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Case Report

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Functional and MRI improvement followed by a mixed trajectory during cannabinoid-terpenoid exposure in glioblastoma: a case report

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22 **Abstract**

23 **Background:** Glioblastoma has limited salvage options, while viable tumour, treatment injury, postoperative
24 change, oedema and corticosteroid effects may produce overlapping clinical and magnetic resonance
25 imaging (MRI) findings.

26 **Materials and Methods:** Clinical records, serial MRI examinations and signed radiology reports were
27 reviewed descriptively for a patient with IDH-wildtype, MGMT-promoter-methylated glioblastoma. The
28 exposure history and contemporaneously documented neurological findings were aligned with seven MRI
29 time points. No blinded central review, standardised volumetry or formal RANO 2.0 adjudication was
30 performed.

31 **Results:** After two operations, radiotherapy, concomitant temozolomide and three adjuvant cycles, serial
32 MRI documented progression before April 2025. During a non-standard exposure state comprising intranasal
33 perillyl alcohol and alpha-bisabolol, individualised cannabinoids and docosahexaenoic acid/medium-chain
34 triglyceride oil, with dexamethasone fixed at 2 mg/day, hemiplegia/KPS 50 improved to hemiparesis with
35 regained walking/KPS 80, coinciding with reduced enhancement. Later MRI showed increasing right
36 temporal and cerebellar enhancement, including a new contralateral cerebellar focus, despite substantially
37 stable postoperative cavity and T2/FLAIR extent. June 2026 lesion perfusion curves were low-amplitude
38 without pathological hyperperfusion. The patient subsequently died after an overall survival of 45 months.

39 **Conclusions:** This uncontrolled case documents early functional and radiological improvement on a stable
40 corticosteroid background, followed by an anatomically progressive but biologically indeterminate
41 trajectory. It does not establish treatment causality, survival benefit, formal tumour response or component-
42 specific efficacy; mixed viable tumour and treatment effect or radiation necrosis could not be excluded.
43 Although this single case does not establish a verified benefit the observed overall survival reached a time
44 span of extraordinarily 45 months.

45

46 **Keywords:** Glioblastoma; cannabinoids; terpenes; perillyl alcohol; alpha-bisabolol

47

48 **Introduction**

49 Glioblastoma commonly recurs despite surgery, radiotherapy and temozolomide, and salvage options remain
50 limited. In treated disease, viable tumour, postoperative change, radiation injury, treatment effect, oedema
51 and corticosteroid exposure can produce overlapping clinical and MRI findings, complicating the
52 interpretation of apparent interval improvement or progression [1, 2]. The standard overall survival is
53 approximately 12-16 months [1].

54 Intranasal perillyl alcohol has been evaluated in malignant glioma and glioblastoma, whereas clinical
55 cannabinoid studies remain in early-phase and exploratory. Evidence for alpha-bisabolol in glioma remains
56 preclinical [3–10]. This report describes the longitudinal course of a patient with IDH-wildtype glioblastoma
57 in whom clinician-documented functional improvement and interval MRI improvement occurred during a
58 complex cannabinoid-terpenoid exposure state on an unchanged and fixed dexamethasone dose, followed by
59 a later compartmentally mixed trajectory. Seven dated MRI examinations are illustrated, with conventional
60 and perfusion imaging from November 2023-June 2026. The imaging record is presented descriptively
61 without assigning efficacy to any individual component or claiming formal response.

62 **Materials and Methods**

63 **Case design and ascertainment.** This single-patient case report was prepared from available clinical
64 records, source MRI images and signed clinical radiology reports. Exposure history and contemporaneously
65 documented neurological findings were aligned with seven MRI time points and reviewed descriptively.
66 Interval measurements and clinical classifications were taken from routine radiology reports; no blinded
67 central neuroradiology review, standardised volumetry or formal RANO 2.0 adjudication was performed.
68 Component-specific cannabinoid identities and doses, formulation concentrations, administration-device
69 details, adherence measures and adverse-event surveillance were not prospectively standardised. The
70 imaging dataset was locked at 8 June 2026, approximately 30 months after temozolomide discontinuation.
71 Subsequent vital-status follow-up established that the patient died after an overall survival of 45 months; no
72 later imaging was evaluated. The CARE timeline and exposure-state details are provided in the online
73 supplementary material. The cannabinoids were sourced from CannaMed, and the terpenes were sourced
74 from Sigma-Aldrich.

75 **Results**

76 A 48-year-old man was first imaged in December 2022 with a right temporal cortical lesion. MRI in April
77 2023 showed a large right temporal mass, and surgery on 16 May 2023 established IDH-wildtype
78 glioblastoma. Radiotherapy was administered from 22 June to 2 August 2023 with concomitant
79 temozolomide 160 mg/day, followed by three adjuvant cycles; temozolomide was then discontinued at the
80 patient's request. Conventional and perfusion MRI in November 2023 favoured residual or recurrent tumour,
81 and a second operation was performed on 22 December 2023. MRI in April 2024 and January 2025

documented continuing progression before the reported exposure interval. Molecular findings included CDKN2A/B homozygous deletion, EGFR and MET amplification, chromosome 7 gain/chromosome 10 loss, TERT promoter mutation, IDH1/2 wild-type status and MGMT promoter methylation.

Figure 1: Pre-Surgical MRI Images

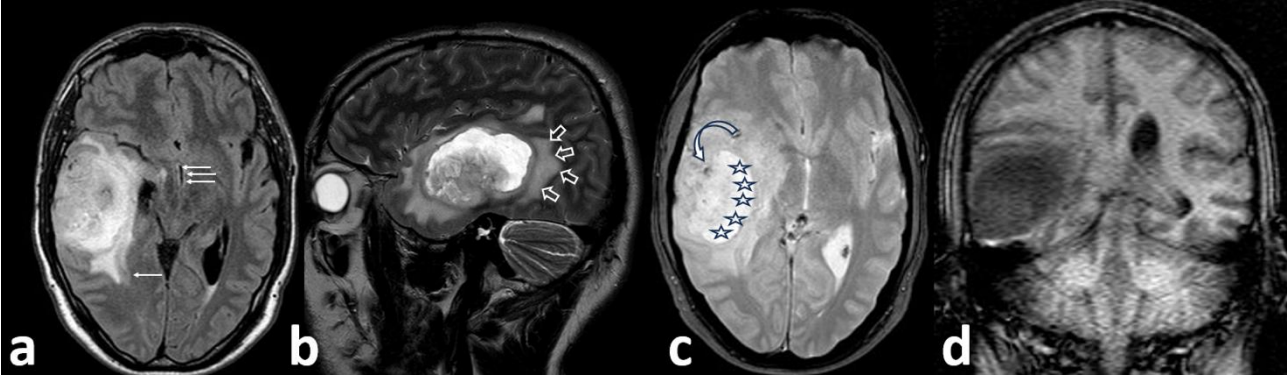


Figure 1: Pre-Surgical MRIs, December 2022. a) FLAIR axial b) T2 Space sagittal images reveal a $6 \times 5 \times 4$ cm expansile, solid mass in the right temporal lobe, with irregular margins and perilesional T2 hyperintense halo (open arrows). Associated mass effect included sulcal obliteration, medialization of the uncus, obliteration of the right basal cisterns, slight left midline shift, and compression of the right lateral and third ventricles (arrows). c) heterogeneous hyperintensity at gradient T2weighted sequence. The minimal area of cystic degeneration within the lesion remained hyperintense (star), while chronic hemorrhage products showed minimal signal loss (curved arrow). d) In this initial examination, no significant enhancement was detected on T1-weighted images.

In April 2025, the patient entered a non-standard exposure state comprising perillyl alcohol approximately 900-1,200 mg/day and alpha-bisabolol approximately 600 mg/day, both administered by intranasal inhalation and initially recorded as 95%-purity preparations, together with individualised cannabinoids administered rectally, sublingually and/or orally in medium-chain triglyceride oil. Dexamethasone remained fixed at 2 mg/day throughout all reported exposure and imaging intervals. At exposure initiation, left hemiplegia and Karnofsky performance status 50 were contemporaneously documented by the treating clinician. During the early interval, improvement to hemiparesis, regained walking and Karnofsky performance status 80 were likewise documented. Mid-2025 MRI showed reduced irregular thickened enhancement around the resection cavity relative to the progressive pre-exposure sequence. The exact dates of the functional transition and mid-2025 MRI were unavailable in the source material. No adverse event attributed to the exposure and requiring discontinuation was identified in the available clinical documentation; adverse-event surveillance was not prospectively standardised.

Figure 2: Post-Surgical MRI Images

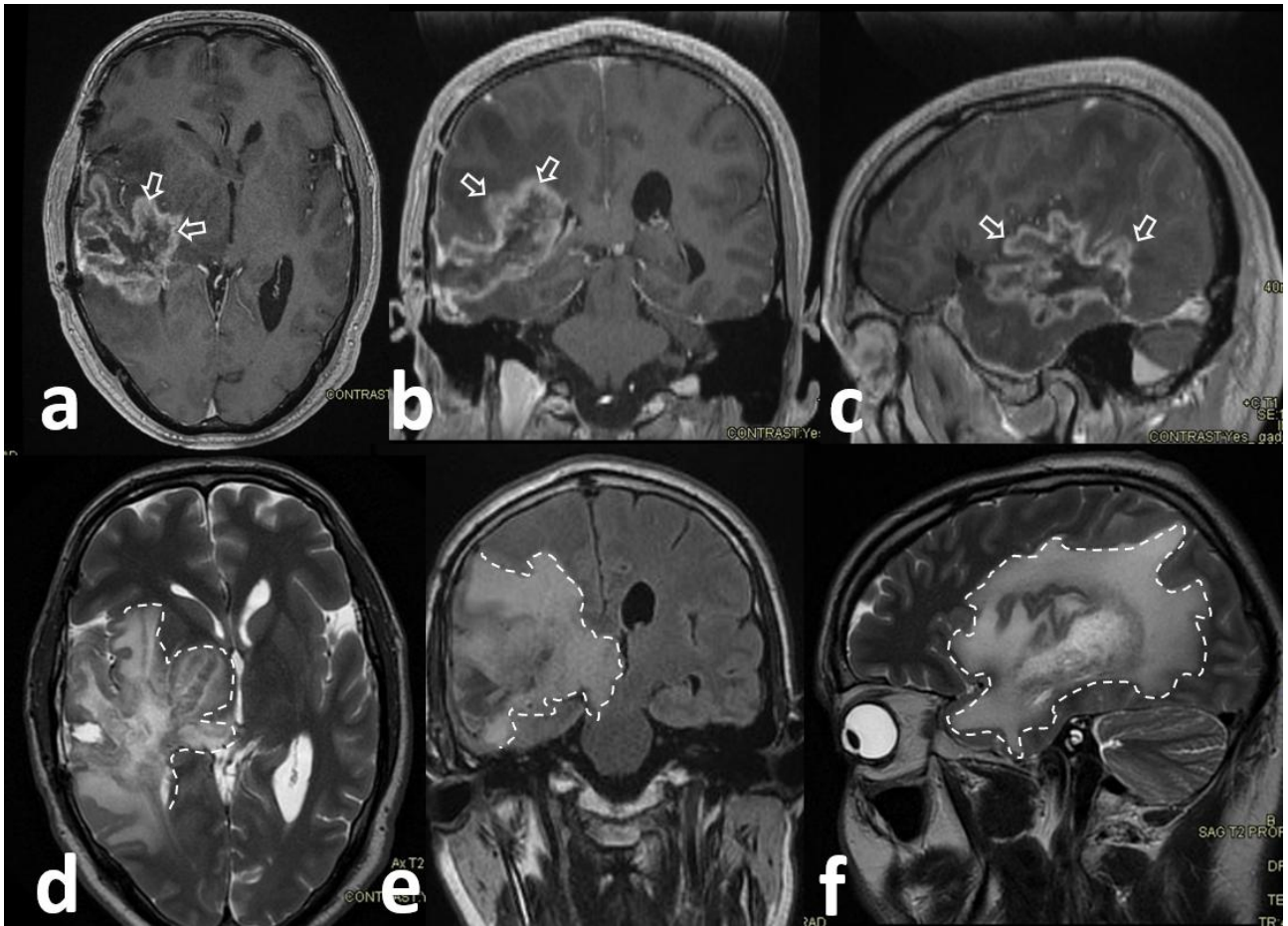


Figure 2: Post-Treatment MRIs, November 2023. a) axial b) coronal c) sagittal T1-weighted, contrast-enhanced slices demonstrate an irregularly enhancing mass surrounding the surgical resection cavity in the right temporal lobe (open arrows). The contrast enhancement appears to extend from the base and periphery of the surgical cavity into the right basal ganglia. The characteristic “ring-like” enhancement pattern suggests aggressive glioblastoma with disrupted blood-brain barrier and neovascularization. d) axial T2W, e) coronal FLAIR and f) sagittal T2W-TSE images show a large hyperintense area in the right temporal lobe. This area shows the extent of perilesional edema as well as the result of the infiltrative nature of the tumor (dashed lines).

Intranasal perillyl alcohol and alpha-bisabolol were reportedly interrupted due to restricted commercial access to terpenes from approximately September 2025 to April 2026, while cannabinoids in medium-chain triglyceride oil continued and docosahexaenoic acid 2,000 mg/day was used. Perillyl alcohol, which was 95% pure, was no longer accessible and has subsequently been reintroduced at approximately 90% purity, along with alpha-bisabolol at 98% purity. Dexamethasone remained fixed at 2 mg/day.

Figure 3: Post-Surgical Perfusion MRI Images

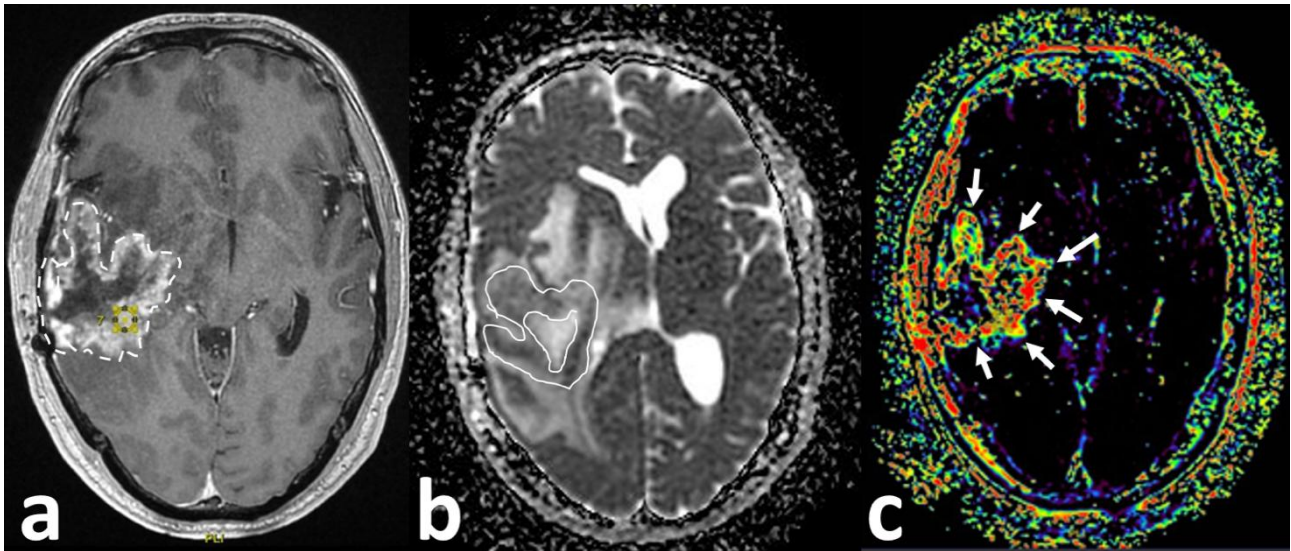
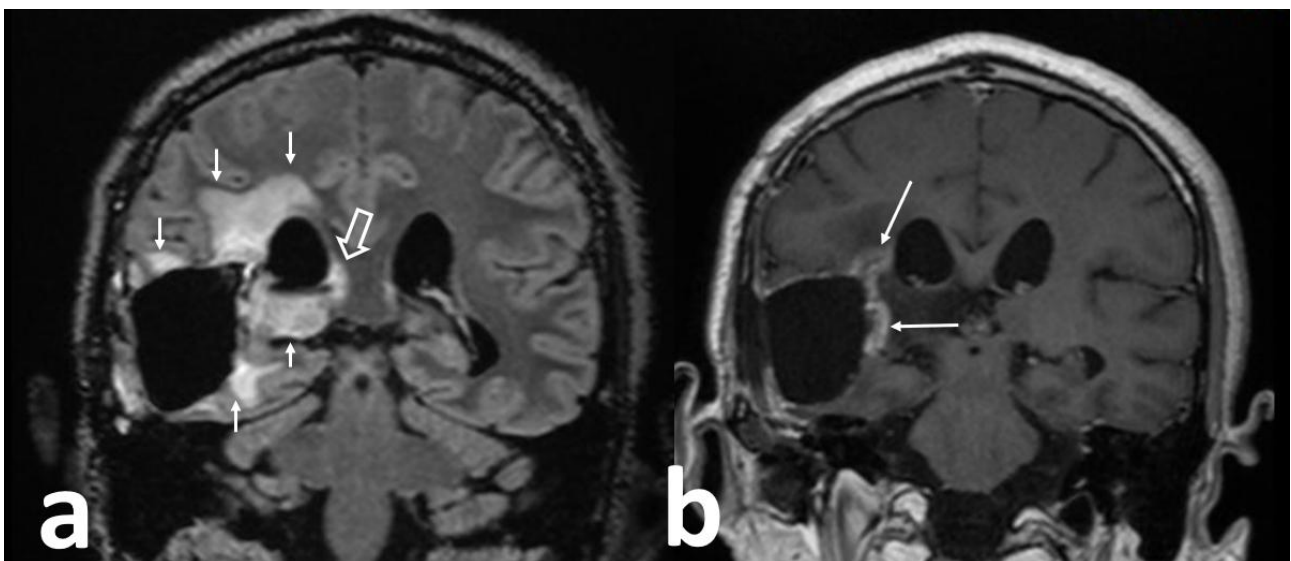


Figure 3: Post-Treatment, conventional and perfusion MRIs. November 2023, a) On the axial postcontrast T-section (dashed lines), irregularly contoured enhancements persisted; b) on the diffusion section ADC map, the area of these interrupted lines restricted diffusion in the form of a thick rim (between the white lines). and c) unlike radiation necrosis, these changes on the T2 perfusion scan rCBF map show increased perfusion in the form of an irregular thick rim (arrows). They show increased perfusion in the form of an irregular rim (compatible with residual + recurrent tumoral infiltrative component).

MRI on 10 February 2026 showed an unchanged approximately 4.5-cm postoperative cavity and similarly extensive leukoencephalopathy and mild oedema, but increased pathological enhancement beneath the right lateral ventricle, new predominantly meningeal infratentorial enhancement and a 1-cm right peduncular intra-axial lesion with restricted diffusion. Perfusion imaging was technically unsuccessful and therefore non-interpretable.

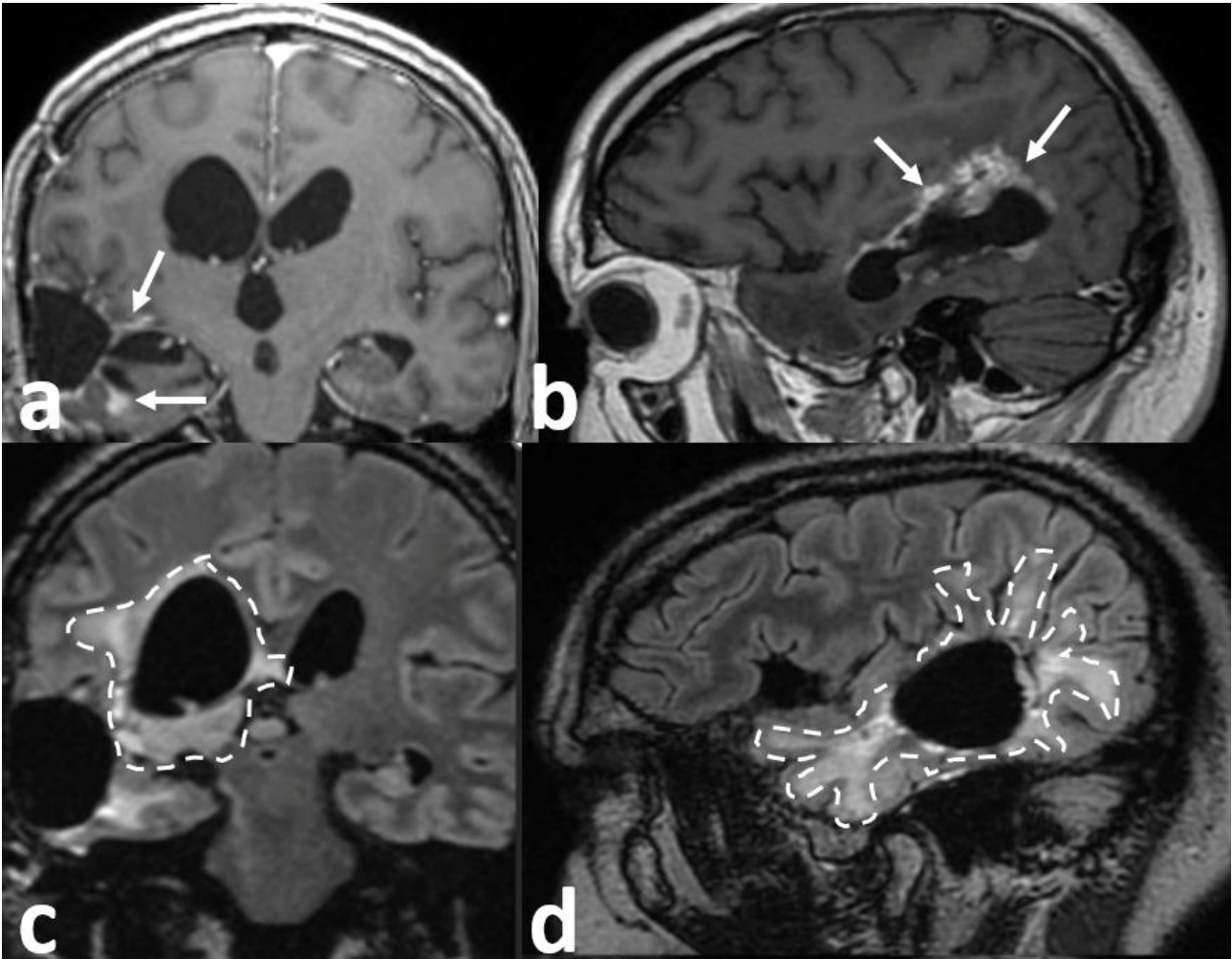
Figure 4: Second-Recurrence MRI in 2024



142 **Figure 4:** Progression in 2024 (April) follow-up MRIs. a) New, prominent hyperintense signals were observed on
143 FLAIR sequences around the previous resection cavity and in the medial temporal lobe and right diencephalon (short
144 arrows). Furthermore, the hyperintense FLAIR signal changes, extending to the corpus callosum and, via this pathway,
145 to the contralateral hemisphere (open arrow). b) The persistence of enhancement (long arrows), together with
146 progression of the non-enhancing component, supports continued tumoral infiltration.

148 On 8 June 2026, the postoperative cavity and extent of the surrounding T2/FLAIR abnormality remained
149 without major change. However, medial enhancement along the postoperative cavity had increased to
150 approximately 36 mm from 27 mm, and a smaller distal focus was slightly larger. The right cerebellar
151 enhancing focus had increased to 14 mm from 10 mm, and a new contralateral 13-mm cerebellar focus had
152 appeared. Dynamic contrast-enhanced perfusion curves within sampled supratentorial and infratentorial
153 enhancing regions were low-amplitude and showed no pathological hyperperfusion. The clinical radiology
154 report considered radiation necrosis possible for the supratentorial change while concluding that further
155 infratentorial progression had occurred.

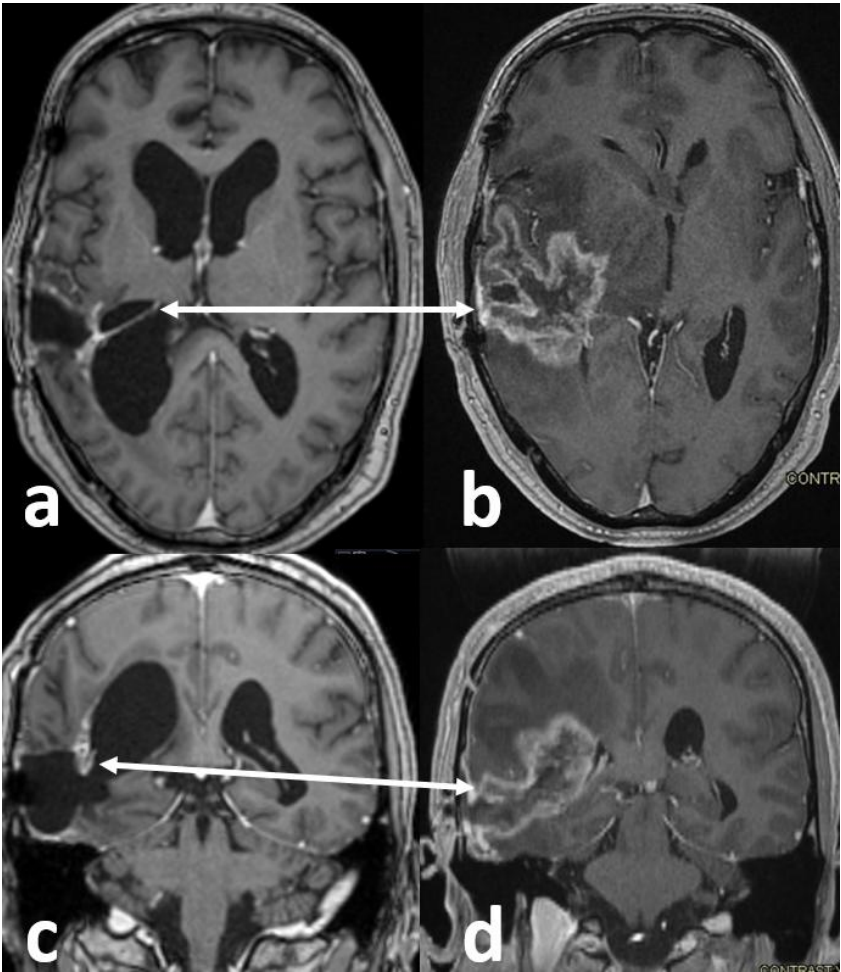
156
157 **Figure 5: Third-Recurrence MRI Images**



159 **Figure 5:** Control MRI examination, January 2025. In a) axial and b) sagittal postcontrast T1w sections, it is seen that
160 the enhancement rim persists (arrows) and in c) axial and d) sagittal FLAIR images, hyperintense perilesional signals
161 extending beyond the enhancement rim are seen to progress.
162

163 The patient reported regaining walking during the early exposure interval. This account corroborated, but did
164 not replace, the treating clinician's contemporaneous documentation of improvement from
165 hemiplegia/Karnofsky performance status 50 to hemiparesis/Karnofsky performance status 80.

166 **Figure 6: Post Treatment-Response MRI Images**



167
168 **Figure 6:** Latest MRI examination, June 2025. Compared with the initial images: a) axial contrast-enhanced T1w
169 image, June 2025 b) axial contrast- enhanced T1w image, Nov 2023, c) coronal contrast-enhanced T1w image, June
170 2025 d) coronal contrast-enhanced T1w image, Nov 2023. Compared with the previous images, the prominent, irregular
171 thickened contrast enhancements surrounding the resection cavity have decreased significantly (curved arrows).
172

173 **Discussion**

174 The most notable observation finding was the temporal concurrence of functional improvement and
175 decreased contrast enhancement following a documented course of progressive recurrent course. The seven-

176 time-point longitudinal imaging record is important because it establishes the original tumour burden,
177 postoperative residual/recurrent disease, continued pre-exposure progression, the immediate January 2025
178 baseline, the mid-2025 interval improvement and the later February-to-June 2026 mixed trajectory. Because
179 the dexamethasone remained fixed at 2 mg/day, the observed improvement cannot be temporally attributed
180 to a change in corticosteroid dosing. Chronic corticosteroid exposure nevertheless remained a co-exposure
181 that could influence neurological status, oedema and enhancement, and the treating clinician's assessments
182 were not independently blinded.

183 The February-to-June transition was discordant across imaging domains. Enhancement increased along the
184 right temporal postoperative margin and in the cerebellum, including a new contralateral focus, whereas the
185 postoperative cavity and surrounding FLAIR extent remained substantially stable and June dynamic contrast-
186 enhanced lesion curves were low-amplitude without pathological hyperperfusion. Dynamic contrast-
187 enhanced perfusion can contribute to differentiating recurrent tumour from radiation necrosis, but it does not
188 provide definitive lesion-level adjudication [11, 12]. The observed pattern makes treatment effect or
189 radiation necrosis plausible for at least part of the supratentorial enhancement, but it neither establishes pure
190 radiation necrosis nor excludes viable tumour within a mixed lesion. The technically unsuccessful and
191 therefore non-interpretable February perfusion study prevents serial perfusion comparison, and the
192 infratentorial foci cannot be assumed to share the same biology as the supratentorial postoperative bed.

193 Clinical evidence for intranasal perillyl alcohol remains limited. Early phase I/II experience and longer-term
194 observational follow-up reported feasibility and possible activity in recurrent malignant glioma [3, 5-7]. That
195 case differs materially from the present IDH-wildtype glioblastoma observation, which involved multiple
196 components, changing formulation and purity states, treatment interruption, continued cannabinoid exposure
197 and a later mixed trajectory.

198 The exposure state also included alpha-bisabolol administered by intranasal inhalation, a sesquiterpene
199 alcohol with preclinical activity in glioma models. In cultured human and rat glioma cells, alpha-bisabolol
200 induced dose-dependent apoptosis and showed lower cytotoxicity towards non-neoplastic glial cells [10].
201 These data are experimental and do not establish clinical efficacy, effective intranasal delivery or an
202 appropriate dose in glioblastoma. The present case therefore should not attribute the observed course to
203 alpha-bisabolol, its intranasal route or any individual component of the multimodal exposure state.

204 Cannabinoid evidence is preliminary. Intratumoural tetrahydrocannabinol was feasible in a small phase I
205 pilot [8], and a randomised phase Ib study of nabiximols with temozolomide supported further investigation
206 [9]. These studies provide clinical context, not a basis for attributing the present course to the individualised
207 cannabinoid preparations or to interaction with the terpenoids.

208 This report is limited by its single-patient design, multi-component and changing exposure architecture,
209 absence of a clean withdrawal period, and incomplete prospective standardisation of component-specific
210 cannabinoid identities and doses, formulation concentrations, administration-device details, adherence,

211 rehabilitation intensity, concomitant medication changes and adverse-event surveillance. Exact dates of the
212 Karnofsky performance status 50-to-80 transition and standardised motor grades were not available in the
213 material used for this report. Imaging limitations include the lack of blinded central neuroradiology review or
214 formal RANO 2.0 assessment, absence of standardised volumetry, reliance on routine clinical reports for
215 interval measurements, and a technically unsuccessful and therefore non-interpretable February 2026
216 perfusion study. Source images were reviewed descriptively rather than through an independent adjudication
217 pathway. The mid-2025 change should therefore be described as interval radiological improvement, not
218 formal response or tumour regression; similarly, low-amplitude June perfusion without pathological
219 hyperperfusion supports but does not establish radiation necrosis. The case documents an unexpected event
220 on a stable corticosteroid background, followed by a mixed later state; it does not establish causality,
221 component-specific efficacy or a receptor-level mechanism. Future reports should prospectively lock
222 formulation provenance, component doses, exposure continuity, administration devices, adherence,
223 corticosteroid dose, concomitant interventions, clinical scales, MRI timing, adverse-event ascertainment and
224 independent radiological adjudication.

225 **Limitations**

226 The restriction on commercial terpene access interrupted intranasal perillyl alcohol and alpha-bisabolol from
227 about September 2025 to April 2026, altering the treatment modality's course and underlying rationale.

228 **Conclusions**

229 This uncontrolled case documents an unexpected functional and radiological event on a stable corticosteroid
230 background, followed by an anatomically progressive but perfusion-discordant mixed trajectory. It may
231 indicate an establish treatment causality, component-specific efficacy, formal response and possibly a
232 uniform viable-tumour progression. Although survival in glioblastoma is heterogeneous and influenced by
233 multiple clinical and molecular factors, including MGMT promoter methylation, repeated surgery and
234 radiotherapy, the patient's observed overall survival of 45 months after early discontinuation of adjuvant
235 temozolomide is clinically noteworthy.

236

237 **Statements**

238 **Statement of Ethics**

239 Written informed consent was obtained from the patient for publication of this case report and accompanying
240 images.

241 **Conflict of Interest Statement**

242 Neither author had a financial, ownership, patent, consulting or supply relationship with the manufacturers or
243 vendors of the products described.

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245 This study received no external funding.

246 **Author Contributions**

247 EY treated the patient and EH contributed clinical care, conceptualisation, investigation, data curation,
248 interpretation, drafting, revision, and guarantor responsibility. GA, OM, HUB, BK, CEM, MA, UMY, AA,
249 and DY contributed investigation, exposure-record verification, validation and manuscript review. All
250 authors approved the final manuscript.

251 **Data Availability Statement**

252 De-identified representative MRI images and longitudinal annotations are included in the article and online
253 supplementary material. Full DICOM studies, signed radiology reports, source clinical records, formulation
254 records and consent documentation are not publicly available because of patient privacy. The imaging data
255 set was locked at 8 June 2026, the latest MRI included in this report. Subsequent vital-status follow-up
256 documented death after an overall survival of 45 months; no later imaging outcomes are evaluated here.
257 Additional de-identified material may be considered by the corresponding author on reasonable request,
258 subject to consent and institutional privacy restrictions.

259

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