Update on Intraoperative Ultra-Rapid PCR for BRAF Mutation Detection in Craniopharyngioma

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INTRODUCTION

Recent molecular studies have shown that approximately 90% of papillary craniopharyngioma contain BRAF V600E mutations.

A phase II trial of BRAF V600E+ papillary craniopharyngioma treated with BRAF/MEK inhibitors showed 94% response rate and 91% tumor volume reduction.

During resection of craniopharyngioma, disruption of the pituitary/hypothalamic axis is often inevitable, requiring hormone replacement.

Determination of tumor genotype prior to surgical resection can alter the available treatments.

Despite interest in developing “liquid-biopsies” for noninvasive preoperative detection and diagnosis of CNS tumors, results thus far have been unsuccessful.

The development of ultra-rapid droplet digital PCR testing can provide accurate information on a tumor’s mutational status within a span of 15-20 minutes.

METHOD

Bead homogenization in the presence of a detergent-free DNA extraction buffer was used to lyse the cells from the tissue sample.

DNA was isolated from associated proteins and cellular debris.

An ultra-rapid ddPCR based assay determined the mutational status intraoperatively.

Histopathological analysis (H&E and immunohistochemistry) was performed on permanent pathology specimen.

Four cases of craniopharyngiomas that underwent standard endoscopic endonasal approaches underwent ultra-rapid ddPCR BRAF V600E analysis and permanent pathology.

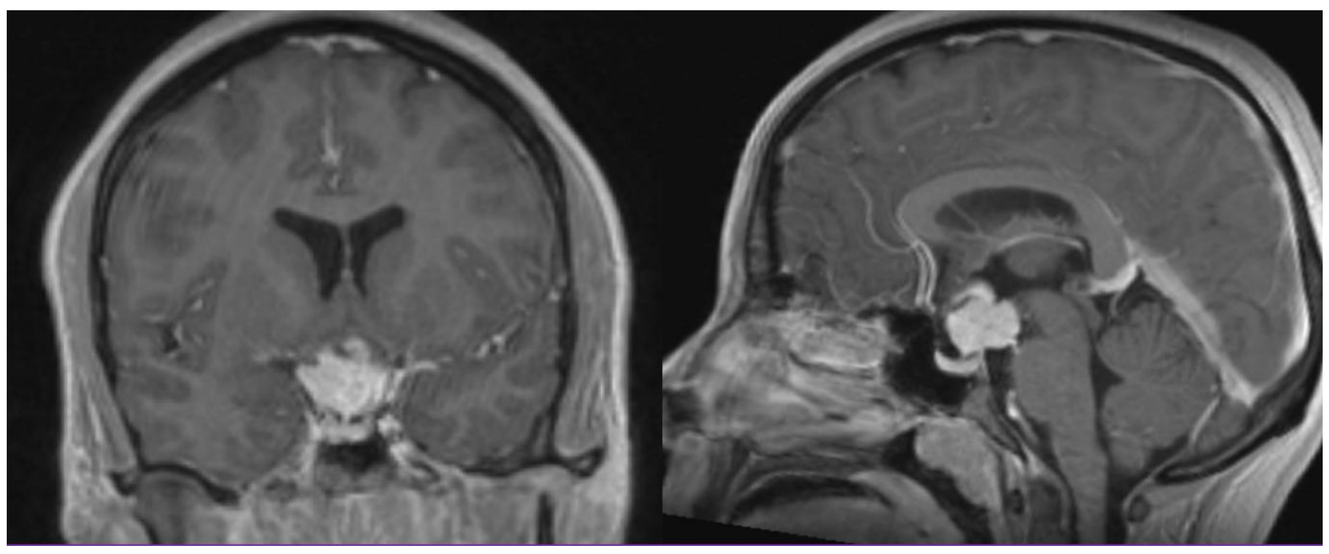
RESULTS

Four craniopharyngioma cases underwent endoscopic endonasal approaches for biopsy or resection.

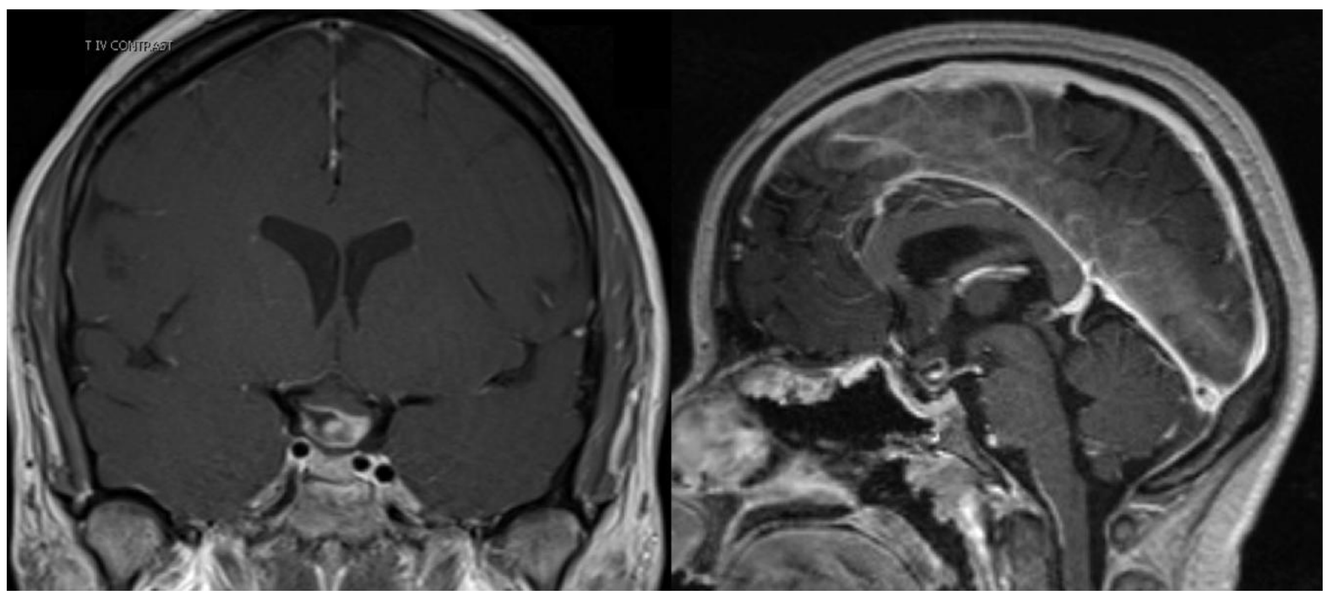
The average time to result for the droplet digital PCR testing was 17 minutes and 12 seconds.

PCR findings were subsequently corroborated by standard immunohistochemical analysis with 4/4 (100%) concordance.

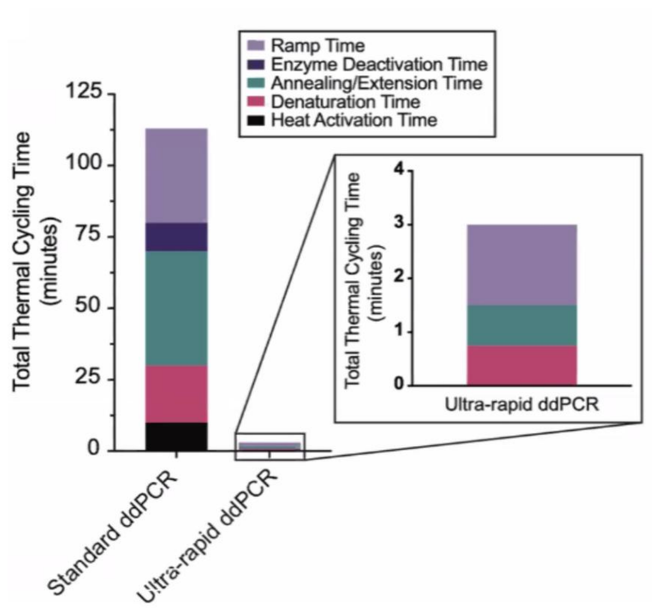
FIGURES



Coronal and sagittal post-contrast T1 weighted MRI demonstrating a 2.5cm lobular, solid mass lesion with mass effect on optic chiasm.



MRI after six months of dual BRAF/MEK inhibition, showing dramatic reduction in size of tumor.



Comparison of processing time for ultra-rapid droplet digital PCR compared to standard PCR with dramatic decrease in time to result.

CONCLUSION

Intraoperative ultra-rapid PCR can rapidly and accurately determine BRAF V600E status, which can directly impact our clinical decision in real-time.

This presents an innovative approach for intraoperative diagnosis and characterization of craniopharyngioma, with significant treatment implications.

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