Pineal Cyst, Glial and Other Rare Tumors

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Dr. Vogel declares he has no conflict(s) of interest to disclose.

Outline

1. Pineal cyst
2. Other cystic lesions: arachnoid (quadrigeminal cistern) cyst, epidermoid cyst
3. Glial tumors, including "tectal plate gliomas"
   1. Pilocytic astrocytoma
   2. Ependymoma
4. Choroid plexus tumors
5. Other rare tumors
   1. Pineal anlage tumor
   2. Atypical teratoid/rhabdoid tumor
   3. Meningioma
   4. Metastatic tumors

A 16-month-old girl was referred for evaluation of a tectal mass and obstructive hydrocephalus.

Previously healthy and developmentally normal until 13 mo of age when she developed ptosis and strabismus in her R eye followed by ptosis and strabismus in her L eye.

Brain MRI performed at 13 months of age showed an ovular, 17 × 13 × 12 mm, rim-enhancing, cystic lesion in the midbrain tectum with adjacent edema.

Intraoperative view of the abnormal tan-gray tissue emanating from the posterior tectal plate. No evidence of extension or contiguity of the lesional tissue toward the more dorsal pineal region.

Intraventricular view of the abnormal tan-gray tissue emanating from the posterior tectal plate. No evidence of extension or contiguity of the lesional tissue toward the more dorsal pineal region.
Differential diagnosis of cystic pineal region lesions

- Pineal cyst
- Arachnoid (quadrigeminal cistern) cyst
- Epidermoid cyst
- Pilocytic astrocytoma
- Usually SOLID: pineal parenchymal tumors, germinomas, other primary pineal tumors

Pineal gland: developmental histology

- Two lobes: superior and inferior
- Astrocytic capsule interconnected with lobular astrocytes
- Pinealocytes, blood vessels, myelinated/unmyelinated nerves, and oligodendrocytes comprise the gland
- Innervated by sympathetic nerves from the superior cervical ganglia
- Pineal rests found in the quadrigeminal plate

Pineal cyst

- Common finding at necropsy
- Small cysts (<0.5 cm.) very common, may affect 1-4% of the population
- Distorts the pineal gland, but rarely causes symptomatic compression of other structures
- Larger cysts present like other pineal neoplasms, tending to affect young adults
- Radiographic findings:
  - Cyst: rounder, regular in shape, minimal enhancement
  - Tumor: usually solid, irregular in shape, stronger enhancement

Sagittal section through the pineal gland of a human fetus. Note the separation into an anterior lobe (AL) and a posterior lobe (PL). H: habenular area, SCO: subcommissural organ, rp: pineal recess.
Pineal Cyst, Glial and Other Rare Tumors

Incidental pineal cyst (courtesy Arie Perry MD)

Pineal Cyst - microscopy

- Lining composed of piloid gliosis, hypocellular compared with the adjacent distorted pineal gland
- Immunohistochemistry: typical three-layered pattern of the cyst wall and highlight the lobularity of the remaining gland
  - The inner layer is gliotic, shows strong expression of GFAP, with numerous Rosenthal fibers, hemosiderin, and siderophages
  - The second layer is pineal parenchyma, usually loss of lobular architecture Strong immunopositivity of the pineal parenchyma for synaptophysin and neurofilament protein
  - Outer layer sclerotic leptomeningeal tissue

Pineal Cyst, Glial and Other Rare Tumors

Pineal Cyst – surgical specimen

39-year-old male with 1.5 cm pineal cyst, with headache, left eye pain, double vision

Pineal Cyst – surgical specimen. Look for characteristic layered appearance

Pineal Cyst, Glial and Other Rare Tumors

Pineal cyst – incidental autopsy specimen

Pineal cyst – considerable piloid gliosis with Rosenthal fibers may be present (Images courtesy Arie Perry MD)
1. Symptomatic pineal cysts may cause:
   - Increased ICP
   - CSF obstruction
   - Neuroophthalmologic dysfunction
   - Brainstem and cerebellar compression
   - Mental status changes

2. Uncommon clinical presentations in 3 cases related to increased cyst size caused by hemorrhage, with sudden death, postural syncope and loss of consciousness.

Other benign cysts of the pineal region?

- Arachnoid (quadrigeminal cistern) cyst
- Epidermoid cyst
- Endodermal cyst
- Choroid plexus cyst

Pineal epidermoid cysts

- Age range 13 to 51 years (mean, 29.2 years): 15 M / 9 F
- Average duration of complaints 7 months; headache, ataxia were the commonest symptoms
- Total excision achieved in 6/24 patients
- Incomplete tumor resection was primarily due to adhesions
- Follow-up:
  - 1 patient had asymptomatic growth of the residual tumor
  - 1 patient with residual tumor with persistent generalized seizures

Pineal arachnoid (quadrigeminal plate) cysts

- Most cause hydrocephalus
- Neurosurgically challenging

Choroid cyst of the pineal region

- Incidental finding
- Arise from the adjacent structures
Remember our case?

2 years later underwent re-biopsy for worsening left III and VI nerve palsies

Dx: Pilocytic astrocytoma, negative for BRAFV600E and BRAF gene rearrangement by FISH, WHO grade I

Other cystic tumors of the pineal region?
- Pilocytic astrocytoma
  - Symptoms due to local mass effect
  - Must distinguish piloid gliosis with Rosenthal fibers of a pineal cyst from a PA
- Usually SOLID: pineoblastomas, pineocytomas, germinomas, other primary pineal tumors

Other glial tumors of the pineal region
- Ependymoma
  - Avoid misdiagnosing PTPR as ependymoma (Brain Pathol 2016 26, 199-205)
- Choroid plexus tumors
  - Exceedingly rare cause of obstructive hydrocephalus
  - Avoid misdiagnosing PTPR as CPP (Brain Pathol 2016 26, 199-205)

Pineal region diffuse midline gliomas with histone H3-K27M mutation

Table 1. IHC results for histone H3-K27M mutant protein

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</table>
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Pineal anlage tumor

- Def: an·la·ge: “the rudimentary basis of a particular organ or other part, especially in an embryo”
- Rare tumor of early childhood, ages 4 months-9 years, mostly males
- “Typical” pineal anlage tumor contains pigmented epithelium, ganglion cells, neuroblasts, glia, cartilage, and striated muscle, but no endoderm-derived elements

Pineal region AT/RT

A disease of adults?

Age 33
Age 19

Pineal region meningiomas

- 6.2-10% of pineal region tumors
- Female predilection
- Indolent growth, producing obstructive hydrocephalus
- Parinaud syndrome infrequent
- Seem to arise from meningothelial cells of the falx-cerebellar junction, or from the roof of the 3rd ventricle, without a dural attachment
- Histology the same as in other locations
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Pineal metastases

- Rare, but remember!
- Most important factor in differentiating metastatic intracranial disease from primary lesion is HISTORY of malignancy.
- In patients with a known history of malignancy, approximately 90% of supratentorial lesions represent metastasis
- Majority: lung, breast, melanoma

Pineal metastases. Case illustration

- 67 Y M with no significant PMH who presented with imbalance and memory problems and was found to have a pineal/tectal lesion with secondary obstructive hydrocephalus concerning for metastasis versus primary brain lesion
- No known malignancy

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- Pathology:
  - PTPR variant?
  - Metastatic neuroendocrine tumor?
  - Pancreatic mass subsequently found

IHC positive:
- Synaptophysin, chromogranin, cytoplasmic (CAM5.2)

IHC negative:
- CAM5.2
- SYN
- NEUROFILAMENT
- S100
- GFAP
- EMA
- NKX3.1
- CDX2
- VIMENTIN
- CAM5.2
Summary

- Diagnosis of pineal cysts requires awareness of the typical histomorphology in order to distinguish them from incidentally biopsied pineal gland versus other cystic tumors.
- Diverse primary glial, embryonal, meningeal tumors may rarely involve the pineal region.
- Metastatic disease is rare but may mimic neuroepithelial features of primary pineal region tumors.

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