Financial Disclosures

• I have no financial interests to disclose.
Case

• 7 year old girl
• Initially parents noticed photophobia
• Then started to complain of blurry vision, headaches, nausea, vomiting
• Eye movements seemed “strange” and she was blinking a lot
Exam

- Well-appearing child
- Visual Acuity 20/40 OU
- Color Vision 6/8 correct Ishihara plates OU
- Pupils
  - Minimally reactive to light
  - Good reaction to near stimulus
  - No rAPD
- Motility
  - Bilateral limitation to upgaze with frequent blinking, possible convergence
- Dilated fundus exam:
  - ?possible optic disc edema
Summary of Findings

- Light-near dissociation
- Supranuclear upgaze palsy
- Convergence/retraction saccades

Many of these findings are part of the Dorsal Midbrain Syndrome:
- Light near dissociation
- Upgaze palsy
- Convergence Retraction
- Lid retraction
- Possible correctopia (due to unequal inhibition of portions of the E-W nucleus)
What would you do next?

- Multiloculated Appearance
- T1W hyperintensity due to fat or lipid
- Heterogenous enhancement
Dorsal Midbrain Tumors

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Dorsal Midbrain Tumors

- Rare in children
- Pineal region tumors
  - Pineoblastoma
  - Germ cell tumors
- Tectal Gliomas
Dorsal Midbrain Tumors Agenda

• We will discuss
  • Presentation
  • Exam Findings
  • Differential Diagnosis for Exam Findings
  • Natural History
  • Treatment
  • Visual Outcomes
  • Systemic Outcomes

• For Pineoblastoma, Germ Cell Tumors, Tectal Gliomas
Pineal Region Tumors

• Account for 2.8% of CNS tumors in children
• Normal pineal gland consists of
  • Parenchymal tissue
    • Germ Cell tumors (50% of pineal tumors)
    • Pineoblastoma and papillary tumors of pineal region (15-25%)
  • Glial tissue
    • Glioma, ependymoma, astrocytoma
  • Connective tissue
• Other pineal region tumors include teratomas and rhabdoid tumors
Tumor Types Discussed Today

- Germ cell tumors
- Pineoblastoma
- Tectal Glioma
Tumor Types: Germ Cell Tumor

• Most common tumors of the pineal region (>50% pineal tumors)
• Male predominance

• Germinoma, choriocarcinomas less malignant
• Embryonal cell carcinoma, endodermal sinus tumors, teratomas more malignant

• Typically diagnosed by neuroimaging but serum markers exist
  • Alpha-fetoprotein (endodermal sinus tumor)
  • Human chorionic gonadotropin (choriocarcinoma and embryonal carcinoma)
  • Germinoma and teratoma do not produce these markers
Tumor Types: Pineoblastoma

- Second most common pineal region tumor but <0.1% of intracranial tumors
- Highly malignant primitive neuroectodermal tumor (PNET)
- WHO grade IV
- May disseminate throughout the CSF
- May occur as part of trilateral retinoblastoma
Tumor Types: Tectal Glioma

- Gliomas of the brainstem represent 10-25% of pediatric brain tumors
- Tectal gliomas <5% of brainstem tumors in children
  - Subset of midbrain gliomas that are slow-growing, low grade
  - Rarely produce neurological deficits
  - Small proportion may show progressive growth with sequelae associated with a space-occupying lesion and obstruction of the aqueduct of Sylvius
Pineal Region Tumors
Typical Presentation: Pineal Region Tumors

- Germinomas typically present in 2\textsuperscript{nd} decade (~12 years)
- Pineoblastomas typically present earlier in 1\textsuperscript{st} decade (~3 years)
- Typical presentation is either:
  - Symptoms from dorsal midbrain compression (~50%)
    - Lid retraction, light near dissociation, impaired upgaze, converge-retraction nystagmus
  - Symptoms from hydrocephalus due to compression of the sylvian aqueduct
    - Headache (75%), nausea/vomiting (70%), altered LOC, weight change, behavior change
  - Symptoms from midline lesion (~10%)
    - Bitemporal hemianopia, diabetes insipidus, precocious puberty, failure to thrive
Exam Findings: Pineal Region Tumors

• Common dorsal midbrain syndrome findings:
  • Pupillary light-near dissociation
  • Lid retraction
  • Impaired upgaze
  • Convergence-retraction

• Less common
  • Myopia due to central disinhibition of Edinger-Westphal nucleus leading to decreased accommodative tone
  • Anisocoria due to asymmetric central disinhibition of Edinger-Westphal
  • Skew deviation
  • Bilateral 4th nerve palsy
Typical Scenario Encountered By Ophthalmologist

- Child presents with:
  - Dorsal midbrain syndrome
  - Headaches, papilledema
- Neuroimaging reveals pineal region mass
- Biopsy (at a minimum) required to differentiate tumor type
- Treat hydrocephalus if present
- Treatment based on biopsy results
Differential Diagnosis: Pineal Region Tumor

- Germinoma
  - Well defined with homogenous enhancement, isointense to gray matter

- Pineoblastoma
  - Mixed signal on T1 and hyperintense on T2, variably enhance

- Choriocarcinoma
  - Heterogeneous on MRI due to hemorrhage, fibrosis, cysts, necrosis

- Teratomas
  - Hyperintense on T1 due to fat, protein with hypointense areas of calcification and blood; mixed signal on T2

Definitive diagnosis is made by excisional biopsy
• Hydrocephalus is typically managed with endoscopic third ventriculostomy (ETV) or VP shunt
• Smaller tumors can be biopsied at the time of the ETV
• Larger tumors may need more complete resection
• Typically found to be benign (germinomas)

• Hydrocephalus often recurs, 50% require at least one shunt revision up to 7 years after initial diagnosis
• Older case series reveal post-op complications
  • Peri-operative death (5%)
  • Neurological worsening (16%)
Treatment – Pineal Region Tumors

- Manage hydrocephalus
  - At time of biopsy or before
- Biopsy (incisional or excisional) – surgical treatment is associated with high morbidity so often biopsy only
- Systemic staging
- Treatment of residual tumor based on pathology
  - Chemotherapy
  - Whole brain or craniospinal irradiation (attempt delay if <3 or <6)
MRI brain/spine and serum markers

ETV/CSF tumor markers

Hydrocephalus?

Yes

No

Marker +

Marker -

No biopsy, treat

Biopsy open or endoscopic

LP/CSF tumor markers

Reproduced from Pettorini et al. Child Nerv Syst 2013
Visual and Oculomotor Outcomes: Pineal Region Tumors

- Symptoms from dorsal midbrain syndrome typically resolve
  - No data on which resolve vs. persist
  - My own personal experience is that pupillary findings and upgaze difficulties often persist more than eyelid findings
- Central fusion disruption has been described post-treatment with radiation
- Most patients do not typically need treatment for eye movement problems
- Optic nerve edema typically resolves over time
  - Visual prognosis dependent on severity and duration of papilledema
Systemic Outcomes: Pineal Region Tumors

• Modern case series reveal extremely rare surgical mortality
• Germinomas are very radiosensitive
  • Long-term progression-free survival rates 90%+ after radiation
  • Studies comparing whole brain to whole ventricle radiation have shown improved IQ measurements in whole ventricle group
  • Increased risk of neurocognitive dysfunction in patients treated <12 years
• Non-germinomas (embryonal cell, yolk sac) are much less radiosensitive
  • Long-term progression-free survival ranges 60-70% after radiation + neoadjuvant chemotherapy
Systemic Outcomes: Pineoblastomas

- Worst survival of all pineal region tumors
- Worse survival in younger patients
  - 5-year survival < 5 years old 15%
  - 5-year survival > 5 years old 57%
- Better 5-year survival with gross total resection than subtotal resection (84% vs. 53%)
- Moving towards gross total resection with adjuvant chemo and radiation as gold standard treatment

Tate et al. Cancer 2012
Monitoring: No standard guideline

• Based on degree of symptoms
• I typically re-evaluate children 4-6 weeks after instituting treatment
  • This may be sooner if papilledema is severe
• Monitor every 4-6 weeks during treatment and in the immediate post-treatment phase
• Spread out follow-up to every three months after one year of stable disease
Tectal Gliomas
Relevant anatomy

• Tectum = most dorsal part of the midbrain
• Consists of superior and inferior colliculi
  • SC: receives retinal inputs, mediates oculomotor responses such as horizontal conjugate gaze
  • IC: receives auditory inputs
Typical Presentation: Tectal Gliomas

- Typical presentation is late and due to symptoms from hydrocephalus
- Mean age at presentation is 8-9 years
- May be seen in association with NF1
- Due to approximation to aqueduct of Sylvius, most patients present with delayed-onset symptoms of increased ICP
  - Nausea, vomiting
  - Transient visual obscurations
  - Rarely cranial nerve palsies, dorsal midbrain syndrome, seizures, behavioral changes
Exam Findings: Tectal Gliomas

- May have decreased visual acuity or abnormal visual field
- Papilledema on dilated fundus exam
- May have mild sixth nerve palsies due to increased ICP
- May (less commonly) have features of dorsal midbrain syndrome
- May have other findings associated with NF1 such as Lisch nodules
Typical Scenario Encountered By Ophthalmologist

- Child presents with headaches and transient visual changes
- Patient found to have papilledema
- Neuroimaging reveals either:
  - well-circumscribed iso- or hypointense on T1 lesions
  - diffuse hyperintense on T2
- Hydrocephalus may also be present
- Biopsy often not necessary
- Hydrocephalus managed by shunt or ETV
- Long-term monitoring vs treatment depending on aggressiveness
Differential Diagnosis: Tectal Gliomas

- For the papilledema/hydrocephalus
  - Any other intracranial lesion/tumor causing increased ICP
  - Pseudotumor cerebri syndrome
  - Venous sinus thrombosis
  - Meningitis
  - Non-accidental trauma
  - Drusen/Pseudopapilledema

- For the MRI findings of midbrain tumor
  - Pineal tumor
  - Non-pilocytic astrocytoma (these enhance post-contrast more)
  - Ganglioglioma
• Tumors are very slow-growing and indolent
• Often no treatment is required for tumor itself after hydrocephalus is controlled
• Serial MRI monitoring
• Less than 10% of patients progress
  • Therefore <10% require treatment
Management– Tectal Gliomas

• Manage hydrocephalus
  • Typically with ETV
• Serial MRI monitoring
• Biopsy/surgery only in cases with rapid growth or questionable diagnosis
  • New neurologic finding
  • Not for simple enlargement on MRI
  • Risks include dorsal midbrain syndrome, acoustic neglect, auditory hallucination, optic atrophy, death
• Radiation and chemotherapy variably recommended
Systemic Outcomes: Tectal Gliomas

- ETV successful in treating aqueductal stenosis in 70%
- Poorer prognosis with:
  - 6th nerve palsy
  - Basilar artery engulfment
  - Pontine location
  - Enhancement on MRI post-contrast
- Follow patients every 6 months to evaluate for progression (occurs in up to 1/3 of patients, usually when > 2 cm)
  - New onset dorsal midbrain
  - Papilledema
Thank you!