AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS COMPANION SOCIETY MEETING

at the 106th ANNUAL MEETING OF THE USCAP

San Antonio, March 4, 2017

SYLLABUS

PINEAL PARENCHYMAL TUMORS

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INTRODUCTION:

Since the original classification by Cushing and Bailey, and the first WHO classification of CNS Tumors (Zulch KJ, 1979) tumors that are presumed to arise from pineal parenchymal cells have been considered as distinct entities. The entities in this category, Pineocytoma (ICD-O 9361/1) and Pineoblastoma (ICD-O 9362/3) were later expanded to include the Pineal Parenchymal Tumor of Intermediate Differentiation (PPTID; ICD-O 9362/3). Other entities and tumor-like lesions in this region will be considered in the following presentations. This review will outline the practical diagnostic issues in these three entities.

PINEOCYTOMA:

Pertinent clinical and radiological findings

- Typically small, rarely cystic but always solid lesions in the pineal regions
- Often calcifications recognized on imaging. Mass effect is exceedingly rare
- Maybe recognized incidentally and typical in adults (median age 30-40s)
- Contrast enhancement variable on MRI
- Occasionally lateral ventricular sizes are increased
- Excellent outcome, adjuvant treatment should be avoided even in cases where a small residual “cannot be excluded” on post-operative radiological images

Pertinent histological and special features

- Moderately cellular often uniform mature cells
- Large “pineocytomatous” rosettes (not a feature of normal pineal)
- Growth in sheets (instead of lobular architecture of the normal pineal)
- Occasionally scattered bizarre cells or Ganglion cells (rare)
- Mitoses exceptional, necrosis absent, calcifications common
- POSITIVE: Synaptophysin, Neurofilament protein, S100 protein, MAP2
- NEGATIVE: OLIG2, GFAP (normal pineal may show patchy staining)
- No specific genetic/molecular pattern recognized for pineocytomas

PINEAL PARENCHYMAL TUMORS OF INTERMEDIATE DIFFERENTIATION:

Pertinent clinical and radiological findings

- Presentation in adulthood (median age 40 yrs) but can be rarely seen in children
- Possible local recurrence
- Larger, more complex radiological appearance, yet still well circumscribed
- Cysts are rare, many show calcifications
- Patient may benefit from adjuvant treatment
- Neuraxis spread in a small percentage of cases

Pertinent histological and special features

- Often more cellular and has fewer pineocytomatous rosettes
- Two distinct histological subtypes
    - Small cell type – sometimes recognized as pineoblastoma in adults. Homogenous population of small cells growing in sheets with rare mitotic figures with scant stroma and cytoplasm. Inconspicuous nucleoli. Resembling central neurocytomas. Scattered mitoses
    - Large cell type – composed of a moderately cellular admixture of small and large cells with occasional rosettes, vesicular chromatin pattern and abundant neuropil-like stroma. Scattered mitoses
- POSITIVE but focal and variable staining with Synaptophysin and Neurofilament protein as well as MAP2. Both cell types demonstrate the same immunostaining pattern.
- NEGATIVE: Neu-N, GFAP, OLIG2
- Slightly higher proliferation index (Ki-67 is often around 5%)
- Molecular features currently unknown.

PINEOBLASTOMAS

Pertinent clinical and radiological features

- Typically in children, most in the first two decades of life
- Large, bulky tumors with mass effect and hydrocephalus
- Presents often with signs of increased intracranial pressure.
- Variable enhancement, calcifications rare
- Cerebrospinal spread may be seen at presentation or later
- Adjuvant treatment almost always necessary, recurrence is the rule

Pertinent histological and special features

- Small blue round cell tumor, with numerous mitoses, apoptoses and necrosis
- Homer-Wright or Flexner-Wintersteiner type rosettes
- High proliferation index, often greater than 20%
- Similar to other malignant small cell tumors such as medulloblastomas

- Less pronounced POSITIVITY is found for Synaptophysin and Neurofilament protein may be weak or negative
- NEGATIVE: Neu-N, OLIG2, GFAP and Neurofilament protein (see above).
- RB1 germline mutations are seen in some patients with pineoblastomas, and the so-called “trilateral retinoblastoma” includes pineoblastoma.
- DICER1 mutations both germline and somatic, have been associated with pineoblastomas

KEY ISSUES RELATING TO PINEAL PARENCHYMAL TUMORS

- ❖ Please make sure the tumor is located within the pineal region, or the quadrigeminal plate. Confirm with neuroradiologist
- ❖ Recognize the normal architecture of the pineal gland, for those not familiar, it may appear like a tumor. Normal pineal has a lobulated appearance, calcifications, and intracytoplasmic pigment that might help.
- ❖ Small biopsies are often encountered, and they may not be representative of the entire lesion.
- ❖ Some pineal tumors are not pineal parenchymal tumors. Recognize the other entities that can be seen in this region (Stay for the other lectures)
- ❖ An elderly patient with a “pineoblastoma” is suspect. Please make sure before calling it a pineoblastoma. The more likely possibility is a metastatic small cell carcinoma.

SUGGESTED READING

1. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol. 2016;131(6):803-20.
2. Vasiljevic A, Champier J, Figarella-Branger D, Wierinckx A, Jouvet A, Fevre-Montange M. Molecular characterization of central neurocytomas: potential markers for tumor typing and progression. Neuropathology. 2013;33(2):149-61
3. Miller S, Rogers HA, Lyon P, Rand V, Adamowicz-Brice M, Clifford SC, et al. Genome-wide molecular characterization of central nervous system primitive neuroectodermal tumor and pineoblastoma. Neuro Oncol. 2011;13(8):866-79
4. Fevre-Montange M, Szathmari A, Champier J, Mokhtari K, Chretien F, Coulon A, et al. Pineocytoma and pineal parenchymal tumors of intermediate differentiation presenting cytologic pleomorphism: a multicenter study. Brain Pathol. 2008;18(3):354-9.
5. Raleigh DR, Solomon DA, Lloyd SA, Lazar A, Garcia MA, Sneed PK, et al. Histopathologic review of pineal parenchymal tumors identifies novel morphologic subtypes and prognostic factors for outcome. Neuro Oncol. 2016. Epub 2016/06/11