




Severe Unilateral Alopecia in a Long-Term Surviving Male Adolescent Glioblastoma Multiforme Patient

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Background: Radiation-induced alopecia (RIA) typically presents as transiently or persistently non-scarring alopecia with a distinct geometric pattern, and minoxidil sometimes serves as an effective therapeutic agent. However, there have been no reported cases of severe unilateral alopecia following radiotherapy for pediatric glioblastoma multiforme (p-GBM), that was unresponsive to minoxidil treatment.

Case Report: This case presents a 17-year-old male with severe unilateral alopecia, who was diagnosed with glioblastoma multiforme (GBM) and consequently received radiochemotherapy. Remarkably, he has survived beyond three years without evidence of tumor recurrence, but with the sole persistent issue being the left-sided alopecia. Despite intensive therapeutic interventions comprising 12 months of topical 5% minoxidil therapy (twice daily) combined with three courses of platelet-rich plasma (PRP) injections administered at 4-week intervals, the alopecic area showed no significant improvement and eventually progressed to permanent alopecia.

Conclusion: The prevention and treatment of RIA remain poorly understood, and this clinical scenario urgently necessitates the exploration of novel therapeutic strategies.

Keywords: glioblastoma multiforme (GBM), pediatric glioblastoma multiforme (p-GBM), alopecia, chemoradiotherapy alopecia, severe unilateral alopecia

Introduction

Glioblastoma (GBM) is one of the most aggressive primary brain cancer. The prognosis for GBM patients remains dismal, with a 5-year overall relative survival rate of merely 4–5% - the poorest among all solid malignancies.¹ Furthermore, pediatric glioblastoma multiforme (p-GBM) cases demonstrate particularly grim outcomes, showing a median survival of just 10.5 months.² The standard treatment for GBM involves a surgical resection followed by radiation therapy and chemotherapeutic temozolomide (TMZ).³ Alopecia is a common side effect of radiotherapy and chemotherapy.⁴ Notably, approximately 20% of RIA cases are associated with GBM.⁵ Alopecia is frequently cited as one of the most distressing adverse events of cancer therapy including chemotherapy and radiotherapy, which commonly lead to psychological distress in cancer survivors, with the impact being especially pronounced in pediatric populations.^{6,7} Chemotherapy-induced alopecia (CIA) is a frequent issue among cancer patients, often resulting in total or diffuse alopecia.^{8–11} RIA occurs less frequently than CIA, typically presenting as transiently non-scarring alopecia, often with a distinct geometric pattern within the radiation field.¹² In most cases, this is a transient state in which full hair eventually regrows within 2 to 4 months,^{7,12} but persistent radiation-induced alopecia (pRIA), defined as the presence of incomplete hair regrowth more than 6 months after cessation of radiotherapy sometimes occurs.^{13–15} It has been reported that topical 5% minoxidil applied twice daily is effective in 82% of patients with pRIA.⁷ Meanwhile, PRP counteracts radiotherapy-induced alopecia through multipathway mechanisms, with stem cell integration synergistically boosting efficacy,

demonstrating clinical translation viability.¹⁶ This case presents a rare instance of p-GBM patient with permanently unilateral alopecia following radiotherapy that was unresponsive to combined minoxidil and PRP therapy.

Case Report

A 17-year-old male presented to our outpatient clinic with hair loss located in the left temporal lobe and upper occipital region, who was diagnosed with WHO Grade IV GBM (located in the left parieto-occipital lobe, left basal ganglia, left thalamus, and splenium of the corpus callosum) at the age of 14. The patient underwent treatment with the Stupp protocol: craniotomy with resection of the supratentorial lesion, followed by TMZ (100mg/d×42d) with intensity-modulated radiotherapy (IMRT) after 3 months (GTVnb D95 64.1Gy/30fx), then maintenance TMZ (cycles 2–6: 250mg/d×5/28d; cycles 7–12: 300mg/d×5/28d). Two weeks after the end of radiotherapy, the patient suffered diffuse hair loss within the irradiated field. Six months after chemotherapy completed, the patient came to our outpatient department for consultation because the hair on the left scalp did not recover. Examination revealed that the alopecic area was primarily confined to the surgical region and the upper left temporal and occipital lobes, with particularly notable hair loss at the rear of the left temporal lobe, presenting as unilateral alopecia. As shown in Figure 1. Dermoscopic examination shows: vellus hair depletion, dystrophic hair shafts (tapered terminal hairs and pigtail hairs), obliteration of follicular ostia, and aberrant arborizing telangiectasia (Figure 2). Pathological results indicated a reduction in hair follicle count, upward displacement of some follicles, atrophy of hair follicles, and disappearance of hair shafts (Figure 3). An extensive hematological evaluation, including trace elements, vitamin D2 and D3, anti-thyroid peroxidase antibodies, sex hormone profiles, complete blood count, and liver/renal function tests, revealed no significant abnormalities. The patient used 5% minoxidil lotion twice daily for 1 year with minimal improvement. Subsequent adjuvant treatment with platelet-rich plasma injections every 4 weeks for 3 sessions also provided no benefit. Hair transplantation was suggested, but he refused. A timeline with relevant data from the treatment is shown in Figure 4. Besides, the patient maintained adequate nutrition with age-appropriate development, preserved hair density in non-irradiated areas (axillary, pubic, facial), and no family history of hereditary hair disorders.

Discussion

Research has shown that over 75% of patients undergoing cranial radiotherapy (CRT) will experience significant scalp alopecia when the single radiation dose exceeds 2 Gy.⁷ The underlying mechanism involves the apoptosis of actively dividing stromal cells within the hair bulb induced by radiotherapy, which disrupts the anagen phase of the hair growth cycle, leading to damage of the hair follicle (HF) and epithelial hair follicle stem cells (eHFSCs). Additionally,



Figure 1 Clinical presentation of a 17-year-old patient, showing areas of hair loss with some coarse and thick hairs remaining, mainly in the left temporal lobe and upper occipital region.



Figure 2 Dermoscopic findings of the patient's skin.

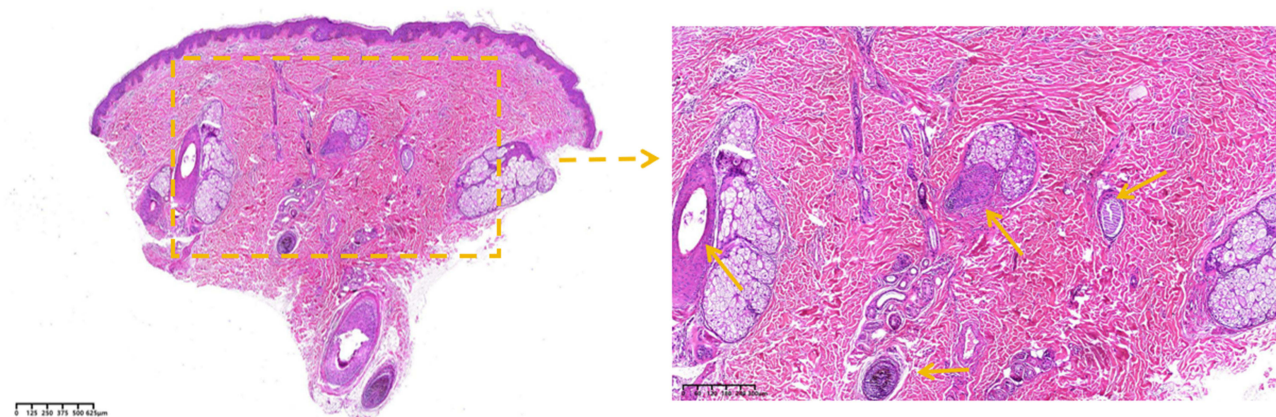


Figure 3 Histopathological HE staining findings from the patient's biopsy.



Figure 4 A timeline with relevant data from the treatment. This figure was created using BioRender.com.

radiotherapy causes DNA damage and accumulates oxidative stress, ultimately resulting in cellular dysfunction and senescence of the hair follicle.^{12,17} The distribution of alopecia is associated with age, type of cancer, and the area of radiotherapy, clinically presenting as non-scarring alopecia, and hair generally regrows within 2 to 4 months.^{7,12} It is reported that pRIA affects approximately 60% of CRT recipients and has a more enduring impact on psychosocial functioning and quality of life.^{13–15} Risk factors for pRIA include the quality of the radiation beam, dose fractionation, cumulative dose, and concomitant treatments.^{7,18} Studies have shown that high-dose radiation therapy (single dose exceeding 2 Gy, total dose exceeding 36 Gy) may lead to permanent alopecia in patients.^{7,19} In our case, the patient received a total radiation dose of 64.1 Gy, which may be the primary cause resulting in the permanent alopecia.

On the other hand, chemotherapeutic agents are cytotoxic and can destroy highly proliferative cells, such as those in the matrix of hair follicles during the initial growth phase, leading to a sudden interruption of mitotic activity and weakening of the hair shaft.^{20,21} The patient in this case received chemotherapy continuously for one year, causing significant damage to the hair follicles, which could be suggested as a contributing factor to the persistent alopecia in the radiation area. Additionally, the GBM of this case was located in the left parieto-occipital-temporal lobe, left basal ganglia, left thalamus, and splenium of the corpus callosum, with extensive vascular damage during surgery, leading to subsequent impediment of hair regrowth. Surgery may damage some capillaries in the surgical area, affecting the nutrient supply to the surrounding hair follicles.²²

Currently, the treatment of RIA primarily includes pharmacological, surgical, and adjuvant therapies. In pharmacological treatment, topical 5% minoxidil solution (applied twice daily) promotes angiogenesis and prolongs the anagen phase by upregulating vascular endothelial growth factor expression and activating prostaglandin-endoperoxide synthase 1.^{7,14} It was reported that topical minoxidil, 5%, solution twice daily produces a subjective response in 82% of cancer survivors with pRIA.⁷ 12-O-tetradecanoylphorbol-13-acetate (TPA) facilitates the re-entry of hair follicles into the anagen phase through activation of the AKT/WNT pathway.²³ Surgical treatment mainly involves hair transplantation, with the impact of radiation dermatitis on transplantation success rates requiring assessment.²⁴ Adjuvant therapies include low-level laser therapy (LLLT, promoting hair follicle metabolism and growth)²⁵ and PRP (enhancing hair follicle repair and regeneration through growth factors).²⁶ However, the patient in this case had been treated with minoxidil twice a day for one year and subsequently with PRP three times, but did not benefit at the end. Hair transplantation was suggested for him, but he declined. Overall, it indicated the urgent necessity of exploring novel therapeutic strategies.

Due to the limitation of the treatment options for pRIA, more and more attention is now focused on its prevention which include two key strategies: reducing follicular radiation exposure and enhancing radiation tolerance. Dose control employs precise calculation and personalized planning, utilizing SRT, conformal blocks, and MLC to minimize non-target doses, while optimizing fixation devices and positioning techniques to control skin dose.^{27,28} Significant progress has been made in radioprotectant development: First-generation agents like Tempol exert antioxidant effects through free radical scavenging.²⁹ Second-generation agents include: ① cell cycle regulators (PGE2 and CDK4/6 inhibitors) that reduce radiation sensitivity via G1 phase arrest;^{30,31} ② PPAR γ agonists (eg, rosiglitazone); and ③ neuroendocrine regulators (melatonin, adrenaline). These agents synergistically protect hair follicles through multiple mechanisms such as promoting angiogenesis, prolonging anagen, activating AKT/WNT, enhancing growth via LLLT, improving repair with PRP, reducing radiation sensitivity, and exerting antioxidants. However, in clinical practice, the prevention of hair loss after radiotherapy has not been paid much attention. This may be due to patients' greater focus on the prognosis of their tumor disease during radiation therapy, overlooking the cosmetic concern of alopecia and thus missing the optimal treatment window. Current research on RIA is constrained by small sample sizes, variable treatment sensitivity, technical barriers, and inadequate attention to psychosocial-biological interactions and the psychological impact of alopecia on adolescents.³² Future studies should emphasize multi-center collaboration (families, schools, hospitals) and interdisciplinary partnerships to establish standardized protocols and strengthen psychological support systems.

Conclusions

This case presented a patient with rare and severe unilateral alopecia, who had been diagnosed with p-GBM and received a long-time survival for three years following treatment of chemoradiotherapy. Although conventional therapies such as minoxidil and PRP have demonstrated certain clinical efficacy for the alopecia induced by both chemotherapy and radiation,

this case of treatment failure poses significant challenges to the management of pRIA. It hints that multidisciplinary treatment approaches and early preventive protection strategies should be urgently emerging as new research directions for the future.

Informed Consent

Patient consented in writing for the publication of his case/photographs both online and in-print and understood that it will be publicly available and was sent a copy of the article to read. And this case report has been approved by the Clinical Trial Ethics Committee of the Affiliated Hospital of Southwest Medical University, with the approval number:KY2024415.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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