

## REVIEW ARTICLE

## Intracranial meningiomas in the present era of modern neuroimaging: diagnostic and management options, with radiological illustrations

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## INTRODUCTION

Etymologically, the term "meningioma" was first introduced by the American pioneer Neurosurgeon, Harvey Cushing in 1922.<sup>1,2</sup> It

originates from the arachnoid cap cells of the meninges, hence, typically attached to the dura.<sup>1,3</sup> Meningiomas are mostly benign tumours of multi-potential mesenchymal cell

## ABSTRACT

**Background:** Intracranial meningioma is the most common primary, intracranial, extra-axial neoplasm. It is mesenchymal in origin and arises from meningothelial cells of arachnoid villi of meninges.

**Objectives:** To re-emphasize the regional anatomic localisation and diagnostic radiological features of intracranial meningiomas, and do a review of their pathology and management, with a view to highlighting the worrisome clinical behaviour of these tumours despite improvement in imaging diagnosis and therapeutic options.

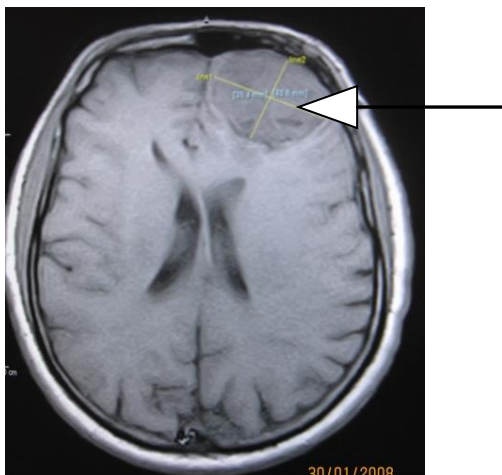
**Conclusion:** Meningiomas can be easily diagnosed radiologically, and characterised according to their sites and peculiar features, in this era. Though most of them are regarded as benign, their clinical behaviour in significant number of cases is not typical of benign tumours as recurrence rates are still worrisome.

**Keywords:** Arachnoid villi, cerebral convexity, CT, MRI, recurrence

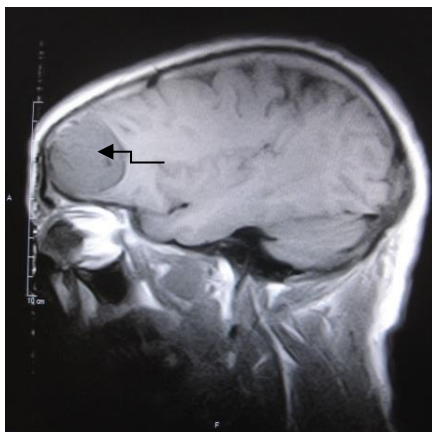
precursors, common in adults. They are relatively slow growing and rarely displaying biologically aggressive behaviour such as invasion of surrounding non-meningial tissues.<sup>4,5</sup> They are the most common type of extra-axial neoplasm as well as the most common primary non-gliar intracranial tumour.<sup>1,6,7,8</sup>

cerebral convexities, cerebellopontine angle and posterior aspect of the spinal cord.<sup>3</sup>

**Figure 1.** Typical vault para-falcine meningioma in axial brain T1W MR

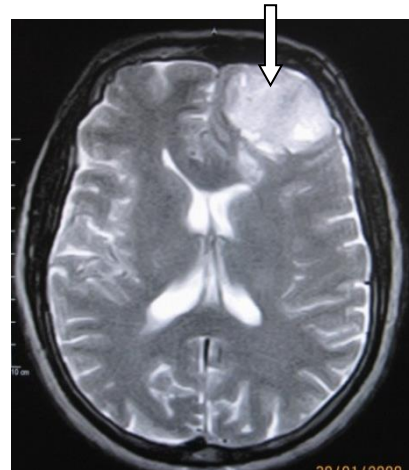


**Figure 2.** Sagittal T1W MRI showing frontal position of this mass



Meningiomas constitute 13 to 20% of all intracranial tumours.<sup>1,9</sup> In Africa, this figure is thought to be closer to 30%.<sup>10</sup> The incidence is ~6 per 100,000 of the population per year with a female bias, and this bias increases with increasing age.<sup>3,4,6,10</sup> The most frequent sites of occurrence are along the sagittal sinus,

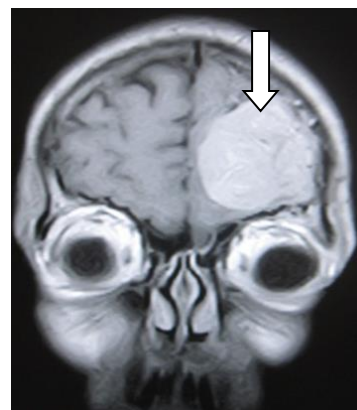
**Figure 3.** Axial T2W MRI showing mass is now hyperintense and devoid of edema



**Figure 4.** Axial FLAIR MRI image showing mass to be hyperintense and focally compressing cerebral cortex



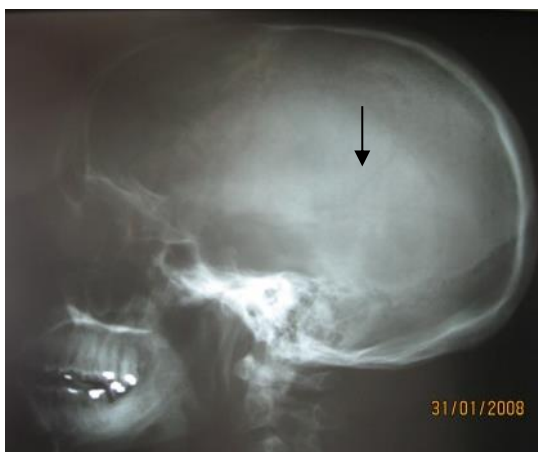
**Figure 5.** Enhanced coronal T1W MRI showing avid tumour enhancement



**Figure 6.** Enhanced axial T1W MRI showing dural tail enhancement



**Figure 7.** Middle meningeal artery prominence



**Figure 8.** Enhanced axial brain CT showing intraventricular meningioma in III<sup>rd</sup> & lateral ventricles – an atypical location



Meningiomas in general are solid tumours of mesodermal origin that appear as intracranial or intraspinal space occupying lesions.<sup>11</sup> In both subtypes, there is female predominance that is more emphasized in the intraspinal meningioma. Female to male ratio in intracranial meningioma is 2:1, but this ratio rises to 4:1 in intraspinal meningioma.<sup>1,5,9,10</sup> Some of these tumours show some levels of estrogen or progesterin immunoreactivity.<sup>10</sup> Progesterone receptors have been found in 80% of meningiomas, thus, leading to an increase in tumour size during pregnancy and luteal phase of menstrual cycle.<sup>9</sup> Meningiomas are rare during childhood and adolescence but more common in the middle-aged and elderly persons (note our two index patients).<sup>3,7,9</sup>

#### EPIDEMIOLOGICAL FACTORS

The majority of meningiomas are found incidentally on serial imaging, accounting for about 2/3 of all diagnosed meningiomas.<sup>7</sup> They are predominantly sporadic and the precise aetiology is not known, though there are risk factors thought to predispose to the development of these tumours. These factors include previous cranial irradiation, trauma, female hormones and neurofibromatosis type 2 (NF2).<sup>1,3,7,9,10.</sup>

Radiation and NF2 are factors associated with multiple intracranial meningioma. In fact, meningiomas are a much more frequent complication of radiotherapy compared to sarcomas or gliomas.<sup>1</sup> Multiple intracranial meningioma have developed even with a low-dose radiotherapy like in tinea capitis treatment in children.<sup>7</sup> Radiation-induced tumours typically have 20-35years' latency period after the exposure.<sup>1,7</sup> Interestingly, some single human leukocyte antigen (HLA) alleles and haplotypes have been noted to protect from or predispose to the developing of symptomatic central nervous system meningioma during adult life.<sup>4</sup>

Suspicion of neurofibromatosis type 2 (NF2) should also be raised in young patients less than 40years of age who developed meningioma.<sup>1</sup> In NF2 there are aberrations of

the Merlin gene on Chromosome-22 with deletion of the chromosome-22.<sup>1,9,10</sup> The NF2 patients are prone to developing multiple meningiomas, meningiomas at a younger age and /or malignant subtypes.<sup>10</sup>

### Sites of Occurrence

Meningiomas can occur in myriads of locations since meningothelial cells can be encountered as small clusters throughout the craniospinal axis with their great abundance in the arachnoid villi of the meninges.<sup>2,6,9</sup> Supratentorial meningioma is much more common than infratentorial meningioma.<sup>10</sup> Typically, the most common locations for meningioma are over the cerebral convexities, falx, para-sagittal region and sphenoid wing.<sup>10</sup> The intraventricular location is one of the sites of intracranial meningioma but the third ventricular location is not very common.

Other atypical development sites are the scalp, nasopharynx, neck, skin, superior sagittal sinus, parotid gland, oral cavity, parapharyngeal space, cranial nerves, peri-neural sheaths, lungs, mediastinum, adrenal glands, fingers and paraspinal regions.<sup>1,5,6</sup> Extracranial meningiomas are rare; the reported incidence is 1-2% of all meningiomas.<sup>5</sup> The meningiomas arising in locations outside the dural compartment have been called ectopic, extradural, calvarial, intra-osseous or extraneuraxial meningiomas. A single term "primary extradural meningioma" has been proposed by Lang, *et al*, for such lesions.<sup>5</sup> This term highlights the origin of these tumours as being separate from the dural coverings of any part of the brain or spinal cord and further differentiates these meningiomas from "primary intradural meningiomas," which may have secondary extracranial extensions and/or have metastasized.<sup>5</sup>

### CLINICAL FEATURES

Symptoms of intracranial pressure rarely occur in meningiomas, thus, they are usually seen as incidental findings on neuro-imaging.<sup>3,6</sup> Clinical presentations include episodic headache that intensifies with

recumbency, slowly progressive paresis, mental status change and focal seizures.<sup>1,3,7,10</sup>

### PATHOLOGY

Regional localisation of meningiomas is as follows:

- 85-90% Supratentorial
  - 45% parasagittal, convexities
  - 15-20% sphenoid ridge
  - 10% olfactory groove/planum sphenoidale
  - 5 - 10% juxtassellar
- 5-10% Infratentorial
- <5% Miscellaneous intracranial
  - intraventricular meningioma
  - optic nerve meningioma
  - pineal gland
  - intraspinal: especially thoracic
- <1% Extra Dural
  - sinonasal cavity (most common)
  - intraosseous (commonly fronto-parietal and orbital regions).<sup>1,5</sup>

If the tumour is invading only the outer layer of the dura and its main mass is extracranial, it should be accepted as primary extradural meningioma.<sup>5</sup> These are thought to arise from ectopic meningiocytes or arachnoid cap cells trapped in the cranial sutures during molding of the head at birth.<sup>5</sup> Misplacement and entrapment of meningothelial cells into suture or fracture lines as a result of trauma has also been speculated as the probable cause of calvarial meningioma.<sup>5</sup> Contrasts exist between usual and ectopic meningiomas.

Although primary intradural meningiomas occur twice as frequently in women as in men, primary extradural meningiomas do not appear to have a gender predilection.<sup>5</sup> Both meningiomas occur predominantly during later decades of life, but primary extradural meningiomas also have a second peak incidence in younger patients (especially during the second decade).<sup>5</sup> Diffuse meningiomatosis and multiple meningiomas also exist.<sup>9,12</sup> The term multiple meningioma is used to describe the simultaneous or sequential appearance of 2 or more

independently situated meningiomas, not necessarily of the same pathologic subtype.<sup>12</sup> The macroscopic features of meningioma correlates with radiological patterns. Two macroscopic forms are recognized viz. globose and en plaque dural based mass.<sup>1</sup>

Since the introduction of CT, the frequency of multiple meningiomas without neurofibromatosis has increased to 4.5-10.5% (from 3% reported in the pre-CT era).<sup>12</sup> Nevertheless, the concomitant occurrence of multiple intracranial and spinal meningiomas in the same patient, though rare, has recently been reported.<sup>12</sup>

### Histology

Histological subtypes of meningioma are varied and include:

1. Meningothelial
2. Fibroblastic
3. Transitional ( whorl formation)
4. Syncytial ( poorly formed polygonal cells arranged in lobules)
5. Angioblastic ( now classified separately as a haemangiopericytoma)
6. Clear cell ( occur in younger patients)
7. Psammomatous
8. Microcystic
9. Secretory
10. Chordoid
11. Lymphoplasmacyte-rich
12. Metaplastic
13. Mixed
14. Papillary
15. Rhabdoid.<sup>1</sup>

Some variants of meningioma arise from degenerative changes, for example cystic meningioma, osteoblastic meningioma, chondromatoid meningioma, meningioma with sarcomatous degeneration, meningioma with fatty degeneration.<sup>1</sup>

### Grading

Grading of meningioma generally follows the World Health Organization (WHO) classification for central nervous system (CNS) tumours.<sup>7,10,11</sup> The WHO 2000 Classification of Meningiomas is into grade 1, II and III.<sup>3</sup>

WHO Grade I - Benign meningiomas (85-90%) include meningoendothelial, fibroblastic, transitional, psammomatous, angiomatous, lymphoplasmacyte-rich, microcystic, and metaplastic meningiomas.<sup>7</sup> These characteristics of the sub-group are not relevant for the prognosis but mere descriptions of different histology.<sup>3,7,11</sup> The angioblastic subtype is the most aggressive grade I meningioma.

WHO II - These are atypical meningiomas, more aggressive with increased mitotic rate and greater tendency of recurrence.<sup>7,9,13,14</sup> In 2007, WHO changed the diagnostic criteria of Grade II meningioma, elevated grade II to 20-30% of all meningiomas instead of the traditional 5-10%, and included the atypical, clear cell, chordoid subtypes.<sup>3,4,13,14</sup> Previous irradiation is associated more with atypical meningiomas and their complete excision is more difficult.<sup>14</sup>

WHO III - Malignant meningioma which subtypes include rhabdoid, anaplastic, papillary.<sup>3,9,11</sup> Some authors have regarded the rare sarcomatous degenerative type as WHO Grade IV.<sup>1</sup>

### Differentials

The differential diagnosis largely depends on location and hyperostosis. They include cerebellopontine angle tumours, parasellar masses, primary glial tumours, chordoma, leptomeningeal metastasis, Bourneville's disease, NF, colloid cyst, pleomorphic xanthoastrocytomas, idiopathic hypertrophic pachymeningitis, sarcoidosis and Paget's disease.<sup>1,3</sup>

### NEUROIMAGING

Conventional radiographs are usually of limited value in the diagnosis of intracranial meningiomas because of the superimposed bony structures. The radiographs will only show enlarged middle meningeal artery grooves, enlarged foramen spinosum, a ball of calcium, hyperostosis or lytic lesions.<sup>1</sup> Hyperostosis is the most common radiographic finding (59%), osteolysis (35%)

and a mixed picture of hyperostosis and osteolysis in 6% of cases.<sup>5</sup>

Conventional angiography demonstrates the *Mother-in-Law sign* (of "comes early, stays late, very dense" tumour blush) and the *spoke wheel appearance* and dense venous filling.<sup>1,6</sup> The arterial phase reveals a tumour blush originating from the middle meningeal artery, highly evocative of the hypervascularization of a meningioma.<sup>6</sup> It could also demonstrate that meningiomas typically narrow arteries by encasement unlike in pituitary macroadenoma.<sup>1</sup>

A CT with bone windows and contrast enhancement with iopamidol is necessary in the detection of a tumour, cortical destruction, intra- and extra-osseous extension and mass effect. On native CT, 60% of meningiomas are slightly hyperdense compared to normal brain, and 20-30% have some calcifications. And on non-native, enhanced CT, 72% of meningiomas are bright with homogenous contrast enhancement, which is a less frequent feature in the malignant or cystic variants. Hyperostosis is typical of meningiomas that abut the base of skull, and reactive hyperostosis is differentiated from skull vault invasion as the latter eventually involves the outer table.<sup>1</sup>

On MRI, a dural-based, extra-axial mass that is intensely and homogeneously enhancing is diagnostic and characteristic of meningioma.<sup>3</sup> Intense enhancement is described as isointensity with choroid plexus signal on gadolinium-enhanced images.<sup>15</sup> About 60-72% of meningiomas exhibit a *dural tail* which is a streak of dural enhancement flanking the main tumour mass.<sup>1,3</sup> However, the MRI provides a better anatomic delineation in the evaluation of the soft-tissue component and extradural extension of the lesion, and so, is diagnostic with superior demonstration of the *dural tail* than CT.<sup>3,5</sup>

On T1W MRI, meningiomas are isointense compared to grey matter in 60-90% of cases, and somewhat hypointense in 10-40%.<sup>1</sup> On T2W, they are isointense in ~50% and

hyperintense in 35-40% which usually correlates with soft textures and hypervascularity.<sup>1</sup> The MRI may also show the *CSF Cleft Sign*.<sup>1</sup> Very hyperintense lesions may represent the microcystic variant and are more commonly associated with atypical features and adjacent brain oedema. Oedema is uncommon in meningioma, but can best be seen on T2W images, and correlates with size, rapid growth, location (convexity and parasagittal more than elsewhere), invasion in the case of malignant meningiomas. The underlying mechanisms for the oedema may relate to venous stasis, thrombosis, compressive ischaemia, aggressive growth and parasitisation of pial vessels.<sup>1</sup>

Positron emission tomography (PET) and single-photon emission CT (SPECT) are ancillary in distinguishing tumour recurrence from post-radiation tissue necrosis. Functional imaging with PET, MRI, or magnetoencephalography assists in surgical planning and definition of the anatomic relationship of tumour to critical brain regions (e.g. the primary motor or language cortex).<sup>3</sup>

#### THERAPEUTIC OPTIONS

There are several therapeutic options available for meningiomas.<sup>3</sup> Advisedly, asymptomatic, stable and incidental small meningioma without cerebral oedema in a patient aged more than 65 years old should be followed-up with MRI every 6 or 12 months.<sup>3,7,9</sup> If observation is elected in other cases, serial MRIs should be obtained at 3 months, 9 months and then, yearly if stable.<sup>7</sup> This is because meningiomas are slow growing tumours with a low mitotic index, therefore, remaining stable on serial imaging.<sup>7,11</sup> Growth rate on the average is a few millimeters in diameter per year.<sup>3</sup>

Surgery can be used in 80% of cases.<sup>6</sup> Total surgical resection is curative.<sup>3,5,11</sup> Surgery aims at total extirpation of the symptomatic meningiomas and of their dural implants thus decreasing recurrence possibilities, and improving the patient's chances of healing.<sup>9</sup> Surgery should be prescribed exclusively for

cases with tumour expansion or cerebral oedema, with the resultant clinical features. Angiographic pre-operative embolisation, especially in skull base meningioma, using particles is favoured 7-9 days prior to surgery to reduce tumour vascularity.<sup>1,2</sup>

Surgical resection is rated using the Simpson's Grading which is based on the extent of resection and is predictive of local recurrence.<sup>1</sup> It ranges from Grade I which is complete tumour excision including resection of underlying bone and involved dura mater to Grade V which is decompression with or without biopsy. Grade I is more difficult if ever possible to attain in the cavernous sinus, petroclival region, posterior sagittal sinus and optic nerve meningiomas.<sup>1</sup>

Cases of incomplete resection, tumour progression, skull base tumours, tumours <3cm, inaccessibility to surgery, atypical/anaplastic histology and brain invasion cases for radiotherapy.<sup>1,5,6,7</sup> Although radiotherapy only rarely achieves a true tumour mass reduction, it can arrest growth in malignant as well as benign meningiomas for some years.<sup>11</sup> Improved outcome has been observed if the dural tail is included in the radiation field.<sup>7</sup>

The use of systemic chemotherapy for treatment of malignant meningiomas has been reported recently.<sup>6</sup> The chemotherapeutic regimen includes cyclophosphamide, adriamycin, and vincristine. Hydroxyurea has also been administered as an adjunct chemotherapeutic agent in recurrent and unresectable meningiomas to achieve dramatic cytoreductive effect on meningioma cells by inducing an apoptotic cascade.<sup>11</sup>

#### COMPLICATIONS

Complications, depending on location, include sinus invasion, thrombosis, haemorrhage, intracranial oedema, intraosseous extension and metastasis to non-neural non-cranial structures. Metastatic disease is rare, but has been reported. Pulmonary metastases from a benign

metastatic meningioma has even been reported lately.<sup>16</sup>

#### FOLLOW-UP

Recurrence in meningiomas occur on an average of 4 years after the initial surgery.<sup>7</sup> It could be monitored with contrast-enhanced MRI, and rates vary with grade and length of follow-up, for instance, WHO I meningioma recurrence rate is 6.9% of cases, WHO II atypical meningioma in 34.6%, and WHO III malignant meningioma is 72.7%.<sup>1,4,11</sup>

Brain invasion, malignancy, multiplicity, location and incomplete excision (even if the lesion has a benign histology), are factors that predispose to recurrence.<sup>3,10</sup> Poor performance status of meningioma include brain invasion, adjuvant radiotherapy, extent of resection, and p53 over-expression.<sup>7</sup> Negative prognostic factors are high grading, young age, chromosome alterations and male gender, whereas positive prognostic factors are elderly age and tumour calcifications.<sup>7</sup>

Although it has been a well stated fact that the extent of resection is the most important factor underlying recurrence, even totally resectable tumours such as convexity meningiomas have a median recurrence rate as high as 10% after 5 years, 20% after 10 years, and 50% after 20 years, of follow-up.<sup>10</sup> Recurrence rates after surgery alone are about 10% in GTR and 40% after STR.<sup>7</sup> With STR, local external-beam radiation therapy or stereotaxic radiosurgery reduces recurrence to <10%.<sup>3</sup> Clear cell, papillary and rhabdoid cell types have a high rate of recurrence.<sup>1</sup>

#### SURVIVAL RATE

The overall survival period is 12 years for WHO Grade II meningiomas, compared with 3.3 years for Grade III meningiomas (anaplastic).<sup>7</sup> No means of prevention are known, presently.<sup>3</sup>

#### CONCLUSION

Meningiomas can easily be diagnosed and characterized radiologically according to their typical sites and peculiar salient features in this era of modern neuroimaging. Though

most of them are regarded as benign, their clinical behaviour in significant number of cases is still not typical of benign tumours. Pathological classifications and therapeutic options are widening, yet, recurrence rates are still worrisome with the most common primary, intracranial, extra-axial neoplasm.

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