Small (and large) Blue Cell Tumors of the Skull Base

Jennifer L. Hunt, MD, MEd
Aubrey J. Hough Jr, MD, Endowed Professor of Pathology
Chair of Pathology and Laboratory Medicine
University of Arkansas for Medical Sciences
jhunt2@uams.edu
Sino-Nasal Lesions

- High Grade Epithelial Tumors
- Tumors with neuroendocrine differentiation
- Other lesions in the differential diagnosis
Sinonasal Undifferentiated Carcinoma

- Incidence: Rare
- Clinical
  - Present with large invasive tumors
  - Metastases are frequent
  - Symptoms include nasal obstruction, epistaxis, visual and headache
  - Prognosis is poor
    - ~20-25% overall survival at 5 years
Sinonasal Undifferentiated Carcinoma

- **Histopathology**
  - Undifferentiated tumor cells
  - Mitoses and necrosis
  - Vascular invasion and adjacent structures

- **Immunohistochemistry**
  - Positive for Cytokeratin
  - Controversy: Neuroendocrine marker positivity
Differential Diagnosis

- Melanoma
- Ewings/PNET
- Rhabdomyosarcoma
- NUT midline carcinoma
- Lymphoepithelial carcinoma
- Lymphoma
- Neuroendocrine carcinoma
Mucosal Melanoma, H&E
Ewing’s, H&E
Rhabdomyosarcoma, H&E
Work-Up of High Grade Tumor

- Cytokeratin stains
- Neuroendocrine stains
- S100
- HMB45
- CD99
- Myogenin
- Desmin
- Lymphoma markers
NUT Midline Carcinoma

- Nut midline carcinomas
  - More common in young people
    - Average age 17 years
  - Very aggressive (lethal) tumors

- Histology
  - Undifferentiated morphology
  - Abrupt keratinization in 82%
  - NUT-BRD4 translocation

French CA, JCO, 22(20):4135, 2004
SNUC and NUT Translocation

• Stelow, et al
  • Undifferentiated carcinomas of UADT
    • NUT rearrangement in 5/28 cases
    • NUT IHC positive in 3/5 cases

• Bishop, et al
  • NUT IHC in 151 primary sinonasal carcinomas
    • 2 of 13 SNUCs positive
    • 1/87 squamous cell carcinomas positive

Stelow E, et al. AJSP, 32(6), 2008
Bishop J, et al. AJSP, 36(8), 2012
Sino-Nasal Lesions

- High Grade Epithelial Tumors
- Tumors with neuroendocrine differentiation
- Other lesions in the differential diagnosis
Olfactory Neuroblastoma

• Incidence
  • Relatively rare (2% of sinonasal tumors)
  • Broad age range
    • Peaks in 2nd and 6th decades

• Clinical
  • Sinonasal symptoms: nasal obstruction, epistaxis, non-specific symptoms
  • Usually arises in the upper nasal cavity (superior nasal concha, upper septum, roof of nose, cribiform plate)
Olfactory Neuroblastoma

• Histopathology
  • Small to medium sized cells in nests
  • Usually minimal pleomorphism
  • Rosettes
    • Homer Wright: Central fibrillary material
      • Up 30-50%
    • Flexner-Wintersteiner: True lumen
      • Rare (~5%)
  • Neuropil
Involvement of the specialized olfactory epithelium
Olfactory neuroblastoma, Homer Wright
Olfactory neuroblastoma: Flexner-Wintersteiner
Olfactory Neuroblastoma

- Immunohistochemistry
  - Synaptophysin, chromogranin positive
  - S100 can have sustentacular pattern
  - CAM5.2 occasionally focally positive
Olfactory neuroblastoma, S100 stain
Olfactory neuroblastoma, Synaptophysin
Olfactory Neuroblastoma

- Hyams grading (histologic grade)
- Kadish stage (clinical staging)
  - Vs. AJCC staging system
Olfactory Neuroblastoma

- **Divergent Differentiation**
  - Often high grade tumors
  - Other components present
    - Rhabdomyosarcoma
    - Epithelial (Carcinoma)
    - Glandular (Adenocarcinoma)
    - Ganglion cells
Olfactory neuroblastoma with divergent differentiation
Olfactory neuroblastoma with divergent differentiation, S100
Olfactory neuroblastoma with divergent differentiation

Synaptophysin

Cytokeratin
Differential Diagnosis

- Sinonasal neuroendocrine carcinoma
- Paraganglioma
- Ectopic pituitary adenoma
Sinonasal Neuroendocrine Carcinoma

- Incidence
  - Rare tumor
  - Sinonasal neuroendocrine carcinoma (SNEC)

- Etiology
  - Possibly from olfactory epithelium

- Treatment and Prognosis
  - Combination therapy
Sinonasal Neuroendocrine Carcinoma

- **Histology**
  - Solid sheets, ribbons, or trabeculae
  - Large cells with coarse chromatin and nucleoli
  - Necrosis and mitoses

- **IHC**
  - Chromogranin, syaptophysin, NSE
  - Cytokeratin
Neuroendocrine carcinoma
Neuroendocrine carcinoma
Neuroendocrine carcinoma, synaptophysin
Ectopic Pituitary

• Clinical
  • Occur along the embryological migration and invagination pathway of Rathke’s Pouch
  • Distinguish radiologically, clinically and surgically from invasive pituitary adenoma
  • Broad age range; most common in 6th decade
  • Frequently mis-diagnosed
Ectopic Pituitary

- **Pathology**
  - Bland appearing neuroendocrine lesion
  - Hormones: FSH, LH, GH, TSH, ACTH, PRL, Calcitonin
Ectopic pituitary adenoma
Ectopic pituitary adenoma, ACTH
Summary

• High Grade Tumors
  • Sinonasal undifferentiated carcinoma
  • Differential Diagnosis: Ewings/PNET, melanoma, Rhabdomyosarcoma

• Tumors with neuroendocrine differentiation
  • Sinonasal neuroendocrine carcinoma
  • Olfactory neuroblastoma
  • Ectopic pituitary adenoma