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SYLLABUS

Papillary Tumor of the Pineal Region and the Differential Diagnosis of Papillary Tumors
Brent A. Orr MD, PhD
St. Jude Children's Research Hospital

INTRODUCTION:

Papillary tumor of the pineal region (PTPR) is a rare neuroepithelial tumor, having less than 200 reported cases in the literature. The tumor is a relatively new entity, first described by Jouvét et al. in 2003 (Jouvét, A 2003) and introduced to the WHO classification of tumors of the Central Nervous System in 2007 (WHO 4th edition). The tumor is believed to arise from specialized ependyma cells of the subcommissural organ.

Clinical and Radiologic Findings

- Typically arises in adults and rarely in the pediatric population (mean: 35, Range: 1-71 years)
- Presentation: obstructive symptoms including headache, gait instability, loss of upward gaze (Parinaud's sign)
- Located in the pineal region near the posterior commissure
- Circumscribed, T1 hyperintense masses with heterogeneous enhancement on MRI

Microscopic Features

- Typically solid and pseudopapillary growth. True papillary growth is often only focal or absent.
- Epithelial surfaces are often present focally
- Hyalinization around vessels is typical
- Geographic necrosis frequently encountered, but not pseudopalisading necrosis
- Definitive grading criteria has not been established, but thought to correspond to grade II or III.

Immunophenotype

- Positive stains:
 - Strong and diffuse cytokeratin immunoreactivity (CAM5.2 or CK18)
 - S-100
 - MAP2
 - CD56
 - PAS-positive; diastase-resistant cytoplasmic inclusions
- Focal immunoreactivity:
 - GFAP (+/-)
 - Synaptophysin (+/-)
 - EMA (typically surface staining), rarely dot-like
- Negative stains:
 - KiR7.1
 - Neurofilament

Molecular Features

- Loss of Chromosome 10 and 22q most frequent finding. Gain of chromosomes 8, 9, and 12 also encountered.
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Treatment and Prognosis

- Frequently recur locally (5-year progression free survival 27%, overall survival 73%)
- Rarely metastasize (~7% in one series)
- No definitive role for chemotherapy
- Radiotherapy is commonly employed, and result in improved progression free survival in some studies
- Gross total resection is the most important predictor of progression free survival
- Mitotic activity and Ki67/Mib-1 labeling frequency may stratify risk. Mitotic activity >3 per 10 high power field or Ki67 index >10 % may be associated with shorter PFS.

Differential Diagnosis

- PTPR vs. Papillary ependymoma
 - Ependymomas are typically diffusely GFAP positive, PTPR are immunonegative or demonstrate only focal immunoreactivity for GFAP

- EMA dot-like perinuclear stain in ependymoma, EMA only focally present in luminal surfaces in PTPR
- Cytokeratin not typically expressed in ependymoma, strong and diffuse in PTPR
- PTPR vs choroid plexus papilloma (CPP)
 - CAM5.2 expression more patchy in choroid plexus tumors, strong and diffuse in PTPR
 - EMA patchy cytoplasmic staining in choroid plexus tumors, but demonstrate only focal surface immunoreactivity in PTPR
 - Kir7.1 is immunopositive in choroid plexus tumors, but negative in PTPR
 - CD56 is often strongly expressed in PTPR, but focal in CPP
- PTPR vs. metastatic carcinoma
 - PTPR are negative for CK7 and CK20 which are frequently expressed in metastatic carcinomas
 - Cytology in metastatic tumors more anaplastic than PTPR
 - EMA frequently expressed in metastatic tumors, but low or focal in PTPR
- PTPR vs Pineal Parenchymal tumor of intermediate differentiation (PPTID)
 - PPTIDs are diffusely immunoreactive for synaptophysin, PTPR demonstrates only focal or absent staining
 - PPTIDs frequently demonstrate NFP staining, PTPR do not express NFP
 - PPTIDs are cytokeratin negative, but PTPR demonstrate strong and diffuse immunoreactivity for CAM5.2 or CK18

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