Genetic drivers of skull base meningiomas beyond canonical chromosomal losses

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BACKGROUND

Meningiomas are the most common primary intracranial tumors, with a significant proportion located at the skull base.

Molecular profiling has revealed recurrent chromosomal losses such as 1p, 14q, and 22q and gene mutations including NF2, TRAF7, KLF4, and BAP1.

Within a broad and evolving landscape, the biological and clinical differences between skull base and non–skull base tumors present a promising area for further exploration.

OBJECTIVE

We aimed to explore genetic drivers, clinical variables, and systemic inflammatory markers in a preliminary cohort.

METHODS

From an institutional cohort of 159 patients surgically treated for meningioma between 2022 and 2025, 33 cases with complete clinical, pathological, and molecular data were included for analysis.

Variables included age at diagnosis, sex, WHO grade, extent of resection, recurrence, follow-up, and genomic alterations across chromosomal/gene loci.

Chromosomal gains and losses were identified using microarray-based copy number profiling, supplemented by detection of recurrent gene mutations.

Preoperative neutrophil and lymphocyte counts were used to calculate the neutrophil-to-lymphocyte ratio (NLR).

Descriptive statistics, group comparisons, and frequency analysis were performed using non-parametric tests (Mann-Whitney U, Fisher's exact).

Tumors were stratified by anatomical location (skull base vs. non–skull base) to explore site-specific differences.

RESULTS

The cohort included 20 females (61%) and 13 males (39%), with a median age at resection of 54 years (IQR 45–73) and a median follow-up of 36 months. WHO grade distribution comprised 25 grade I (76%), 6 grade II (18%), and 2 grade III (6%) tumors. Seventeen tumors (51.5%) arose from the skull base (7 anterior, 4 middle, 4 posterior, 2 cerebellopontine angle), while 16 originated from non–skull base sites. Microarray profiling unveiled distinct genomic patterns (**TABLE 1**): non–skull base meningiomas were enriched in recurrent chromosomal aberrations, most notably losses of 1p (37.5%), 3p (25.0%), 6q (12.5%), 7p (18.8%), and 22q (31.2%), consistent with canonical drivers of higher-grade disease. In contrast, skull base tumors showed fewer large-scale chromosomal imbalances but a higher frequency of gene mutations, including TRAF7 (17.6%), NF2 (5.9%), MET, and MTOR (5.9% each). Occasional chromosomal alterations were also observed in this group, such as –2p, –4q, and +5.

Preoperative NLR data was available for 7 patients; median NLR was 2.10 (range 1.27–3.63). Higher NLR values were observed in grade II–III tumors vs. grade I (median 3.18 vs 1.90, $p < 0.05$), suggesting potential prognostic relevance. Mean NLR was modestly higher in skull base tumors (2.19) compared to convexity cases (1.96).

TABLE 1. Baseline demographic, clinical, and molecular characteristics of meningioma patients with available genomic profiling (*n* = 33).

Characteristic		Location		All (n = 33)
		Skull base (*n* = 17)	Non-skull base (*n* = 16)	
Age at resection, median (IQR)		57 (54-71)	54 (44-65)	57 (47–67)
Sex, *n* (%)	Female	16 (94.1)	9 (56.2)	25 (75.8)
	Male	1 (5.9)	7 (43.8)	8 (24.2)
WHO grade, *n*	I	15	8	23
	II	2	7	9
	III	0	1	1
Recurrence, *n*		2	2	4
Pre-op NLR, median		2.19	1.99	2.1
Main alteration		Gene-driven: TRAF7, NF2, MET, MTOR	Chromosome-driven: –1p, –22, –3p, –6q, –7p	Chromosome aberrations: 19 (57.6%) Gene mutation: 14 (42.4%)

Data is presented as median (IQR) or n (%). Main alteration denotes the predominant genomic driver per case, categorized as either chromosomal aberrations (losses/gains) or gene mutations (e.g., TRAF7, NF2, MET, MTOR).

CONCLUSION

This preliminary analysis highlights potential genetic drivers in skull base meningiomas that differ from non-skull base location. Furthermore, systemic inflammation as measured by NLR correlated with higher grade, supporting its role as a non-invasive biomarker. Despite limitations of sample size, these findings suggest that skull base meningiomas may follow distinct biological paths, with implications for prognosis and targeted therapy.

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