

End-of-Life Inpatient Palliative Care for Glioblastoma Multiforme: Lessons Learned from One Case

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ABSTRACT

Glioblastoma multiforme (GBM) is the most common malignant primary brain tumor with a poor prognosis and limited survival. Patients with GBM have a high demand for palliative care. In our present case, a 21-year-old female GBM patient received inpatient palliative care services including symptom management, mental and psychological support for the patient, psychosocial and clinical decision support for her family members, and pre- and post-death bereavement management for the family. Furthermore, we provided the family members with comprehensive psychological preparation for the patient's demise and assisted the patient's family throughout the mourning period. The aim of this study is to provide a reference and insights for the clinical implementation of palliative care for patients with malignant brain tumors.

Key words: glioblastoma; glioblastoma multiforme; palliative care; end-of-life care

INTRODUCTION

Glioblastoma multiforme (GBM) is the most common and fatal primary brain tumor in adults, accounting for 57.3% of all gliomas and with an incidence of 3.22 per 100,000. GBM is highly invasive, making complete surgical resection difficult. The median survival time is 12–15 months after diagnosis, and less than 5% of patients survive more than 5 years^[1-3]. Currently, standard treatments include maximal safe surgical resection, radiation, chemotherapy, targeted therapy, and immunotherapy^[4-10]. Postoperative concurrent radiotherapy with or without adjuvant temozolomide (TMZ) could be beneficial for increasing survival time

up to 2 years^[11]. Despite the best efforts of neuro-oncologists to treat glioblastoma, there is a high recurrence rate, limited survival, poor prognosis, rapid decline in physical function and behavioral and neurocognitive changes, and a high burden of symptoms, especially at the end of life. However, palliative care can, to some extent, improve the quality of life of patients with glioblastoma and their caregivers. The practice of palliative care can also reflect the doctor-patient and nurse-patient relationships and medical humanistic care^[12]. However, in areas where palliative care is developing and the status of palliative care is insufficient, the training of palliative care nurses has become a hot topic in China, where palliative care services for glioblastoma patients are still inadequate. The modalities and timing of palliative care interventions are still being explored all around the world^[13-15]. In the form of storytelling, we narrate here a case of glioblastoma palliative care. In addition, we offer perceptions and ideas to ponder with the aim of providing enlightenment for the development of palliative care for patients with malignant brain tumors.

Received July 2, 2024; accepted September 14, 2024; published online November 3, 2024.

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CASE DESCRIPTION

Course of treatment

The patient was a 20-year-old female. On May 25, 2017, the patient had sudden onset of headache with persistent bilateral swelling and pain accompanied by dizziness, nausea, and vomiting. She was admitted to a local hospital with contrast-enhanced head magnetic resonance imaging (MRI) for consideration of glioma. Left occipital craniotomy was performed on May 31, 2017. Postoperative pathology revealed intracranial high-grade glioma with necrosis, which was consistent with a diagnosis of glioblastoma (World Health Organization [WHO] grade IV, IDH-wildtype). Postoperatively, the patient developed a nasal field defect in the right eye and was followed up regularly. From July to August 2017, concurrent chemoradiotherapy was performed, followed by 6 cycles of TMZ chemotherapy (the first cycle: 200 mg qd, days 1–5; the second cycle: 280 mg qd, days 1–6). During the chemoradiotherapy, blood cell counts, liver function, renal function, and head status were regularly monitored. Leukocytopenia and vomiting occurred and were improved after symptomatic treatment. Head MRI was performed for possible glioma recurrence in November 2018. The patient was admitted to our hospital on December 7, 2018. After exclusion of surgical contraindications,

total resection of high-grade glioma of the left occipital lobe was performed by neuronavigation craniotomy under general anesthesia on December 12, 2018. The operation was successful and the postoperative recovery was good. After tumor resection and discharge, the patient continued to receive nine sessions of adjuvant TMZ chemotherapy (last chemotherapy on March 7, 2019). The patient had Hashimoto thyroiditis with hypothyroidism and received oral levothyroxine sodium tablets 87.5 mg qd as recommended. (Fig. 1)

Clinical management and palliative care

Management of symptoms

The patient's intracranial pressure increased due to the space-occupying effect of the tumor, causing symptoms such as headache, dizziness, and vomiting. The clinical approach to managing these symptoms includes oral glycerol sodium chloride or intravenous mannitol infusions. The tumor was located in a vital area of the brain and resulted in a postoperative visual field defect on the nasal side of the right eye. The patient also developed epilepsy, a common problem following craniotomy, for which intravenous valproate sodium was administered and continued postoperatively. When the patient resumed food intake, treatment was changed to valproate sodium tablets or oral

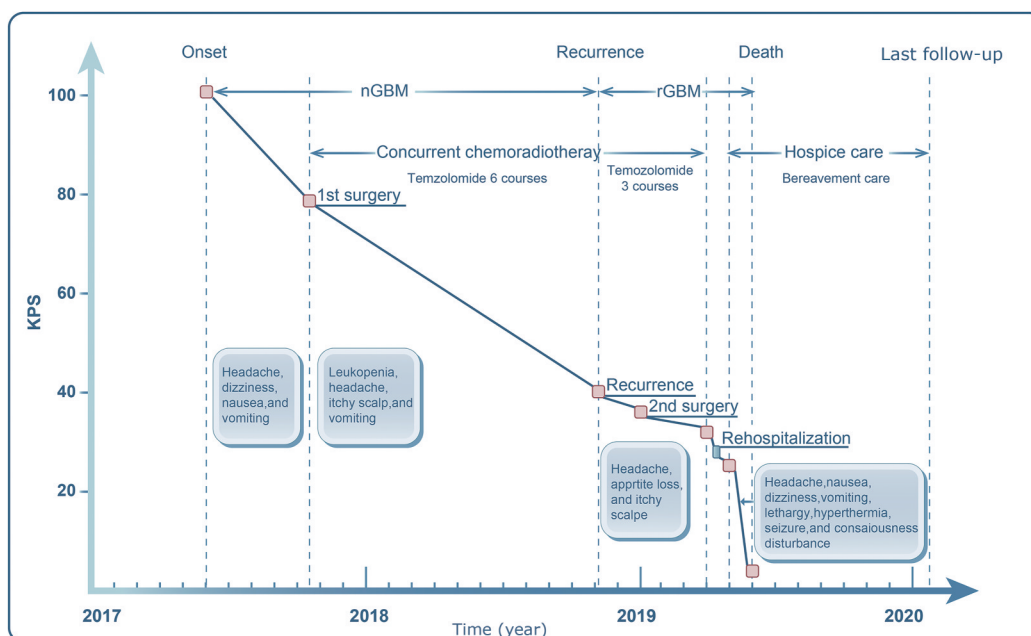


Figure 1. Disease course and treatments of a 21-year-old patient with GBM.

KPS: Karnofsky performance status; nGBM: newly diagnosed glioblastoma multiforme; rGBM: recurrent glioblastoma multiforme; CCRT: concurrent chemoradiotherapy. Radiotherapy combined with temozolomide chemotherapy was offered for one month after surgery, followed by continued temozolomide chemotherapy (28 days each cycle).

liquid formulations. The patient subsequently developed hand rashes and pruritus. Dermatologic consultation suggested a fixed drug eruption, probably induced by the antiepileptic drug. The skin lesions were healed after discontinuation of sodium valproate and application of topical treatments. Finally, the patient experienced consciousness problems, with symptoms of weakness and decreased communication, which required strong support from her family. We taught her mother hair washing and body massage techniques; meanwhile, we also encouraged open conversations between the mother and the patient. As the patient complained of difficulty defecating, she was given a glycerin enema to relieve the discomfort.

Mental and psychological support for the patient

When we first saw the patient, she was emaciated, mentally weak, and sleeping most of the time. We helped the patient wash her hair to make her more comfortable. We told the patient that her family would like to spend more time with her and that they would do anything for her. Accompanied by her family members, the patient was transferred from the neurosurgical intensive care unit (NsICU) to the general ward. The patient's mood improved and she was not irritable. We helped the patient move in a wheelchair to the window of the ward, accompanied by her sister. We guided the family members to talk to the patient about her interests and hobbies and whether she wanted to do anything. We consistently demonstrated care, greetings, companionship, and empathy. Pertinent information about the patient's condition was disclosed gradually.

Psychosocial and clinical decision support for family members

As the patient showed changes in consciousness and symptoms of brain herniation, she was transferred back to the NsICU 4 days before her death. Doctors, nurses, and social workers held meetings to inform family members of changes in the patient's condition and possible prognosis. The family was informed that if the patient died in the hospital, she could only leave Beijing after being cremated. The family accepted the progression of the disease and prepared to return to a local hospital for further treatment, stating that they would not agree to any invasive procedures. We helped the family members prepare for discharge and end-of-life care. We prepared medications en route and provided them our contact information. Her mother hugged us crying, said "we

never gave up" and thanked us.

End-of-life condition of the patient

At the end of life (15 days before her death), the patient was admitted to the NsICU after an epileptic seizure. She became noncompliant, irritable, and unwilling to communicate with others, and only wanted to sleep and urinate. She was most uncomfortable with the urinary tube. When the family visited, the patient was unwilling to communicate. The patient had a medical condition that caused loss of appetite. When we visited the patient 11 days before her death, she was able to take a small amount of protein solution. The patient refused to use the wheelchair because of dizziness and nausea and asked herself, "What is wrong with me? How long will it take to get better? What's wrong with this?" As mentioned before, the patient had altered mental status and symptoms of brain herniation and was transferred back to the NsICU 4 days before her death.

Family bereavement management

Her father told us that the patient had died and thanked us for our service. We told him to cry if he wanted to, and to support the patient's mother by accompanying her. Two days later, we contacted the patient's sister to express our concern and to inquire about the parents. The patient's twin sister, the elder, assured she had prepared mentally over two years, would care for their parents, and would experience the world on her younger sister's behalf. The patient's twin sister kept her passing a secret from classmates, feeling her presence lingered. The older twin sister also revealed that the patient yearned to return to school and wished for a healthy life where she could do so.

Nine months after the patient's death, we contacted the sister to express our concern and ask about the family. The sister said the parents were coping well, occasionally crying softly, but not overly sorrowful. The family continuously offered each other comfort and support. We acknowledged the sister's efforts and encouraged her to spend more time with her parents. The sister said that the patient would be glad that others still remembered her.

DISCUSSION

The in-hospital palliative care has many new insights and experiences. First, specialized palliative care for GBM requires a multidisciplinary team that includes

neuro-oncologists, oncologists, specialized nurses, social workers, psychologists, volunteers, specialized palliative care teams, and larger teams for holistic care^[13-15]. Second, early palliative care intervention improves patients' global health status and quality of life and reduces length of hospital stay and costs^[16-19]. GBM is associated with rapid disease progression, poor prognosis, and limited survival, and impaired consciousness can occur at all stages of the disease. In our current case, the patient had been hospitalized several times throughout the disease course and was admitted into our center for a long period of time, especially at the end of life. The lessons learned from this case underscore the importance of early intervention in the care of GBM patients. Early and open communication about the prognosis of the disease and the potential for rapid deterioration is critical, which allows patients and their families to understand the gravity of the situation and make informed decisions about their care. By involving patients early in the decision-making process, they are empowered to express their preferences and values, which can lead to a more personalized and patient-centered approach to care. The optimal time point for early palliative care with respect to glioma has not been proposed, although the American Society of Clinical Oncology (ASCO) guidelines suggest a definition of "early" as "within 8 weeks of diagnosis"^[20]. However, due to the uniqueness of the central nervous system, especially in patients with glioma, "early" needs to be better defined and verified, which will be one of our research priorities. Palliative care integration may span from diagnosis through the patient's death and extend to follow-up and bereavement support for families post-mortem.

GBM patients experience a long period of time with a core set of tumor- and treatment-related symptom burden^[21-24]. The goal of palliative care is to improve the physical, psychological, social, and spiritual comfort of patients and to enhance the quality of life for patients and their families^[25, 26]. Hospice care provides end-of-life palliative care, ensuring comfort for both patients and their family members. In our practice, palliative care extends to the end-of-life stage, often starting at glioblastoma diagnosis prior to medical intervention. Technically, hospice care falls under the category of end-of-life care^[21, 22, 27, 28].

Patients with GBM present with a variety of symptoms, both disease- and treatment-related. GBM patients present with more specialized and complex symptoms,

like nausea and vomiting, often due to increased intracranial pressure, although other causes cannot be ruled out. The patient in this case exhibited a range of symptoms including headache, dizziness, nausea, vomiting, lethargy, fever, constipation, seizures (epilepsy), and drowsiness, as described in literature^[29, 30]. The patient had glioma-specific symptoms, which were effectively managed through symptomatic supportive care. Epilepsy is a common symptom in glioma patients, especially at the end of life. In our current case, epilepsy was managed by oral sodium valproate 0.5 g bid. For patients with swallowing disorders, we typically switch the sodium valproate tablets to oral solution or to an intravenous pump of sodium valproate injection. Intravenous or intramuscular diazepam is administered as appropriate in patients with seizures. Alternative routes, including intranasal, sublingual, buccal, rectal, subcutaneous, or intravenous administration, should be considered if necessary^[31]. Meanwhile, patient safety is protected.

In our practice, we incorporate both symptom control and comfort measures in palliative care^[32-33]. We steadfastly provide compassionate care, including greetings, companionship, empathy in medical decision-making, and post-death bereavement and grief counseling for families. In the current case, we served as a resource for the medical decisions. We provided support and assistance, especially at the end of the patient's life, and bereavement counseling after patient death. Communication was smooth with the patient and her families, and the family overcame anxiety, depression, and grief. After the patient died, we provided ongoing support to her families, including care, condolence, and psychological support, with the goal of providing comfort and assistance to the bereaved family. Most Chinese families go through a long period of mourning for the loss of a loved one. Palliative care aids in understanding illness and death and helps families cope with patient death. In the context of traditional Chinese culture, it is particularly difficult for family caregivers to accept the departure of their beloved family members. In some cases, they cling to beliefs in miracles, causing them to persist in hope, even in instances where the possibility of recovery seems unlikely, which represents a significant barrier to the adoption of palliative care.

Palliative care hurdles for glioma patients in China include a cultural taboo against discussing death, which is feared to invite misfortune^[34, 35]. Palliative care in China remains in a developmental stage, and inpatient palliative care beds are not widely available, especially

for glioma patients. However, there are also relatively few beds in the surgical wards of tertiary and public hospitals, and patients are treated in the hospital only during the perioperative period. While many Chinese patients tend to seek medical treatments in resource-rich metropolises, they have to choose local medical institutions for follow-up treatments, and most of them have a long recovery period at home, which makes continued palliative care services almost impossible. Finally, there is also a lack of nursing home or hospice settings^[13-15,33], and the models of community-based palliative care are still developing. In our present case, applying palliative care principles to the patient deepened our disease understanding and pinpointed key areas for future palliative interventions. Without palliative care, GBM-induced distress will persist for patients and families, making palliative care for glioma patients critically urgent. The implementation of comprehensive inpatient palliative care in the current patient has offered invaluable experience in this area.

Under the visionary leadership of Prof. Ning XH, our center has pioneered an innovative model for inpatient palliative care. This model includes three key components: the "Outpatient Palliative Care" service, which provides accessible and timely care; the "Comorbidities Co-Management", which ensures a holistic approach to treating patients with multiple health conditions; and the "Peking Union Medical College Hospital-Secondary Hospital-Community and Family Continuous Service" framework, which facilitates a seamless continuum of care across multiple healthcare settings. This integrated model is expected to improve patient outcomes by prioritizing comprehensive care and continuity of care^[36]. As most patients have a long recovery period at home, community- and home-based palliative care may become the primary way for glioma patients to receive palliative care. Finally, for patients and their families, most medical information on glioma comes from doctors and Internet searches. They lack an adequate understanding of the disease, and it takes time for them to accept bad news, let alone prognosis and care. These factors also present challenges for inpatient palliative care providers. Home-based palliative care programs may be more advantageous^[37].

ARTICLE INFORMATION

Acknowledgement

We thank the medical and nursing teams for their diligent ef-

forts during the patient's hospitalization.

Conflict of interests

The authors declare no conflict of interests.

Authors' contributions

Conceptualization: Xiao ZY and Zhang Y; methodology: Xiao ZY, Zhang Y, and Sun YX; writing - original draft preparation: Xiao ZY and Zhang Y; writing - reviewing: Sun YX, Xu DR, Wang Y, and Ning XH; visualization: Sun YX, Xu DR, Wang Y, and Ning XH; funding acquisition, project administration, and supervision: Ma WB.

Funding

This work was funded by the National High Level Hospital Clinical Research Funding (2022-PUMCH-B-113).

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(Edited by Liang-Jun Gu)