Papillary Craniopharyngioma Management in the Era of BRAF and MEK Inhibition

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Introduction

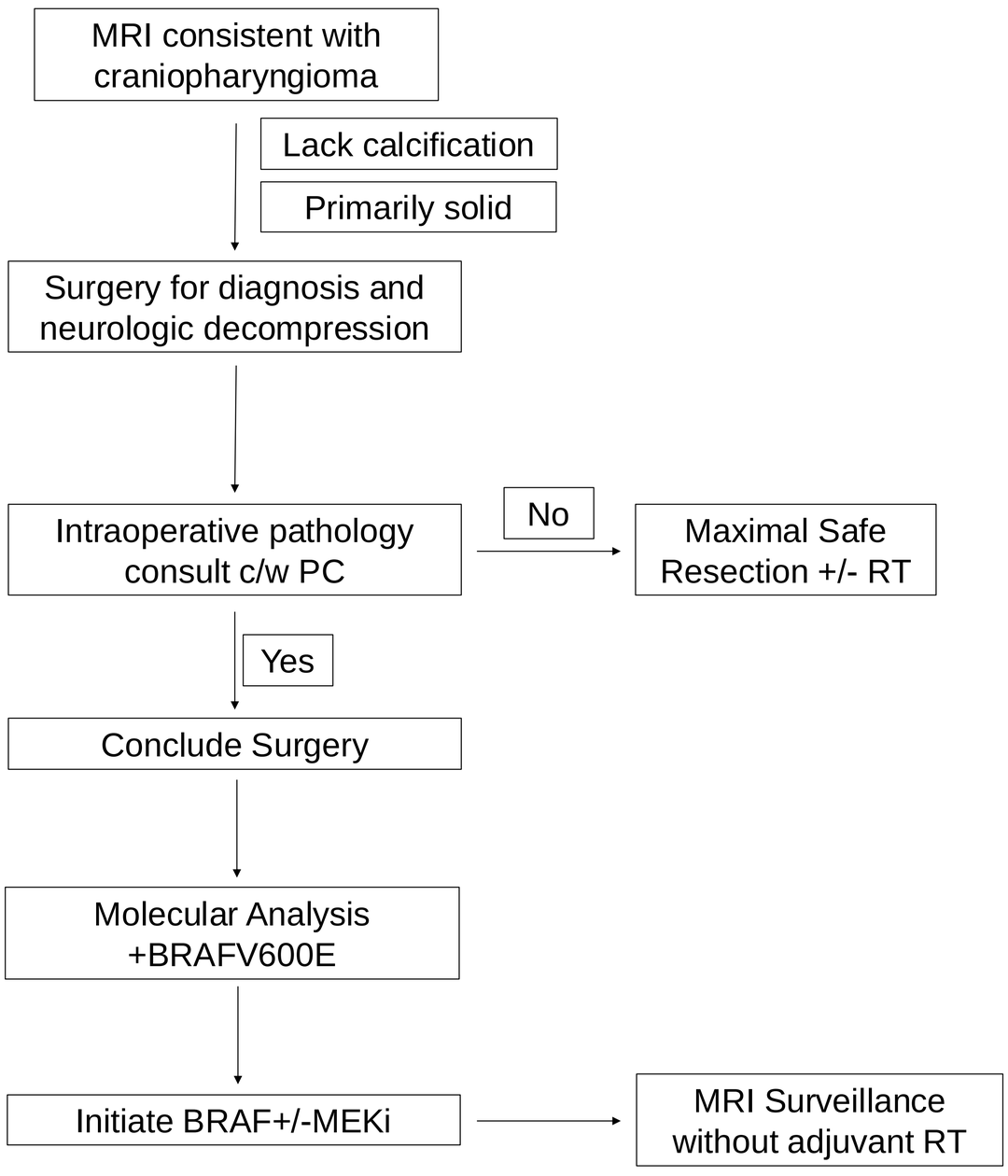
- Papillary craniopharyngioma (PC) is a histopathologic diagnosis with the presence of the BRAFV600E mutation in 95% of patients
- BRAFV600E is a targetable mutation with available FDA approved inhibitors, BRAF inhibitors, and downstream target, MEK inhibitors.
- Recent clinical trial (n=16) demonstrated high rates of complete (CR) or partial (PR) response, with generally low toxicity
    - Allowed for radiation at the discretion of the treating physician
- Up to 94% of patients will demonstrate new or progressive endocrinopathy after radiotherapy within 5-years
- We describe a potential treatment algorithm for patients with high preoperative suspicion for papillary craniopharyngioma in the BRAF/MEKi era

Methods

- Retrospective case series (n=4)
- Post-resection and last follow-up volumetric analysis of residual
- Details on operative procedure, medical therapy; no patients received radiotherapy
- Evaluation of grade 3 and 4 adverse events (CTCAE)

Results

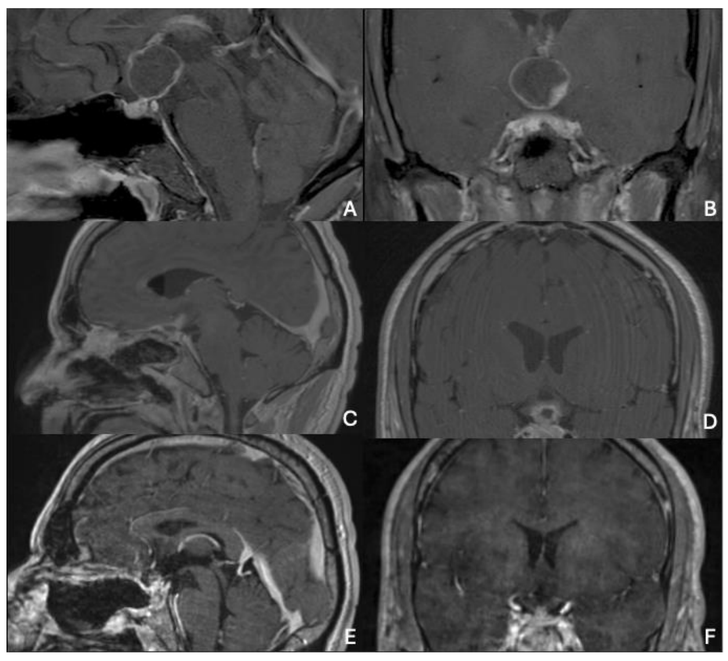
Proposed Algorithm



Results (cont.)

Case 1:

- 40M with blurry vision and DI
- Preop MRI in Figure 1A-B
- EEA-transsellar/transtubercular for diagnosis and optic decompression
- Postop residual along optic and infundibulum
- Started on BRAF/MEKi, no adjuvant RT
- Involution of remaining tumor with CR to tx
- No recurrence at 19-months without adverse medication effects



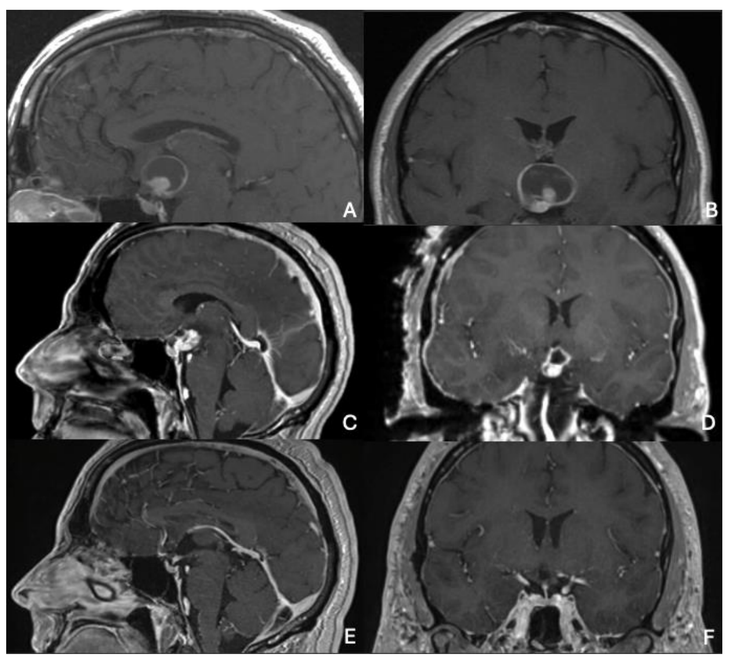
Preop Volume:
Cystic: 5.04 cm^3
Nodule: 0.33 cm^3

Postop Volume:
Cystic: 0 cm^3
Nodule: 0.72 cm^3

Post Tx Volume:
Cystic: 0 cm^3
Nodule: 0.07 cm^3

Case 2:

- 46M with fatigue, weight gain, panhypopit
- Preop MRI in Figure 1A-B
- R pterional subfrontal, trans-lamina terminalis approach for diagnosis and neurologic decompression
- Postop hypothalamic residual
- Started on BRAF/MEKi, no adjuvant RT
- Involution of remaining tumor with CR to tx
- Continue BRAF/MEKi for 7 cycles c/b cardiomyopathy
    - Discontinued MEKi, continued BRAFi for total 24m
- No tumor recurrence off all therapy for 51 months since surgery



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Conclusion

- BRAF V600E mutation is a readily targetable and consistent mutation in papillary craniopharyngioma
- Durable and fast response to BRAF/MEKi mitigate need for aggressive surgical resection and adjuvant RT
    - May have more favorable neuro-endocrinologic outcomes by focusing on neurologic decompression and avoidance of adjuvant RT
- multiple subtleties to these evolving treatment paradigms that have yet to be answered, including utility of dual versus monotherapy and exact duration of treatment necessary to obtain a durable response.