Non-Traditional Presenting Grade II Brain Meningioma: A Case Study

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Background

Meningioma is a relatively common form of cancer, occurring in approximately 97 out of 100,000 individuals. Although it arises from the meninges surrounding the central nervous system (CNS) rather than from neurons, it is classified with CNS tumors due to overlapping symptoms caused by compression of nerves and vessels in the head. Extracranial metastases are rare (liver and thigh in this case), at less than 1%, and correlate with reduced survival rates.

Methods

Patient was treated at the Hoag Hospital in Orange County, California using surgical craniotomies, chemotherapy, gamma knife radiation, and immunotherapy; and Magnetic resonance imaging (MRI) and immunohistochemistry (IHC) diagnostically. Whole exome sequencing (WES) was used to determine somatic karyotype and point mutations.

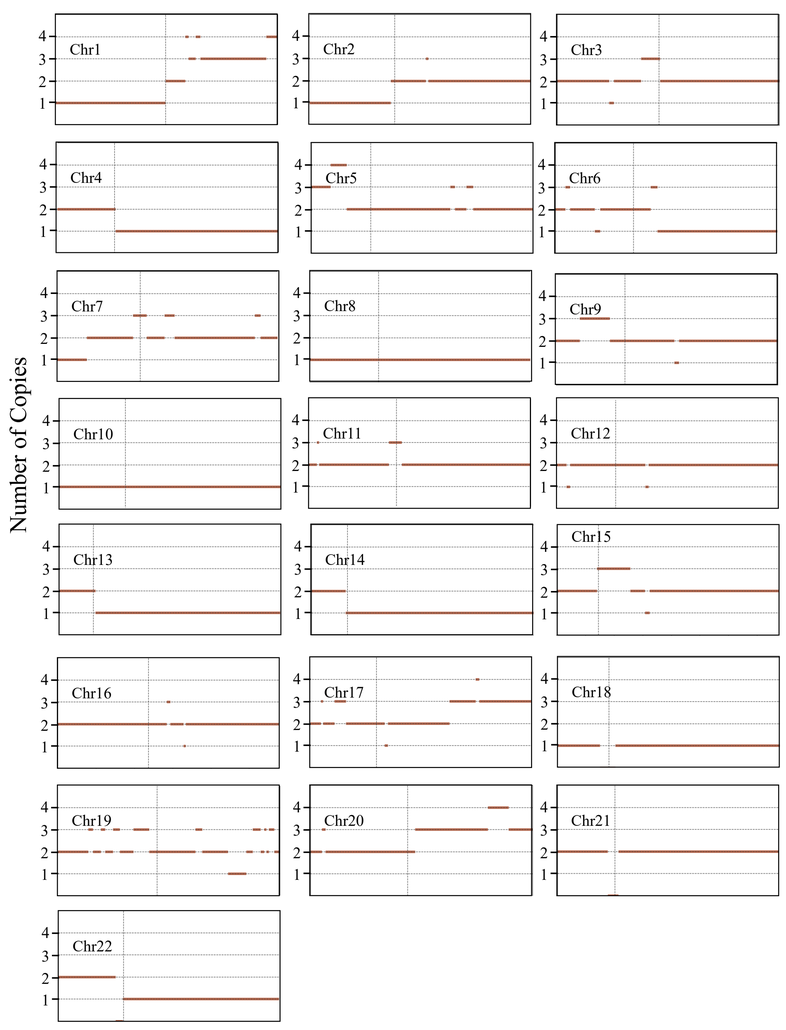

Figure 2: Tumor karyotype as computed from whole exome sequencing

Results

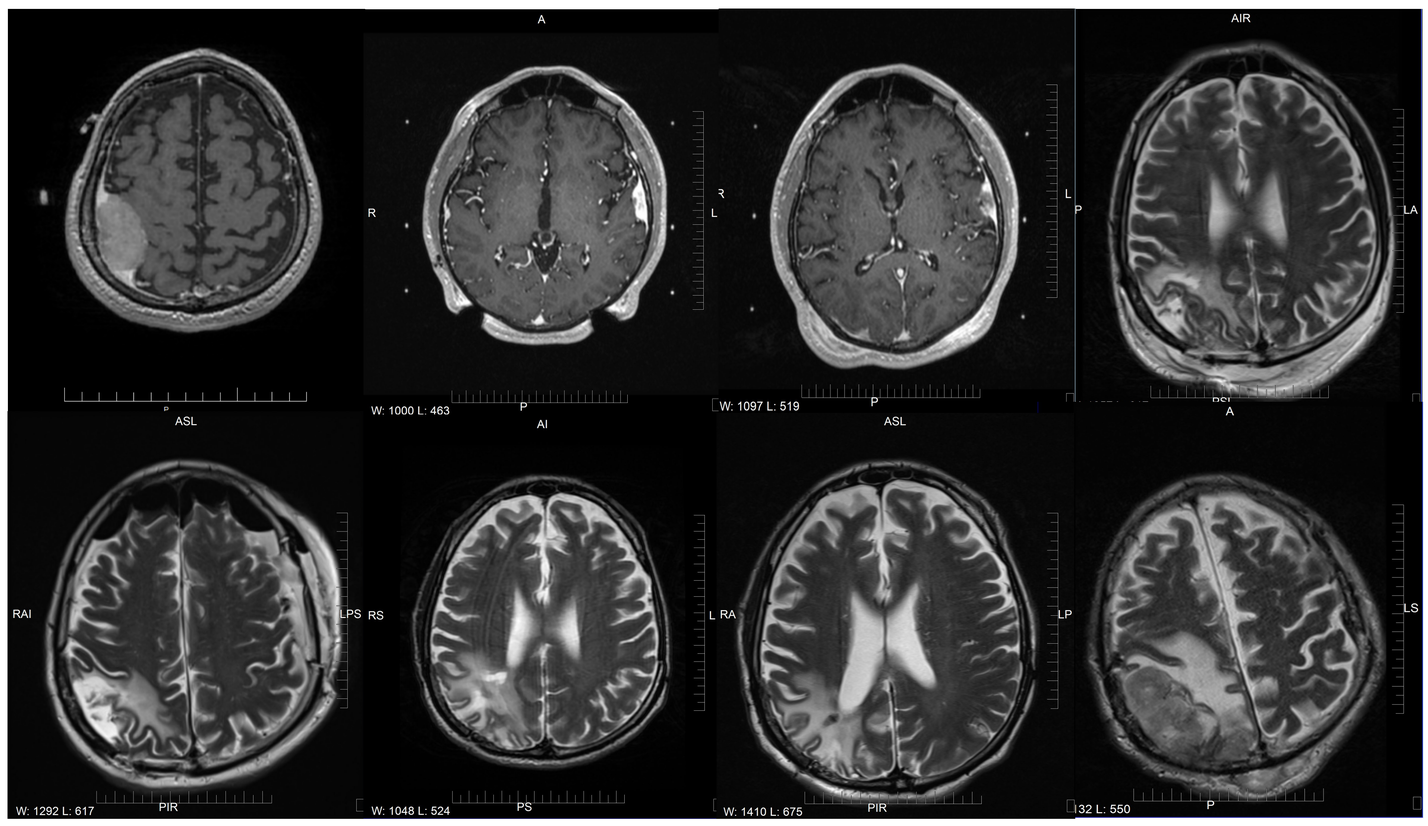

Figure 1a-h: (top left to right: 2015, 2019, 2020, early 2021, bottom left to right: late 2021, 2022, early 2023, late 2023) MRI scans displaying meningiomas pre/post procedures.

Case: 49-year-old male presented with chronic migraines, unresponsive to traditional treatments. MRI found a unilateral mass in the right parietal region. Patient underwent surgical removal, and the patient was diagnosed with atypical grade II meningioma. Somatic mutations were detected in NF2 (p.Y144fs) and SUFU (p.N374fs).

Over the next eight years, the patient underwent 12+ procedures in response to recurrent meningiomas in various locations, including 6 additional surgical craniotomies, chemotherapy, gamma knife radiation, and immunotherapy. Further analysis of sequencing data revealed several somatic copy number variants, including the deletion of the unmutated copies of both NF2 and SUFU, which are suspected to have been deleted in the original tumor.

Eight years after the initial tumor diagnosis, patient was found to have masses in the liver, L5 vertebrae, and right femur. The liver mass was removed and was stained positively for SSTR2, suggesting that it originated from the meninges. The tumor grade was raised to level III following the discovery of metastases. Chemotherapy is planned to shrink metastases and prevent further spread.

Year	Type	Time Since Diagnosis (years)	Location	Dimensions (cm)	Progesterone Receptor	Ki-67	Epithelial Membrane Antigen	S100	Vimentin	Estrogen Receptor
2015	Craniotomy	Initial Diagnosis	R Parietal	5.8x4.1x2.2	+		+	Focal +		
2019	Gamma Knife	3.4	R Parietal							
2019	Gamma Knife	4.3	R Temporal, R Frontoparietal, R Convexity, R Parietal							
2020	Gamma Knife	5.2	L Frontal, R Parietal							
2021	Craniotomy	5.4	R Parietal	3.5x2.6x2	+	≤20%	-			-
2021	Craniotomy	5.5	R Frontotemporal	5.6x5.2x1	Strong Nuclear +		Weakly +	Weak Patch	+	
2023	Craniotomy	7.4	R Parietal	4.2x3.5x1						
2023	Craniotomy	8	L Temporal	5.7x5x3.3	Focal +	50-60%	Weakly +			
2023	Craniotomy	8.1	R Subglial Midline	7x4x2	Focal +	70%	+			
2023	Gamma Knife	8.3	R Parietal, R Anterior Temporal							

Table 1 Meningioma description: procedure type, timelines, size, location, and genetic markers.

Future Direction

Gene-specific investigation of tumor development presents a compelling frontier in medical research that focuses on the effects of specific genes in tumor formation and progression. Gene-karyotyping revealed that our patient had NF2 and SUFU gene mutations

- NF2 Gene Modulation: Neurofibromin 2 (NF2) encodes for a protein involved in the mTOR pathway. Dysregulation leads to increased progression of cell cycle and leads to cell proliferation.
- SUFU Gene Targeting: Suppressors of fused homologues, or SUFU, encodes for tumor suppressor protein oncogenes. Mutation or deletion has been linked to various cancers, which suggests that it has a significant role in adult tissue homeostasis maintenance.

Investigating the specific mechanism through which NF2 or SUFU mutations contribute to meningioma growth and development will lead to clinicians being able to prescribe targeted therapies based on individual genetic markers.