Histopathology and Grading of Meningiomas

2

Declan McGuone and Anita Huttner

Meningiomas are one of the most common intracranial tumor types encountered by neuropathologists in routine surgical pathology practice. When neuropathologists receive a tissue biopsy from a patient with a meningioma, they typically follow the mandate of the World Health Organization (WHO) Classification of Tumors of the Central Nervous System (2016), to accurately classify and grade the tumor. Although meningiomas are usually benign and are often slow-growing tumors, they are notable for their striking histologic diversity, and many different microscopic subtypes have been described over the years. Relatively few of these distinct histologic patterns are clinically significant, and, in practice, the most commonly encountered subtypes are the meningothelial, fibrous, and transitional variants. In this chapter we will consider the fundamental principles of tumor grading as they apply to meningioma, discuss the major morphologic subtypes of meningioma currently recognized by the WHO, and review common immunohistochemical studies that may be utilized to facilitate a diagnosis of meningioma. The tremendous histologic diversity of meningiomas means that they occasionally mimic other tumor types, including several malignant tumors, and this can be diagnostically problematic in centers that lack a dedicated neuropathologist. In this chapter we will also consider some of the major differential diagnoses that occasionally masquerade as meningioma.

D. McGuone
Department of Pathology, Yale New Haven Hospital, New Haven, CT, USA
e-mail: declan.mcguone@yale.edu

A. Huttner (✉)
Department of Pathology, Yale School of Medicine, New Haven, CT, USA
e-mail: anita.huttner@yale.edu

J. Moliterno, A. Omuro (eds.), *Meningiomas*,
https://doi.org/10.1007/978-3-030-59558-6_2

Meningioma Histogenesis

Although meningiomas usually occur as dural-based masses along the craniospinal axis, their histologic features actually resemble arachnoid rather than dura mater. As a result, they share many histologic similarities with normal arachnoidal cells, particularly the arachnoid cap cell, and have a tendency to occur at locations where this cell type is found most frequently [1–3]. Moreover, most meningiomas have an immunohistochemical profile that is similar to normal arachnoid mater including a characteristic patchy staining pattern for epithelial membrane antigen (EMA). In some instances, meningiomas recapitulate the functional properties of normal arachnoidal cells including a tendency to form whorls similar to the normal wrapping function of arachnoidal cells at cerebrospinal fluid (CSF) barrier sites [4]. Occasionally meningiomas occur at atypical locations in which arachnoidal cap cells are found such as the choroid plexus stroma, and this is the presumed basis for the rare intraventricular meningioma. Meningiomas that lack a dural connection are referred to as primary extradural meningiomas, and these have a predilection for head and neck regions such as the sinuses, orbit, skull bone, and scalp, although other sites including the lungs, mediastinum, and liver are described [5–9].

Grading of Meningioma

The most reliable morphologic predictor for tumor recurrence is the WHO grade, and the grade of a meningioma also plays an important role in guiding therapeutic decisions. The principles of meningioma grading are well established and enable meningiomas to be grouped into three categories, based on the extent of progressively atypical features that are defined by microscopic criteria (See Table 2.1). The vast majority of meningiomas correspond histologically to WHO grade I and are

Table 2.1 Meningioma morphologic variants grouped according to WHO grade and biological behavior

WHO grade I	WHO grade II	WHO grade III
Meningiomas with low risk of recurrence or aggressive behavior	Meningiomas with increased risk of recurrence or aggressive behavior	Meningiomas with high risk of recurrence or aggressive behavior
Meningothelial meningioma	*Atypical* meningioma	*Anaplastic* meningioma
Fibroblastic meningioma	*Clear cell* meningioma	*Rhabdoid* meningioma
Transitional meningioma	*Chordoid* meningioma	*Papillary* meningioma
Psammomatous meningioma		
Angiomatous meningioma		
Microcystic meningioma		
Secretory meningioma		
Lymphoplasmacyte-rich meningioma		
Metaplastic meningioma		

clinically benign [10]. The risk of recurrence for a grade I meningioma is 7–25% [11]. Higher-grade meningiomas arise either de novo or by transformation of a preexisting lower-grade tumor. Based on the degree to which atypical microscopic features are present, the tumor is classified as either atypical (WHO grade II) or anaplastic (WHO grade III). The risk for recurrence increases with progressively increasing grade, and grade III meningiomas are associated with a markedly elevated risk for recurrence and overall shorter survival times [12]. Cellular proliferation, as assessed using the Ki67 proliferation index, correlates well with tumor grade and biologic behavior [13]. An elevated proliferative index (i.e., >4%) is associated with a similar recurrence rate to atypical meningioma, while a markedly elevated proliferative index of >20% has been associated with death rates comparable to those of anaplastic meningioma [14]. Although the Ki67 proliferative index is an important adjunct in evaluating meningiomas, it is not currently recognized as a formal component of the WHO grading scheme, partly due to significant interlaboratory differences in technique and interpretation. It is worth noting that the boundary points between histologic tumor grades are also somewhat arbitrary. The relatively subjective nature of some of the softer morphologic criteria introduces inter- and intra-observer variability, which is sometimes associated with inconsistent tumor grading within institutions [15]. A subset of patients with grade I meningioma have one or two atypical features but not brain invasion or increased mitotic activity, and in these patients, the risk of recurrence is increased compared to individuals with otherwise benign grade I meningiomas that have no atypical features at all [16]. In patients who undergo a large tumor resection, grading of the excision specimen can be further complicated by the fact that meningiomas usually do not exist in a pure histologic form and often show significant heterogeneity between different regions within the tumor. This means that accurate grading often requires considerable sampling of different areas to exclude regions that could behave in a more clinically aggressive fashion. Several variants of meningioma have distinctive microscopic patterns that are associated with a significantly increased risk of recurrence and are automatically classified as higher grade based on these appearances alone. Examples of higher-grade meningiomas with distinctive microscopic appearances include the rhabdoid and papillary subtypes described below [11]. Progesterone receptor (PR) expression is inversely associated with tumor grade, and most grade III meningiomas do not express PR; however, this test has limited clinical utility because a significant number of grade I and grade II meningiomas also show no PR expression [17, 18].

WHO Grade I (Benign) Meningiomas

Tumors corresponding to grade I meningioma are characterized by striking histologic diversity, with nine variants currently recognized in the WHO Classification of CNS Tumors (see Table 2.2). By definition grade I tumors lack microscopic criteria of higher-grade atypical or anaplastic (i.e., malignant) meningiomas (see Table 2.1). Grade I meningiomas are permitted to have up to two atypical cytologic features

Table 2.2 WHO 2016 grading criteria for meningiomas

WHO grade I	WHO grade II Atypical meningioma	WHO grade III Anaplastic meningioma
Low grade with Any predominant morphology, except for clear cell, chordoid, papillary, or rhabdoid Mitoses <4/10HPF Lacks criteria of atypical or anaplastic meningioma	Intermediate grade with Brain invasion on histology Increased mitotic activity (Mitoses >4/10 HPF) Or *at least 3* of the following features: Sheet-like growth Small cells with high N/C ratio Increased cellularity Foci of spontaneous necrosis Macronucleoli	High grade with Overtly aggressive phenotype with sarcoma-, carcinoma-like histology Mitoses >20/10 HPF

HPF high-power fields, *N/C ratio* nuclear-to-cytoplasmic ratio

(but not brain invasion or increased mitotic activity) before being classified as a grade II tumor. Moreover, invasion of the bone or skeletal muscle does not influence tumor grade, and some grade I tumors will exhibit considerable permeation of the skull bone, including occasional extension into the subcutaneous tissues of the scalp, without a corresponding change in grade [19]. The main features of the nine grade I variants are discussed in the following section.

Meningothelial Meningioma This is one of the most common and classic variants of meningioma that consists of well-demarcated lobules of arachnoidal cells partly surrounded by thin collagenous septa. Inside the lobules the tumor cells typically have imperceptible cell borders and appear to form a multinucleated syncytium. The tumor cells contain bland nuclei that tend to be relatively uniform with open chromatin and often contain nuclear pseudoinclusions which are a characteristic finding in this variant (Fig. 2.1). Unlike the transitional and fibrous subtypes described below, whorls and psammoma bodies are not a prominent finding although they can be seen in some cases. This variant has a predilection for the anterior skull base.

Fibrous Meningioma This is another common and classic grade I variant that typically has elongated tumor cells with a spindled appearance and intervening collagenous fibers. Whorls and psammoma bodies are often present, and the tumor cells may exhibit the classic nuclear features of meningothelial meningioma, at least focally. These features are helpful in distinguishing a fibrous meningioma from other spindle cell tumors such as schwannomas and tumors that contain abundant collagen such as solitary fibrous tumor/hemangiopericytoma. Fibrous meningiomas tend to have a convexity distribution (Fig. 2.2).

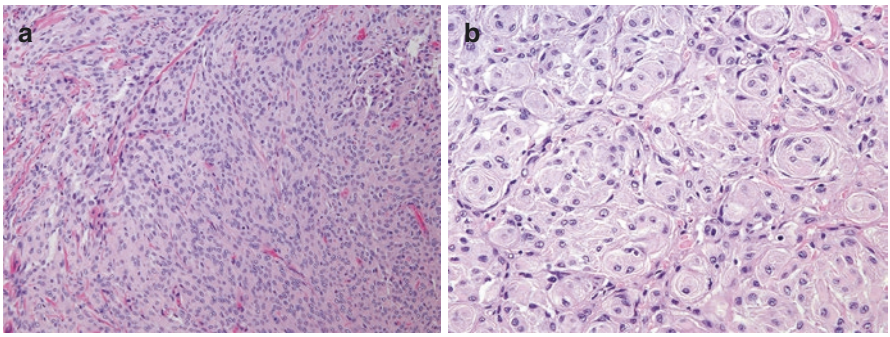

Fig. 2.1 (**a**) Meningothelial meningioma. Hematoxylin and eosin (H&E) stained section demonstrates a meningioma with lobular architecture, syncytium-like appearance due to ill-defined borders. (**b**) Variant with prominent whorl formation

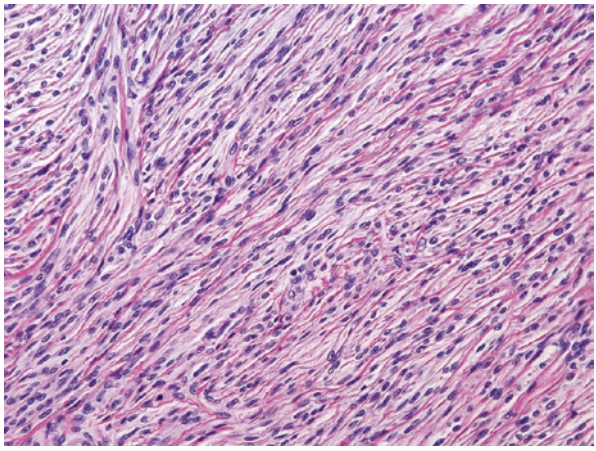

Fig. 2.2 Fibrous meningioma with intersecting fascicles of spindled cells and variable collagen deposition (H&E stained section)

Transitional Meningioma This is a common variant with microscopic features in transition between meningothelial and fibrous variants. The tumor often consists of meningothelial lobules with admixed fascicles of spindle cells, psammoma bodies, and whorls. Similar to the fibrous meningioma, these tumors tend to arise on the convexity dura.

Psammomatous Meningioma Psammomatous meningiomas have a striking microscopic appearance and contain innumerable psammoma bodies which sometimes outnumber the tumor cells. In some cases, tumor cells can be difficult to identify due to the sheer abundance of psammoma bodies. Occasionally psammoma bodies coalesce and calcify or form metaplastic bone. These tumors classically occur in the thoracic spine of middle-aged women.

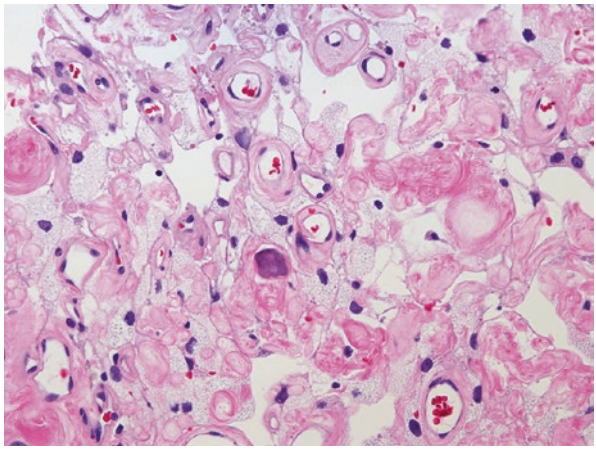

Fig. 2.3 Angiomatous meningioma. Composed of dense accumulation of numerous small blood vessels (H&E stained section)

Angiomatous Meningioma This is a vascular variant characterized by innumerable blood vessels that comprise most of the tumor. The blood vessels typically vary in size and caliber and are often hyalinized. This tumor can mimic a vascular malformation or hemangioblastoma. A classic finding is degenerative atypia of the tumor nuclei which is sometimes striking and does not indicate a higher grade. Angiomatous meningiomas are sometimes associated with considerable peritumoral brain edema (Fig. 2.3).

Microcystic Meningioma This uncommon variant is characterized by numerus microcystic spaces demarcated by tumor cell processes and sometimes contains macrocysts detectable on imaging [20]. As with angiomatous meningioma, hyalinized blood vessels and degenerative atypia may occur. Microcystic meningiomas are thought to arise from arachnoid trabecular cells, and the microcysts are vaguely reminiscent of small subarachnoid spaces.

Secretory Meningioma This variant shows focal epithelial differentiation and contains intercellular eosinophilic secretions known as pseudopsammoma bodies. These secretions are usually periodic acid-Schiff-positive and can occur singly or in small clusters, in a background of otherwise classic meningioma. Focal epithelial differentiation can be highlighted by labeling with antibodies for cytokeratin and carcinoembryonic antigen (CEA) [21]. Pseudopsammoma bodies also label strongly for CEA, and this variant may be associated with elevated circulating CEA levels. Peritumoral edema is sometimes striking [22] (Figs. 2.4 and 2.5).

Lymphoplasmacyte-Rich Meningioma This is an uncommon variant characterized by a preponderance of chronic inflammation that often obscures the meningothelial component. The major differential diagnostic considerations are a clonal lymphoproliferative disorder, pachymeningitis, and other systemic hematologic and autoimmune conditions [23].

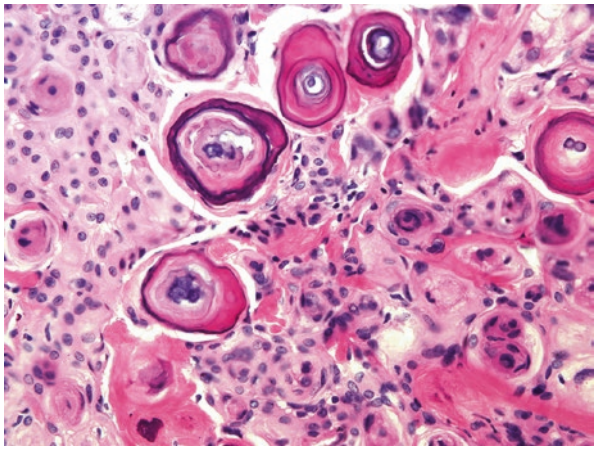

Fig. 2.4 Psammomatous meningioma. Numerous psammoma bodies dominate the tumor (H&E stained section)

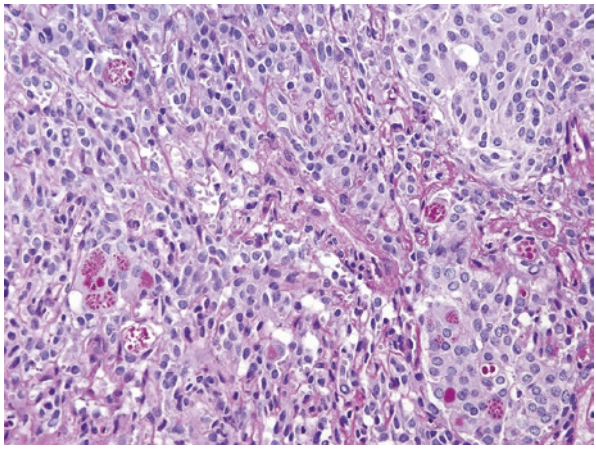

Fig. 2.5 Secretory meningioma shows gland-like spaces with brightly eosinophilic globules, also known as pseudopsammoma bodies (H&E stained section). These are PAS positive (not shown)

Metaplastic Meningioma This uncommon variant is characterized by focal or widespread mesenchymal differentiation that includes osseous, cartilaginous, lipomatous, myxoid, and/or xanthomatous tissue. Although the histologic appearances are striking, this variant has no known clinical significance.

WHO Grade II Meningiomas

Grade II meningiomas are a group of tumors characterized by a significantly increased risk of recurrence [11, 24]. Three entities are recognized in this group, the most common of which is the atypical meningioma, defined by the presence of atypical microscopic features (see Table 2.1). Two other grade II tumors, the clear cell and chordoid meningioma, are relatively uncommon and are defined by their distinctive microscopic appearances. Any previously mentioned grade I variant may

also qualify for a diagnosis of atypical meningioma if microscopic criteria are met, even focally (see Table 2.1).

Atypical Meningioma The diagnosis of atypical meningioma is established by a mitotic count of greater than 4 mitotic figures per 10 high-power fields, evidence of brain invasion, and/or three or more microscopic criteria, including hypercellularity, small cell change, architectural sheeting, spontaneous necrosis, and macronucleoli (see Table 2.1). Despite the name, nuclear atypia is not a criterion for diagnosis. Moreover, nuclear atypia is not a reliable indicator of tumor grade because some grade I meningiomas such as the angiomatous and microcystic variants described above may also have considerable nuclear atypia. Only spontaneous tumor necrosis is scored, and correlation with clinical history is sometimes necessary to distinguish between embolization-induced necrosis and spontaneous necrosis [25]. Brain invasion is associated with a higher risk of recurrence and if present automatically indicates a grade II meningioma [26]. Demonstration of brain invasion requires confirmation of pial breach which is characterized by islands of meningioma cells completely surrounded by GFAP-positive brain parenchyma, often with reactive astrogliosis. Direct extension of a meningioma from the subarachnoid space along perivascular Virchow-Robin spaces, but without direct extension into the brain parenchyma, does not constitute invasion. Atypical meningiomas are more in common in males and tend to have a non-skull base location. The 5-year recurrence rate for atypical meningioma with gross total resection is significantly greater than grade I meningioma and has been estimated at up to 40% in some series [27] (Fig. 2.6).

Clear Cell Meningioma This rare meningioma variant has a predilection for the posterior fossa and spinal canal of younger patients and is recognized by its typical microscopic appearance. The tumor has a sheeting or patternless architecture and consists of polygonal cells with clear cytoplasm that are surrounded by interstitial and prominent perivascular collagen. This is a biologically aggressive tumor type, and frequent recurrence with occasional CSF seeding is described. *SMARCE1* mutations are described in familial and some sporadic cases, and loss of expression

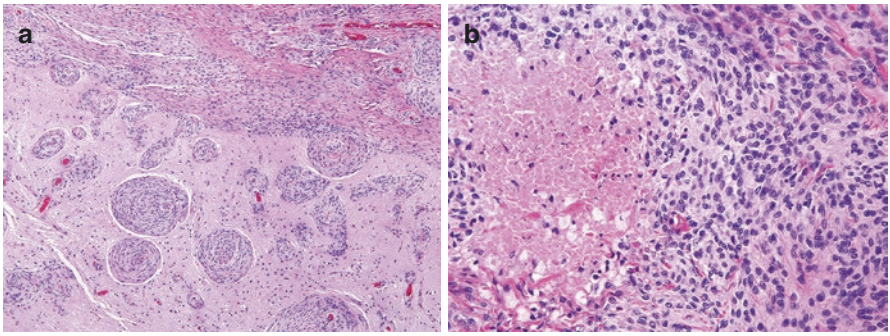

Fig. 2.6 Atypical meningioma. (**a**) H&E stained sections show brain invasion and (**b**) a focus of spontaneous necrosis

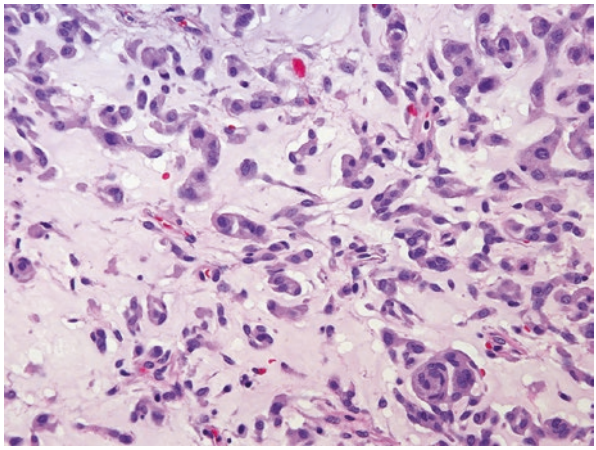

Fig. 2.7 Chordoid meningioma characterized by cords of epithelioid cells within a myxoid background (H&E stained section)

of SMARCE1 detected by immunohistochemistry may be a sensitive marker for clear cell meningioma [28].

Chordoid Meningioma These are rare tumors composed of nodules of vacuolated cells set in a myxoid stroma, with admixed regions of classic meningioma. The tumors histologically resemble chordoma. Psammoma calcifications are not common. In some instances, chronic inflammation and plasma cells are abundant, and rare cases are associated with Castleman disease and anemia (Fig. 2.7).

WHO Grade III (Malignant) Meningiomas

This is a group of malignant tumors characterized by markedly increased risk of recurrence and decreased overall survival when compared to other meningioma types. Three entities are recognized: anaplastic (malignant) meningioma, rhabdoid meningioma, and papillary meningioma.

Anaplastic (Malignant) Meningioma Anaplastic meningioma accounts for 1–3% of all meningiomas and is characterized by frankly anaplastic cytology that resembles undifferentiated carcinoma, melanoma, or sarcoma. Often the tumor is so poorly differentiated that it is difficult to discern the tumor as meningioma without additional immunohistochemical studies for confirmation. These tumors typically exhibit brisk mitotic activity (i.e., greater than 20 mitotic figures per 10 high-power fields), and atypical mitotic figures are usually found [29]. The Ki67 proliferative index is often markedly elevated, and tumor necrosis and brain invasion are frequent. Some anaplastic meningiomas also exhibit focal epithelial or mesenchymal differentiation, and this can sometimes pose additional diagnostic difficulties. In most instances a history of a prior meningioma at the same site, with immunohistochemical or genetic support, is required to establish the diagnosis (Fig. 2.8).

Rhabdoid Meningioma This is an uncommon high-grade variant characterized by tumor cells with eccentric nuclei, prominent nucleoli, and globular hyaline cytoplasmic material [30]. Most rhabdoid meningiomas have other overtly malignant features such as necrosis and brisk mitotic activity. Occasional grade I tumors have focal rhabdoid cytology without other malignant features, and this is acceptable as a minor component of those tumors, although closer clinical follow-up may be indicated. Unlike the rhabdoid cells of atypical teratoid/rhabdoid tumors of the posterior fossa of childhood, rhabdoid meningiomas retain expression of SMARCB1 (Fig. 2.9).

Papillary Meningioma This is a rare variant with a predominant papillary or perivascular pseudopapillary growth pattern comprising greater than 50% of the tumor. True papillary tumors have a classic cauliflower-like appearance; however, in most cases the appearance is actually pseudopapillary with tumor cells clinging to blood vessels that are separated by intervening clefts. Some papillary tumors exhibit focal rhabdoid features.

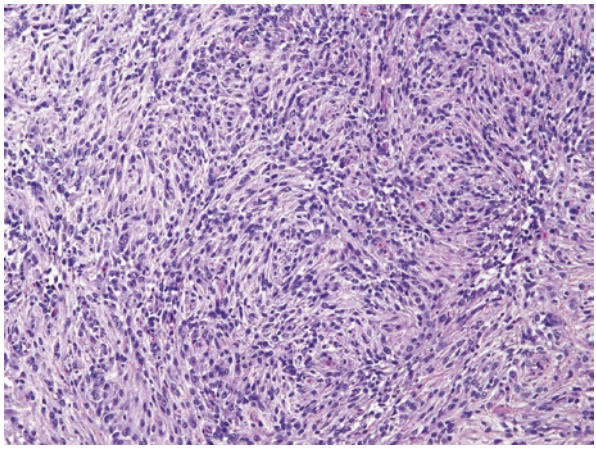

Fig. 2.8 Anaplastic (malignant) meningioma with high mitotic activity and markedly atypical cells (H&E stained section)

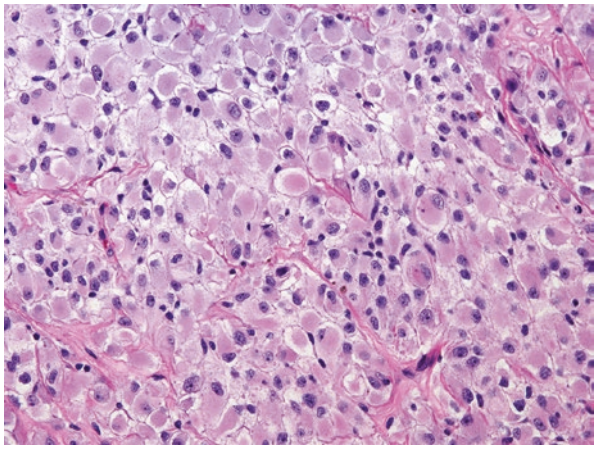

Fig. 2.9 Rhabdoid meningioma. Characterized by eccentrically displaced nuclei and prominent paranuclear eosinophilic globular inclusions (H&E stained section)

Other Meningioma Variants Acknowledged by the WHO Several additional meningioma variants are acknowledged by the WHO although the clinical significance of these individual variants is currently unknown due to their overall rarity. Examples of these unusual variants include oncocytic, sclerosing, whorling-sclerosing, GFAP-expressing, granulofilamentous inclusion-bearing, rosette-forming, and mucinous meningiomas [4, 11, 31–34].

Meningioma Immunophenotype

The canonical confirmatory immunostain for meningioma is EMA, with most meningiomas having a characteristic wispy pattern of positive staining. Malignant tumors may show less intense EMA staining. Vimentin is expressed by all meningiomas, but as this protein is broadly expressed by many other cell types, it is of limited diagnostic utility. Somatostatin receptor 2A is expressed in most meningiomas and can be helpful in confirming arachnoidal lineage particularly in poorly differentiated tumors, although caution is required because this stain is also positive in many neuroendocrine neoplasms. GFAP is negative in meningioma cells but can be helpful in confirming brain tissue invasion by the tumor. Keratin stains are usually negative unless the meningioma shows focal epithelial differentiation, as in the secretory variant. Ki67 has an important role in evaluating cell proliferation, as discussed above.

Differential Diagnoses of Meningioma

Most meningiomas are slow-growing masses with characteristic imaging and clinical findings. In the majority of cases, a diagnosis is often clinically suspected before pathologic confirmation. In some instances, non-meningothelial tumors will present with unusual clinical or radiologic features or have a dural attachment, and this may pose a diagnostic challenge. Moreover, the histologic diversity of meningiomas can be problematic if the tumor is one of the rarer microscopic variants or if the tumor is of higher grade and poorly differentiated. Some of the more common differential diagnostic considerations are discussed below.

Non-meningothelial Mesenchymal Tumors

Non-meningothelial soft tissue tumors are a large and heterogeneous group of neoplasms ranging from benign to locally invasive or overtly malignant. They share similar histologic features with soft tissue tumors found at extracranial sites and are classified by cell lineage into adipocytic, vascular, fibroblastic, smooth muscle, skeletal muscle, nerve sheath, and undifferentiated types. The most common tumor belonging to this category is the solitary fibrous tumor/hemangiopericytoma, a tumor characterized by diffuse STAT6 nuclear expression [11]. This tumor typically has prominent staghorn-shaped blood vessels and either a solitary fibrous pattern comprising alternating hypercellular and hypocellular areas, bland spindled cells,

and prominent collagen or a hemangiopericytoma pattern with high cellularity and prominent reticulin. These tumors typically express CD34 and lack EMA which facilitates their distinction from meningioma.

Metastatic Neoplasms

Dural-based metastatic neoplasms are sometimes confused for meningioma, particularly if the metastatic deposit is a solitary lesion, a primary origin for the tumor is not known, or there is no systemic disease. A diverse range of tumor types can exhibit dural metastases with tumors of the breast, prostate, lung, and other unusual locations such as uterus and gastrointestinal tract overrepresented in some series [35, 36]. Microscopic examination of the tumor typically reveals cytologic anaplasia with evidence of glandular or squamous differentiation, thereby confirming a diagnosis of metastatic carcinoma. Melanoma is often recognized by its brown cytoplasmic pigment and prominent nucleoli although non-pigmented variants of melanoma occur. Metastatic sarcomas typically have a spindled appearance and often require detailed immunohistochemical studies to differentiate them from anaplastic meningioma or other more common meningioma types. Occasionally clear cell and secretory meningiomas (see above) may resemble metastatic carcinoma, but these variants are readily distinguished from carcinoma by their distinct immunohistochemical profiles. In rare instances meningiomas can act as a receptor bed for metastatic tumor, and coexistent meningioma and metastatic carcinoma are occasionally described [37].

Other Differential Diagnoses

Specific variants of meningioma are also associated with specific differentials particular to the histologic features of that subtype. Examples include the microcystic meningioma which may resemble hemangioblastoma, angiomatous meningioma which can be confused for a vascular malformation, and the chordoid meningioma which can resemble a chordoma. The differential diagnosis of spindle cell tumors occurring at the cerebellopontine angle includes schwannoma and fibrous meningioma. The rare lymphoplasmacyte-rich meningioma raises several differentials including infectious and inflammatory etiologies, as well as low-grade lymphoma. In these diagnostically challenging cases, the histopathologic differential diagnosis is usually readily resolved by detailed immunohistochemical analysis of the tumor, careful clinicopathologic correlation, and ancillary studies.

References

1. Langford LA. Pathology of meningiomas. J Neuro-Oncol. 1996;29(3):217–21.
2. Kepes JJ. Presidential address: the histopathology of meningiomas. A reflection of origins and expected behavior? J Neuropathol Exp Neurol. 1986;45(2):95–107.

3. Cyril B, Courville KHA. The histogenesis of meningiomas: with particular reference to the origin of the 'meningothelial' variety. J Neuropathol Exp Neurol. 1942;1(3):337–43.
4. Perry A, Brat DJ. Practical surgical neuropathology: a diagnostic approach. Philadelphia: Churchill Livingstone/Elsevier; 2010.
5. Lang FF, Macdonald OK, Fuller GN, DeMonte F. Primary extradural meningiomas: a report on nine cases and review of the literature from the era of computerized tomography scanning. J Neurosurg. 2000;93(6):940–50.
6. Liu Y, Wang H, Shao H, Wang C. Primary extradural meningiomas in head: a report of 19 cases and review of literature. Int J Clin Exp Pathol. 2015;8(5):5624–32.
7. Bae SY, Kim HS, Jang HJ, et al. Primary pulmonary chordoid meningioma. Korean J Thorac Cardiovasc Surg. 2018;51(6):410–4.
8. Luo JZ, Zhan C, Ni X, Shi Y, Wang Q. Primary pulmonary meningioma mimicking lung metastatic tumor: a case report. J Cardiothorac Surg. 2018;13(1):99.
9. Zulpaite R, Jagelavicius Z, Mickys U, Janilionis R. Primary pulmonary meningioma with rhabdoid features. Int J Surg Pathol. 2019;27(4):457–63.
10. Alahmadi H, Croul SE. Pathology and genetics of meningiomas. Semin Diagn Pathol. 2011;28(4):314–24.
11. Louis DN. International Agency for Research on C, Deutsches Krebsforschungszentrum H, Organització Mundial de la S. WHO classification of tumours of the central nervous system. Lyon: International Agency for Research on Cancer; 2016.
12. Greenfield JG, Love S, Budka H, Ironside JW, Perry A. Greenfield's neuropathology. Boca Raton: CRC Press; 2015.
13. Mukhopadhyay M, Das C, Kumari M, Sen A, Mukhopadhyay B, Mukhopadhyay B. Spectrum of meningioma with special reference to prognostic utility of ER, PR and Ki67 expression. J Lab Physicians. 2017;9(4):308–13.
14. Perry A, Stafford SL, Scheithauer BW, Suman VJ, Lohse CM. The prognostic significance of MIB-1, p53, and DNA flow cytometry in completely resected primary meningiomas. Cancer. 1998;82(11):2262–9.
15. Willis J, Smith C, Ironside JW, Erridge S, Whittle IR, Everington D. The accuracy of meningioma grading: a 10-year retrospective audit. Neuropathol Appl Neurobiol. 2005;31(2):141–9.
16. Marciscano AE, Stemmer-Rachamimov AO, Niemierko A, et al. Benign meningiomas (WHO Grade I) with atypical histological features: correlation of histopathological features with clinical outcomes. J Neurosurg. 2016;124(1):106–14.
17. Perry A, Cai DX, Scheithauer BW, et al. Merlin, DAL-1, and progesterone receptor expression in clinicopathologic subsets of meningioma: a correlative immunohistochemical study of 175 cases. J Neuropathol Exp Neurol. 2000;59(10):872–9.
18. Roser F, Nakamura M, Bellinzona M, Rosahl SK, Ostertag H, Samii M. The prognostic value of progesterone receptor status in meningiomas. J Clin Pathol. 2004;57(10):1033–7.
19. Ironside JW. Diagnostic pathology of nervous system tumours. Edinburgh: Churchill Livingstone; 2002.
20. Paek SH, Kim SH, Chang KH, et al. Microcystic meningiomas: radiological characteristics of 16 cases. Acta Neurochir. 2005;147(9):965–72; discussion 972.
21. Colakoglu N, Demirtas E, Oktar N, Yuntem N, Islekel S, Ozdamar N. Secretory meningiomas. J Neuro-Oncol. 2003;62(3):233–41.
22. Buhl R, Hugo HH, Mehdorn HM. Brain oedema in secretory meningiomas. J Clin Neurosci. 2001;8(Suppl 1):19–21.
23. Bruno MC, Ginguene C, Santangelo M, et al. Lymphoplasmacyte rich meningioma. A case report and review of the literature. J Neurosurg Sci. 2004;48(3):117–24; discussion 124.
24. Champeaux C, Dunn L. World Health Organization grade II meningiomas. Acta Neurochir. 2016;158(5):921–9; discussion 929.
25. Ng HK, Poon WS, Goh K, Chan MS. Histopathology of post-embolized meningiomas. Am J Surg Pathol. 1996;20(10):1224–30.

26. Brokinkel B, Hess K, Mawrin C. Brain invasion in meningiomas-clinical considerations and impact of neuropathological evaluation: a systematic review. Neuro-Oncology. 2017;19(10):1298–307.
27. Perry A, Stafford SL, Scheithauer BW, Suman VJ, Lohse CM. Meningioma grading: an analysis of histologic parameters. Am J Surg Pathol. 1997;21(12):1455–65.
28. Tauziede-Espariat A, Parfait B, Besnard A, et al. Loss of SMARCE1 expression is a specific diagnostic marker of clear cell meningioma: a comprehensive immunophenotypical and molecular analysis. Brain Pathol (Zurich, Switzerland). 2018;28(4):466–74.
29. Perry A, Scheithauer BW, Stafford SL, Lohse CM, Wollan PC. "Malignancy" in meningiomas: a clinicopathologic study of 116 patients, with grading implications. Cancer. 1999;85(9):2046–56.
30. Perry A, Scheithauer BW, Stafford SL, Abell-Aleff PC, Meyer FB. "Rhabdoid" meningioma: an aggressive variant. Am J Surg Pathol. 1998;22(12):1482–90.
31. Roncaroli F, Riccioni L, Cerati M, et al. Oncocytic meningioma. Am J Surg Pathol. 1997;21(4):375–82.
32. Berho M, Suster S. Mucinous meningioma. Report of an unusual variant of meningioma that may mimic metastatic mucin-producing carcinoma. Am J Surg Pathol. 1994;18(1):100–6.
33. Elmaci I, Altinoz MA, Sav A, et al. Whorling-sclerosing meningioma. A review on the histological features of a rare tumor including an illustrative case. Clin Neurol Neurosurg. 2017;162:85–90.
34. Zheng J, Geng M, Shi Y, Jiang B, Tai Y, Jing H. Oncocytic meningioma: a case report and review of the literature. Surg Oncol. 2013;22(4):256–60.
35. Nayak L, Abrey LE, Iwamoto FM. Intracranial dural metastases. Cancer. 2009;115(9):1947–53.
36. Kleinschmidt-DeMasters BK. Dural metastases. A retrospective surgical and autopsy series. Arch Pathol Lab Med. 2001;125(7):880–7.
37. Sayegh ET, Burch EA, Henderson GA, Oh T, Bloch O, Parsa AT. Tumor-to-tumor metastasis: breast carcinoma to meningioma. J Clin Neurosci. 2015;22(2):268–74.