behaviour
- **T1 C+ (Gd):** avid enhancement that may extend into the bone if associated with bone destruction
- **MR spectroscopy:** elevated level of alanine at short TE

CT image above and MRI Images courtesy of Dr Azza Elgendy, Radiopaedia.org, rID : 33802.

Left image is axial FLAIR, centre- sagittal T1W and right is axial T1W with Gd contrast.
**Microscopic:**

Characterized by the presence of perinuclear eosinophilic cytoplasmic bodies, which represent masses of intermediate filaments which displace the nuclei eccentrically.

Rhabdoid morphological features may be expressed in a large number of diverse and histogenetically unrelated tumours, including meningioma. The expression of the rhabdoid phenotype is almost always associated with aggressive behavior and poor prognosis, regardless of the nature of the underlying neoplasm. The acquisition of a rhabdoid phenotype represents a phenotypic marker of anaplastic transformation in meningioma.

**Clinically,** rhabdoid meningioma follows a very aggressive course, characterized by repeated local recurrence and in some cases metastatic spread.

In the largest series of rhabdoid meningiomas published to date, rhabdoid histology was defined by the presence of loosely cohesive sheets of cells with abundant eosinophilic cytoplasm, eccentrically placed nuclei and hyaline and often fibrillary paranuclear inclusions. The presence of macronucleoli, although a feature of many cases, is not an essential diagnostic requirement for inclusion. The hyaline and fibrillary cytoplasmic inclusions correspond ultrastructurally to large whorls of tightly packed intermediate filaments, which often indent and displace the nucleus and entrap surrounding cytoplasmic organelles.

Rhabdoid features in meningioma may be evident at the time of first presentation and diagnosis, but in a significant proportion of cases, emerge or become more prominent with the development of one or more recurrences. In general, areas with the microscopic appearance of conventional meningioma are present, but in some cases, the morphology may be purely rhabdoid, either at presentation or in recurrent disease. Most rhabdoid meningiomas demonstrate other histological features of malignancy.

A minority have only focal rhabdoid features, and lack other histological features of malignancy; the behaviour of these tumours remains to be determined.
A small proportion of rhabdoid meningiomas may demonstrate combined papillary and rhabdoid features. Pseudo-papillary patterns may manifest as a result of a loss of cellular cohesion, but strictly speaking, papillary patterns rely upon the identification of perivascular pseudo-rosette formation.

**Immunohistochemically,** all rhabdoid meningiomas are strongly and diffusely vimentin positive, show at least some membranous EMA staining and rarely express GFAP.

**The differential diagnosis** of pure or extensive rhabdoid patterns includes melanoma, carcinoma, sarcoma and malignant glioma with dural attachment or invasion. Considerable morphological overlap exists with melanoma, particularly the presence of large nucleoli and nuclear pseudo-inclusions.

Gemistocytic astrocytoma and ependymoma may enter the differential diagnosis, the latter particularly when a papillary pattern with perivascular pseudo-rosettes and GFAP positivity are identified.

**Prognosis:** The tumour has a tendency for recurrence and has a poor prognosis.

**MENINGIOMA versus METASTASIS**

Metastases can be solid and mimic the transitional type of meningioma or they can be necrotic and thus cystic so able to mimic the microcystic variety of meningioma.

The images below are from the CT scan of a 38 year old female who had been taking a contraceptive pill and presented with hemiplegia, so the provisional diagnosis was occlusive stroke related to the pill.

Image (a) Non-contrast - shows a mass lesion in the left posterior parietal region – white solid broad arrow. Anterior to this and contiguous with the mass, is severe localized oedema – thin white arrow.

Image (b) – post contrast - The severe mass effect has caused the falx to be bowed markedly to the right of midline – black arrow. Such severe shift would result in herniation of the left frontal lobe under the free edge of the falx and this in turn could cause ischaemia in the territory of the left or
even both anterior cerebral arteries but this had not yet occurred. The mass was mostly necrotic and so appears cystic but has a solid perimeter, especially on its medial aspect.

There is no indication of compression from without – the picture is of a mass within brain. Compare this with another patient with a meningioma - below -where the CT scan shows the grey-white junction is displaced internally. Posterior to the mass is focal oedema – upper arrows. Both frontal horns are attenuated (the right almost obliterated). The septum pellucidum is displaced to the left. – middle arrow. The choroid plexuses are unequally visualized which is not of any significance – lower single arrow.

The differential diagnosis therefore rests between a necrotic primary tumour, a secondary metastasis or abscess. Chest radiograph disclosed a mass in the lung which was biopsied and found to be a squamous cell carcinoma of the lung. SCC metastases frequently become necrotic, as do all metastases from tumours of squamous origin.

**MULTIPLE MENINGIOMA vs MULTIPLE METASTASES**

Multiple lesions can occur with meningioma and also with metastases. Single lesions occur more often than multiple in the case of meningioma but these have still to be distinguished from the solitary dural- based metastasis.
The patient in image (a) had multiple partially calcified, partially contrast enhancing meningiomas. One could see the attachment to the anterior falx cerebri – single arrow.

The left temporal meningioma arises from the pterion which is another common site of origin – double arrows. There is associated peritumoural oedema which is a frequent association with meningioma – black solid arrow.

The patient in image (b) has a solitary lesion attached to the dura of the anterior falx but it was not a meningioma, despite the uniform enhancement and peritumoural oedema. It was a dural metastasis from melanoma – see arrow.

So the take home message is: multiple lesions are not necessarily metastases and a single extra-axial lesion does not exclude metastases.
Ionising radiation has sufficient energy to displace electrons from molecules. Free electrons can damage human cells. At very high doses damage can be evident within days of exposure. Late onset effects, such as cancer may develop even with exposure to relatively low doses.

Radiation-induced meningioma is the most common brain neoplasm known to be caused by ionizing radiation. Grouped into 3 categories: those due to high-dose (> 20 Gy), intermediate-dose (10-20 Gy), and low-dose (< 10 Gy) radiation.

High-dose RIMs were reported in the literature between 1953 and 2002. The radiation doses ranged from 22 to 87 Gy, and the majority of patients had undergone radiotherapy as children. The mean latency from irradiation to diagnosis of the meningioma was ~ 19 years, with a tendency for shorter latency in patients treated with higher doses and those who had undergone radiotherapy at younger ages.

The increased incidence of meningiomas following exposure to low-dose radiation has been reported in patients who, as children, had undergone radiation treatment for tinea capitis, those whose heads and necks were exposed to medical and dental x-rays at a young age, and survivors of the atomic explosions in Hiroshima and Nagasaki.

1974, a retrospective cohort study in Israel showed a significantly higher risk of malignant and benign head and neck tumors among ~ 11,000 Israeli adults treated for tinea capitis as children.


This major epidemiological work is widely credited as proving the causal role of radiation in the development of meningiomas in some patients. Follow-up studies of the Israeli cohort showed that a radiation dose of only 1-2 Gy administered during childhood led to a 9.5-fold increase in meningioma incidence. Continuing follow-up shows that elevated risk of brain tumor, including meningioma, is positively associated with dose, with excess relative risk for benign meningioma rising to 18.82 for doses > 2.6 Gy. These studies showed a higher prevalence of calvarial tumours and multiple meningiomas, and higher recurrence rates in RIMs than sporadic meningiomas (SM).

The mean latency was ~ 36 years.

1980, Preston-Martin et al. noted a higher incidence of meningioma in women with a history of full-mouth dental x-rays. The risk in this cohort study was higher in patients who had undergone radiographic examinations as children or teenagers and in those in whom radiographic examinations were conducted before 1945, when doses were higher. The majority of tumours were located in the tentorial or subtentorial region. The authors of more recent case-control studies in Sweden and the US have found that dental radiographic examinations performed during the adult years may also increase the risk of meningioma.

The increased incidence of meningiomas among survivors of the 1945 atomic explosions in Japan was not shown until 1994, when Shibata et al. demonstrated a higher incidence of meningiomas in survivors of the bombing in Nagasaki.

In 1997 Shintani et al. published similar findings obtained in Hiroshima survivors. Due to the relatively low-dose exposure to ionizing radiation among these survivors compared with those undergoing radiotherapy for tinea capitis, the average latency was greater in the Japanese studies.
**The risk of meningioma induction was shown to increase with closer proximity to the bombs' epicenters and in those exposed during childhood.**

**Radiation-induced meningiomas (RIM)** are more frequently multiple and have a very long latency. Meningiomas are a much more frequent complication of radiation exposure compared to sarcomas or gliomas.

**Epidemiology**

The exact incidence of radiation-induced meningiomas is unknown - one study had an incidence of 22%. There is increasing incidence of developing RIMs over time, unlike radiation-induced gliomas that have a stable/decreased incidence 5-years post treatment. RIM tend to occur in younger patients when compared to spontaneous meningiomas.

Etiology;

- whole brain radiotherapy for childhood *leukaemia*
- radiotherapy for *tinea capitis*
- whole mouth *dental radiographs* (increased risk in examinations performed pre-1945 when doses were higher)
- survivors of Hiroshima and Nagasaki atomic bombs

**CT scan non contrast** below shows hyper-density in 4 locations, which later enhance with contrast.

Images courtesy of HenryKnipe. Radiopaedia.org, rID : 28317
**Pathogenesis:**

Radiation-induced meningiomas (RIM) may also exhibit more aggressive clinical behaviour than sporadic meningiomas (SM), including high recurrence rates following surgery and radiotherapy. Rubinstein et al. noted a 25.6% recurrence rate in 43 patients with RIM, and 11.6% of this group experienced multiple recurrences, compared with an 11.4% recurrence rate in 258 patients with SMs in their series. Both groups were followed for only 4 years. Higher recurrence rates in patients with RIMs than those with SMs have also been reported elsewhere.


This patient had a minor head injury which required a CT scan and this was negative for trauma but did show a small lesion in the left frontal convexity – see arrow in A. Six months later she had symptoms of raised intracranial pressure. A further CT scan showed the left frontal lesion had enlarged greatly – see MRI B. The MRI scan revealed 2 other small mass lesions in the right middle and frontal fossae – see C and D. Surgical resection of the left frontal mass was performed. The tumour was adherent to the dura mater of the left frontal convexity and the wall of the superior sagittal sinus.

**Histopathology** revealed frequent mitoses (D), hypercellularity (A), and focal necrosis (B), whorl formation (C) in the tumour specimens.
Immunohistochemical analysis revealed an MIB-1 labeling index of approximately 20%. The immunohistochemical profile revealed approximately 20% Ki-67-positivity (E).

The pathological diagnosis was atypical meningioma.

Radiation-Induced Meningiomas Subtypes. – meningotheliomatous, transitional and fibroblastic histological subtypes are the most common in RIM. Appear different from those seen in sporadic meningiomas. Have high cellularity, nuclear pleomorphism, an increased mitotic rate, focal necrosis, bone invasion and tumour infiltration of the brain. There may also be numerous multinucleated and giant cells and nuclei with vacuolated inclusions, psammoma bodies, foam cells and thickened blood vessels. RIMs were more often atypical, like the above example, or aggressive and multifocal with higher proliferation indices than sporadic meningiomas

There is a long latency between radiation exposure and diagnosis of RIM - on average ~35 years. They are more likely to be multiple, have a higher frequency of atypical (WHO grade II) and anaplastic (WHO grade III) and there are higher rates of recurrence than spontaneous meningiomas.

Treatment:

Surgical removal is the treatment of choice for most cases of RIM, although complete and safe resection may not be possible due to the lesion’s frequent multiplicity, involvement of osseous structures and vessels, and aggressive nature. Paradoxically, stereotactic radiosurgery or fractionated stereotactic radiosurgery may be appropriate adjuncts to surgery or may be performed in lieu of surgery in some patients, despite the radiation-related origins of RIMs. In some patients, angiography may be appropriate for visualization of the tumour's vascular anatomy and pre-operative embolization.

A large percentage of RIMs are located at the calvaria, and in cases of parasagittal or falcine meningiomas preoperative assessment of the superior sagittal sinus is critical in planning surgery.

MR imaging with MR venography is used for assessment of patency of the superior sagittal sinus, although angiography may be required in rare cases. In patients with highly vascular tumours, preoperative embolization may be beneficial.

The abnormal study due to occlusion of the superior sagittal sinus due to invasion by a meningioma is courtesy of Islam O. Medscape, Mar 20, 2016.

Left image – Normal MRV right image shows invasion of the SSS – see white arrow.

Radiation-induced meningiomas are characterized by associated marked changes to the scalp, including alopecia, atrophy, and poor vascularization. Poor skin condition may necessitate adjustment of the surgical approach and skin flap placement. Paradoxically, stereotactic radiotherapy may be used to treat patients with unresectable or residual/recurrent tumours.

Prognosis:

Recurrence rates are higher among patients with tumours involving the skull base or a major cranial sinus, where wide resection margins are often impossible to achieve.

ACKNOWLEDGEMENTS:

Pathology images: those not individually acknowledged in the text have as their source PathWest Laboratory Medicine WA.

Radiology images: those not individually acknowledged in the text have as their source Sir Charles Gairdner Hospital, The Queen Elizabeth II Medical Centre.

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