An Unusual Case of a Massive Mitotically Active Pineocytoma

Ishaq Asghar, M.B.B.S., Hanae Benchbani, M.D., Mark Edgar, M.D., Ian Dryden, M.D.
Department of Laboratory Medicine and Pathology, Mayo Clinic, Jacksonville, Florida

Introduction

- Pineal region tumors are rare accounting for 0.5% of CNS tumors (1,2).
- Pineocytomas account for 25% of pineal region tumors (1,3).
- They are WHO grade 1 tumors with unique histology, rare mitotic activity (<1% Ki-67), no recurrent genetic alterations, and distinct DNA methylation profile (1,4).
- This differentiates them from the higher grade pineal parenchymal tumor of intermediate differentiation (PPTID) and pineoblastoma.
- We present a case of an unusually large pineocytoma with focally increased mitotic activity.

Clinical Findings

- A 75-year-old male who presented with a new onset tremor in right hand.
- He had a history of midbrain mass in the pineal region, identified fifteen years ago, but was not biopsied for unknown reason.
- At the time it was noted that he had hydrocephalus and was treated with ventricoperitoneal (VP) shunt.
- MRI with and without contrast shows 5.5 x 4.6 x 3.4 cm heterogeneously enhancing T2 hyperintense midline hemorrhagic mass involving the bilateral thalami and midbrain including the tectal plate.
- The initial radiologic differential diagnosis included a diffuse midline glioma versus a low grade glioma.

Histopathologic Findings

- Stereotactic core biopsies were performed showing a well-differentiated, moderately cellular, pineocyte neoplasm with occasional large pineocytomatous rosettes and rare cells with gangliocytic differentiation.
- Up to 5 mitotic figures per 10 HPF were identified.
- Brain tissue and thick hyalinized vessels were noted in the background.
- Immunohistochemistry reveals that the neoplastic cells were positive for synaptophysin and neurofilament. They were negative for GFAP, CAM5.2, and EMA.
- GFAP highlights background gliotic brain parenchyma.
- The Ki-67 proliferation index was low, estimated to be around 3 to 5%.

Molecular Findings

- Next-generation sequencing (NGS), chromosomal microarray (CMA), and DNA methylation profiling were performed.
- NGS showed a truncating loss-of-function alteration in ATRX p.F2113Sfs*9 and a variant of uncertain significance EGFR p.N540K.
- KBTBD4 alteration was not detected with NGS.
- Relevant CMA findings included loss of 2q, gain of 9q, and loss of whole chromosome 13 (RB1).
- DNA methylation profiling classified the neoplasm as pineocytoma with a high confidence score (0.99 NCI-Bethesda; 0.97 DKFZ).

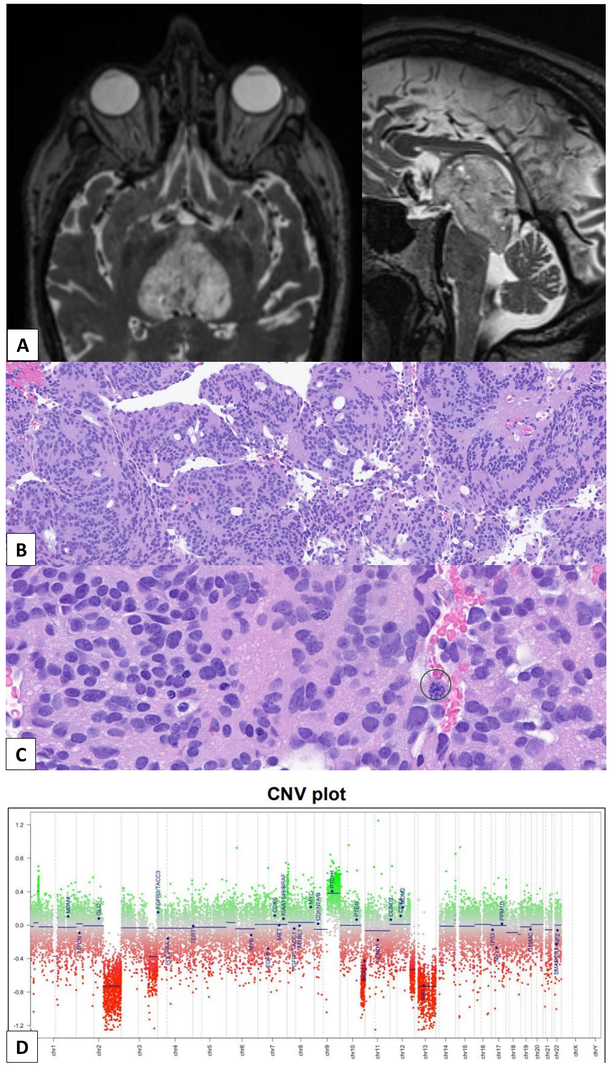

Figure 1: A) MRI showing axial and sagittal views of T2 hyperintense pineal region mass, B) pineocytoma with large rosettes (10x), C) Pineocytoma with up to 5 mitosis/10hpf (40x, circled mitosis), D) CNV plot obtained from NIH/NCI DNA methylation profiling.

Conclusions

- To our knowledge, a pineocytoma of this size with mitotic activity has not been reported.
- A PPTID (WHO grade 2) neoplasm is considered less likely given the lack of characteristic histologic features, KBTBD4 gene alteration, and a defining DNA methylation profile (1,4).
- Similarly, a pineoblastoma (WHO grade 4) is considered less likely given the lack of characteristic histologic features, recurrent genetic alterations (DICER1, DROSHA, DGCR8, RB1, and MYC/FOXR2), and the defining DNA methylation profile (1,4).
- Given the rarity of pineocytoma, this case sheds light on the potential biologic spectrum of this neoplastic entity.
- Furthermore, the findings in this case suggest that further discussion is necessary regarding a potential subclassification for this neoplasm, such as "atypical pineocytoma," along with studying its clinical, therapeutic, and prognostic implications.

References

1. Dominique Figarella-Branger, editor. Chapter 5: Pineal Tumours. In: WHO Classification of Tumours Editorial Board. Central nervous system tumours. Lyon (France): International Agency for Research on Cancer; 2021. . (WHO classification of tumours series, 5th ed.; vol. 6). https://publications.iarc.fr/601.
2. Price M, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2017-2021. Neuro Oncol. 2024 Oct 6;26(Supplement_6):vi1-vi85. PMID: 39371035; PMCID: PMC11456825.
3. Jouvet A, Saint-Pierre G, Fauchon F, Privat K, Bouffet E, Ruchoux MM, Chauveinc L, Fèvre-Montange M. Pineal parenchymal tumors: a correlation of histological features with prognosis in 66 cases. Brain Pathol. 2000 Jan;10(1):49-60. PMID: 10668895; PMCID: PMC8098427.
4. Pfaff E, et al. Molecular subgrouping of primary pineal parenchymal tumors reveals distinct subtypes correlated with clinical parameters and genetic alterations. Acta Neuropathol. 2020 Feb;139(2):243-257. PMID: 31768671.