Common Mesenchymal Neoplasms in and around the CNS

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Disclosures

I have no relevant financial relationships to disclose.
Learning Objectives

• 1. Summarize updated grading criteria for meningiomas and solitary fibrous tumors
• 2. Identify diagnostic morphologic and immunohistochemical features of common skull base neoplasms
• 3. Discuss relevance of ancillary molecular testing for grading and subclassifying meningiomas
Meningiomas

- Most common primary brain tumor in adults (least common in children)
- Median age at diagnosis is 66
- Varied histologic appearances, but syncytial arrangement of tumor cells with occasional whirls and nuclear pseudo-inclusions characteristic
- EMA+/SSTR2A+
- May rarely occur as purely intraosseous lesion
Histologic subtypes of meningioma
Grade 2 morphologies

Chordoid

Clear cell

SMARCE1

Grade 3 morphologies

Papillary

Rhabdoid

BAP1
Meningioma grading (histologic)

- Grade 1 (Benign) – recurrence risk up to 20% at 20 yrs:
  - Mitoses less than 4/10 high-powered fields (HPF)
  - AND no other criteria (below) for higher grade fulfilled

- Grade 2 (Atypical) – recurrence risk up to 50%:
  - Mitoses equal or more than 4/10 HPF but fewer than 20/10 HPF
  - OR 3 or more of the following histologic criteria:
    - Increased cellularity
    - Sheetlike growth
    - Prominent nucleoli
    - Small cell change
    - Spontaneous necrosis
  - OR one of the following histologic variants:
    - Clear cell meningioma
    - Chordoid meningioma
  - OR brain invasion

- Grade 3 (Anaplastic) – recurrence risk up to 94%:
  - Mitoses more than 20/10 HPF
  - OR one of the following histologic variants:
    - Rhabdoid meningioma
    - Papillary meningioma
IHC in meningioma

Caveats/tips:

1) Fibroblastic meningioma is often diffusely S100+, but schwannoma is never EMA+
2) SSTR2A can often show positivity in other mesenchymal tumors, including some rare CD34+ fibroblastic tumors in children
3) High-grade tumors can lose antigens
4) Don’t diagnose CCM without SMARCE1 loss
5) BAP1 loss in rhabdoid meningioma uncommon, usually associated with germline syndrome
Molecular alterations in meningioma correlate with clinical behavior
Copy number analysis of meningiomas reveals occasional disconnect between histologic grade and genomic disruption
Individual and covariate analysis of molecular features revealed strong associations with survival outcomes.

A | Feature | HR
---|---------|-----
1 | CDKN2A/B loss | 72.16
2 | Mitoses (per each act\(\ddagger\)) | 1.24
3 | MIB-1 (per each %) | 1.10
4 | 18q loss | 7.82
5 | 6q loss | 6.89
6 | 1q loss | 7.66
7 | 10q loss | 6.32
8 | 18p loss | 7.31
9 | 1p loss | 1.10
10 | CNV (per each act\(\ddagger\)) | 5.58
11 | 10p loss | 6.11
12 | 4p loss | 3.69
13 | 14q loss | 1.72
14 | Atypical features (per each) | 6.48
15 | 4q loss | 5.03
16 | 6p loss | 7.80
17 | 13q loss | 3.79
18 | 7p loss | 5.17
19 | 22q loss | 6.31
20 | 9q loss | 2.91
21 | Necrosis | 3.54
22 | 1q gain | 3.74
23 | 11q loss | 5.27
24 | 3p loss | 3.13
25 | Prominent nucleoli | 2.34
26 | 2q loss | 3.11
27 | Brain invasion | 2.73
28 | 9q loss | 8.90
29 | 1p gain | 8.78
30 | Nuclear atypia | 6.20
31 | 19q loss | 2.19

B | LASSO
---|---
Gradient boosting | Random survival forest
1p-6q-10q-18q-19p-CDKN2A/B-mitoses | 6p-4q-18p-19p-9p-3p-10q-4q-

WHO grade | Integrated grade
---|---
I | 1
I* | 2
II | 3
III | 1 (grade I with two atypical features)
II | II
III | III
Integrated grade appears superior to conventional WHO grade at predicting long term clinical behavior
Tumors with low-risk histology (angiomatous/microcystic, secretory, psammomatous) need no additional testing

Similarly for clear cell and perhaps chordoid morphologies

Most others may benefit from ancillary cytogenetic testing for 1p and 9p loss
58M with calcified frontotemporal extra-axial mass
Fibrous dysplasia

- Can occur in both monostotic and polyostotic forms
  - Polyostotic form associated with McCune-Albright syndrome
- Usually presents in first 3 decades of life in long tubular bones, ribs, and craniofacial skeleton
- Possess characteristic GNAS mutations
- Histology shows monotonous spindle cell proliferation with irregular fragments of admixed woven bone lacking obvious osteoblastic rimming
- When arising in skull, frequently show cementoid bodies (concentrically laminated calcified structures)
66F with history of breast ca and frontal skull lesion
Solitary fibrous tumor

• Overlapping clinical features with meningioma, though considerably less common
• Irrespective of histology, high propensity to recur or metastasize to distant locations, sometimes decades after presentation
• Characteristic NAB2::STAT6 fusion gene (result of paracentric inversion on 12q13)
• Variable break points described, often correlating with cellularity
Histology of SFTs

- Haphazardly arranged ovoid to rounded cells with variable intervening collagen
- ‘Staghorn’ vessels
- CD34+/STAT6+ IHC
- May show extensive pseudopapillary morphology
- Fat-forming SFTs uncommon, but may be clue to dx
Grading of SFTs

Recurrence-Free Survival by Soft Tissue WHO Grade (2013) and Necrosis From the Time of Surgery

WHO Grade 1: Mitotic count: < 2.5 MF/mm² (< 5 MF/10 HPF)
WHO Grade 2: Mitotic count: ≥ 2.5 MF/mm² (≥ 5 MF/10 HPF without necrosis)
WHO Grade 3: Mitotic count: ≥ 2.5 MF/mm² (≥ 5 MF/10 HPF with necrosis)

Virtual slide
Chondrosarcoma or chordoma?
Chondrosarcoma

- Malignant cartilaginous matrix producing tumor
- Graded by degree of cellularity/atypia
- Nonspecific IHC profile (usually S100+)
- Many tumors possess IDH1/2 mutations (38-70%)
- Skull base chondrosarcomas frequently show extensive myxoid features; however, this is still considered grade 1 histology ONLY in this anatomic location
- 5 and 10 yr PFS of skull base CSA is 99% and 98%, while only 70% and 45% for chordoma
Chordoma

• Malignant tumor of notochord origin that usually arises in axial skeleton and midline skull base
• Stains for keratins, brachyury
• Physaliferous cells
• 5-year PFS up to 60-70%
  – Large tumor size, age > 40, with worse outcomes
Dedifferentiated chordoma

Poorly differentiated chordoma

- Unlike conventional chordoma, PD chordoma arises in children and young adults (median age 11 yrs)
- Predilection for clivus and c-spine
- Poorly differentiated, epithelioid to rhabdoid morphology
- Stain like conventional chordoma, but have INI1 loss
- Highly aggressive malignancy

Q&A