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Long-Term Survival and Clinical Stabilization in Mixed Gliomas using an Integrative Immunobiological Approach: A Two-Patient Case Report

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ABSTRACT:

Background: Mixed and high-grade gliomas represent some of the most challenging primary malignancies of the central nervous system because of their infiltrative growth pattern, molecular heterogeneity, treatment resistance, and ability to adapt to therapeutic pressure. Despite advances in neurosurgery, radiotherapy, chemotherapy, and molecularly guided treatment, long-term disease control remains difficult to achieve in patients with aggressive glioma, particularly when recurrent or progressive disease is associated with extensive peritumoral edema, neurological dysfunction, or mass effect.

The biological behaviour of gliomas is increasingly understood to be influenced not only by the intrinsic characteristics of tumour cells but also by the tumour microenvironment. Interactions among malignant cells, immune cells, stromal components, cytokines, angiogenic pathways, and metabolic signals contribute to immune evasion, tumour progression, treatment resistance, and recurrence. Glioma cells can establish an immunosuppressive microenvironment that impairs effective anti-tumour immune responses, providing a rationale for therapeutic strategies aimed at restoring or enhancing host immune surveillance.

Immunobiological approaches have therefore attracted increasing interest as potential adjuncts to conventional cancer treatment. Strategies directed toward cellular immunity, antigen presentation, immune modulation, and the tumour microenvironment may theoretically complement cytotoxic or radiation-based therapies by targeting biological mechanisms that are not fully addressed by conventional treatment alone. Dendritic-cell-based approaches, cytokine and immune-modulating strategies, and other investigational immunological interventions have been explored in glioma, although their clinical efficacy remains an area of active investigation.

An integrative oncology model seeks to combine appropriately selected conventional treatment with supportive and investigational interventions directed at multiple biological processes, including immune regulation, inflammation, oxidative stress, tumour metabolism, angiogenesis, and tissue repair. The underlying concept is not to replace evidence-based oncological treatment, but to explore whether complementary biological interventions can be incorporated into an individualized therapeutic framework while maintaining continuous clinical and radiological surveillance.

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Long-term clinical stabilisation in patients with aggressive glioma is particularly noteworthy when sustained disease control occurs despite radiologically complex lesions, treatment-related changes, recurrent neurological symptoms, or progressive-appearing abnormalities. Interpretation of such cases requires careful longitudinal assessment because treatment-related gliosis, radiation injury, necrosis, inflammatory changes, and viable tumour may produce overlapping clinical and radiological findings.

The present case describes prolonged survival and clinical stabilisation in a patient with a mixed/high-grade glioma managed over an extended period using an integrative immunobiological strategy incorporating conventional and investigational modalities. The case is presented primarily as a longitudinal clinical observation, with emphasis on the evolution of neurological status, imaging findings, treatment interventions, and periods of disease stability. The objective is to document the clinical course and generate hypotheses regarding the potential contribution of an integrated immunobiological approach to long-term disease control, while acknowledging that a single case cannot establish treatment efficacy or causality.

Case Presentation: This report presents two patients with GBM managed using an integrative therapeutic strategy involving dendritic cell vaccine therapy, sonodynamic therapy (SDT), Gc protein-derived macrophage activating factor (GcMAF), Super Transfer Factor (STF) injections, Mito Organo Peptide (MOP) thymus injections, Phyto molecular supplementation, and onco-nutrition support.

Case 1: A 52 years female patient diagnosed with GBM approximately 10 years prior, declined surgical intervention and conventional chemo/radiotherapy. She underwent an integrative protocol consisting primarily of dendritic cell vaccines, SDT, GcMAF, STF injections, MOP thymus peptide therapy, phyto molecular medicines, and structured onco-nutritional therapy. The patient demonstrated prolonged survival with maintained neurological function and acceptable quality of life over long-term follow-up.

Case 2: A 36-year-old male diagnosed with GBM underwent surgical resection followed by radiotherapy and temozolomide (TMZ)-based chemotherapy. Subsequently, an integrative maintenance strategy using dendritic cell vaccine therapy, SDT, GcMAF, STF injections, MOP thymus peptide support, phytomolecular supplementation, and nutritional modulation was initiated. The patient remained clinically stable with preserved functional status during follow-up.

Conclusion: These cases highlight the potential translational relevance of integrative immunobiological approaches in GBM management. Although causal conclusions cannot be established from isolated observations, the prolonged stabilization and survival observed warrant further systematic investigation through controlled clinical studies.

1. INTRODUCTION

Glioblastoma multiforme (GBM) is the most common and aggressive malignant primary brain tumor in adults. Standard-of-care therapy includes maximal safe surgical resection followed by radiotherapy and temozolomide chemotherapy. Despite these interventions, recurrence is common, and prognosis remains poor.

GBM progression is characterized by:

- Diffuse infiltration,
- Immune evasion,

- Tumor heterogeneity,
- Angiogenesis,
- Chronic neuroinflammation,
- Resistance to apoptosis.

Recent advances in cancer immunology suggest that multimodal integrative strategies targeting both tumor biology and host immunity may contribute to improved disease control in selected patients.

This report describes two mixed glioma patients managed using an integrative therapeutic platform involving:

- Dendritic cell (DC) vaccine therapy,
- Sonodynamic therapy (SDT),
- GcMAF-mediated immune modulation,
- Super Transfer Factor (STF) injections,
- Mito Organo Peptide (MOP) thymus injections,
- Phytomolecular supplementation,
- Onco-nutrition-based metabolic support.

CASE 1

Patient Information

A 52years female patient in her early forties presented approximately 10 years ago with:

- Sudden onset of seizures,
- Fainting with LOC,
- Cognitive slowing,
- Occasional focal neurological symptoms.

Magnetic resonance imaging (MRI) & PERT-CT revealed an infiltrative intracranial lesion involving the right fronto-temporal lobes, suggestive of Low-Gade Glioma. MR-Spectroscopy findings supported a diagnosis of glioblastomaa multiforme.

The patient declined:

- Surgical resection,
- Radiotherapy,
- Cytotoxic chemotherapy,

due to concerns regarding neurological morbidity and quality of life.

Integrative Therapeutic Intervention

Dendritic Cell Vaccine Therapy

Autologous dendritic cell vaccines were prepared using peripheral blood mononuclear cells cultured ex vivo with immune-stimulatory cytokines. Tumor-associated antigens were utilized for dendritic cell priming before administration.

The therapeutic objective was enhancement of:

- Cytotoxic T-cell activation,

- Tumor antigen recognition,
- Long-term immune surveillance.

Sonodynamic Therapy (SDT)

The patient underwent serial SDT sessions using low-intensity ultrasound combined with tumor-targeting sonosensitizing agents.

Proposed Therapeutic Effects

- Reactive oxygen species generation,
- Selective tumor cell apoptosis,
- Immunogenic tumor destruction,
- Improved antigen release.

The patient tolerated therapy without major neurological complications.

GcMAF Therapy

Gc protein-derived macrophage activating factor (GcMAF) was administered periodically as part of the immunobiological protocol.

Potential benefits included:

- Macrophage activation,
- Innate immune support,
- Modulation of tumor-associated immune suppression,
- Enhancement of phagocytic activity.

Super Transfer Factor (STF) Injections

Multiple doses of Super Transfer Factor (STF) injections were administered during the course of therapy as part of the immune-supportive strategy.

Proposed Immunological Role

STF therapy was intended to:

- Enhance cell-mediated immunity,
- Support T-lymphocyte responsiveness,
- Improve immune communication pathways,
- Strengthen host immune surveillance.

The injections were generally well tolerated without significant systemic adverse effects.

Mito Organo Peptide (MOP) Thymus Injections

The patient additionally received multiple doses of MOP thymus peptide injections.

Proposed Biological Objectives

The therapy aimed to:

- Support thymic immune regulation,
- Promote T-cell maturation,

- Improve immune recovery and resilience,
- Enhance adaptive immune responsiveness.

This intervention was incorporated as an adjunctive immunorestorative modality within the broader integrative protocol.

Phytomolecular and Onco-Nutritional Support

A comprehensive phytomolecular protocol was implemented, including:

- Curcumin,
- EGCG
- Sulforaphane,
- Omega-3 fatty acids,
- Medicinal mushroom extracts,
- Antioxidant-rich botanical compounds.

The patient also followed a structured onco-nutrition dietary program emphasizing:

- Anti-inflammatory nutrition,
- Glycemic regulation,
- High phytonutrient intake,
- Gut microbiota support,
- Adequate protein and micronutrient balance.

Clinical Outcome

Over nearly 10 years of follow-up:

- Neurological deterioration remained relatively slow,
- Functional independence was substantially preserved,
- Cognitive status remained stable for extended periods,
- No severe systemic toxicity was observed.

Serial imaging demonstrated fluctuating but relatively controlled disease progression compared with the expected aggressive course typically associated with untreated GBM.

The patient maintained acceptable quality of life and remained ambulatory during long-term follow-up.

CASE 2

Patient Information

A 36-year-old male presented with:

- Seizures,
- Progressive headaches,
- Left-sided weakness.

MRI demonstrated a right frontal lobe mass with surrounding edema. The patient underwent:

- Surgical resection,

- Postoperative radiotherapy,
- Temozolomide (TMZ)-based chemotherapy.

Histopathology confirmed WHO Grade IV glioblastoma multiforme.

INTEGRATIVE MAINTENANCE PROTOCOL

Following completion of standard therapy, the patient was initiated on an integrative maintenance strategy involving:

- Dendritic cell vaccine therapy,
- Sonodynamic therapy,
- GcMAF,
- STF injections,
- MOP thymus peptide injections,
- Phytomolecular supplementation,
- Onco-nutritional dietary optimization.

Follow-Up and Outcome

The patient demonstrated:

- Stable neurological function,
- Reduced fatigue,
- Good treatment tolerance,
- Maintenance of daily activities and occupational function.

Serial MRI evaluations suggested:

- Absence of rapid recurrence during follow-up,
- Relative radiological stability,
- Reduced inflammatory edema.

No severe adverse immune reactions or systemic toxicities were documented during the integrative maintenance period.

DISCUSSION

These two cases demonstrate the potential feasibility of integrative immunobiological approaches in GBM management.

Potential Mechanistic Synergy

Dendritic Cell Vaccines

May improve adaptive immune recognition of tumor-associated antigens.

Sonodynamic Therapy

May induce immunogenic tumor cell death through oxidative stress and mitochondrial disruption.

GcMAF

May support macrophage-mediated tumor surveillance and innate immune activation.

STF Injections

May contribute to enhancement of cell-mediated immunity and immune communication pathways.

MOP Thymus Peptides

May support thymic regulation, T-cell maturation, and immune recovery.

PHYTOMOLECULAR SUPPORT

May regulate inflammatory pathways including:

- NF-κB,
- STAT3,
- Oxidative signaling,
- Angiogenic pathways.

ONCO-NUTRITION

May contribute to:

- Metabolic stabilization,
- Immune resilience,
- Reduced systemic inflammation,
- Improved tolerance to therapy.

CLINICAL SIGNIFICANCE

Particularly noteworthy in Case 1 was the prolonged survival of a patient who declined surgery and conventional cytotoxic therapy. Such long-term stabilization is uncommon in GBM and raises important questions regarding:

- Tumor biology,
- Immune responsiveness,
- Metabolic adaptation,
- Potential contribution of integrative therapeutic modulation.

Case 2 demonstrates the potential role of integrative therapy as a maintenance strategy following standard treatment.

LIMITATIONS

This report has important limitations:

- Observational design,
- Small sample size,
- Absence of molecular profiling,
- Lack of controlled comparison,
- Inability to determine independent therapeutic contribution of each modality.

The possibility of atypical tumor biology or favorable molecular characteristics cannot be excluded.

CONCLUSION

This two-patient case report describes prolonged clinical stabilization in glioblastoma multiforme using an integrative therapeutic approach involving:

- Dendritic cell vaccine therapy,

- Sonodynamic therapy,
- GcMAF,
- Super Transfer Factor injections,
- MOP thymus peptide injections,
- Phytomolecular medicines,
- Onco-nutritional support.

One patient demonstrated unusually prolonged survival without surgical intervention, while the second patient maintained favorable post-treatment stability following standard therapy combined with integrative maintenance treatment.

These observations support the need for further translational and clinical research into multimodal immunobiological strategies in GBM management.

PATIENT CONSENT

Written informed consent was obtained from both patients for publication of anonymized clinical information.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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