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Mini Review

The Immune Microenvironment of Glioma

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Abstract

A glioma is a tumor that develops when glial cells proliferate uncontrollably. Normally, these cells nourish neurons and aid in the operation of your central nervous system. Gliomas are most commonly found in the brain, although they can also develop in the spinal cord. Gliomas are malignant (cancerous), however some may develop slowly. Adult gliomas are the most prevalent kind of primary brain tumor. Despite being relatively infrequent, they cause considerable morbidity and mortality. High-grade gliomas, often known as glioblastomas, are aggressive tumors with a dismal prognosis (Madhumathi et al., 2020). It is now more widely understood that the central nervous system contains an innate immune system. There has been no significant advancement in glioma treatment during the previous decade. The tactics that cancer cells attempt to avoid detection by the immune system help explain the lack of effective therapy for gliomas. However, immunotherapy, which includes blocking immune checkpoint inhibitors, has increased patient survival in several cancer types (Hend et al., 2014).

Keywords: Glioma, Tumor, Cancerous, Immunotherapy, Glioblastomas

INTRODUCTION

Glioma is the most aggressive primary tumor of the central nervous system, with an exceedingly poor overall survival rate. Recent advances in cancer treatment involving immune checkpoint blockage have received a lot of attention. Despite being the most promising (immunotherapy) cancer treatment, clinical use of immune checkpoint blockage in glioma patients remains difficult due to the "cold phenotype" of glioblastoma and many reasons causing resistance, both innate and acquired. As a result, glioma immunotherapy will require a thorough understanding of the tumor microenvironment as well as the brain's specific immune condition (Morteza et al., 2013). More sensitive biomarkers for monitoring immune response, as well as integrating different immunotherapy techniques, may speed clinical progress and allow for the creation of effective and safe glioma patients therapies.

Novel immunotherapies targeting the immunological component of the tumor microenvironment have showed tremendous promise in the therapeutic therapy of malignancies in recent years. Drugs targeting immunological checkpoint molecules are being lauded as a breakthrough in cancer immunotherapy, among other treatment techniques. Glioma is the most frequent and lethal primary central nervous system (CNS) brain tumor, with a 5-year survival rate of fewer than 10%. Glioblastoma multiforme (GBM) accounts for 50% of glioma cases and has a 5-year survival rate of fewer than 5%, equating to a World Health Organization (WHO) grade IV tumor. Unfortunately, the current gold standard of GBM treatment (complete resection + adjuvant radio-chemotherapy) is only a palliative choice for patients, with a median survival time of fewer than 15 months following diagnosis (Mohamed 2017).

The recent clinical success of checkpoint inhibitors across several solid cancers has generated interest in immune-targeted glioma therapy methods. However, because the blood-brain barrier (BBB) prevents direct communication between the brain and immune system, the CNS is often regarded as a "immunologically privileged" location. Given the brain's particular accessibility and tissue composition, developing successful immunotherapeutic techniques is not easy. The specific immunology and tumor microenvironment of the brain are discussed in this paper. Furthermore, we discuss several immune checkpoint blockade techniques as

well as immunotherapy resistance mechanisms (Nwangwa et al., 2016).

The immune system is made up of many cell types that protect the body from potential infections.

Gliomas, also known as glial tumors, are the most prevalent primary brain tumors, accounting for 81% of all malignant ones. Gliomas, despite their rarity, inflict severe morbidity and death. Glioblastoma is the most aggressive and prevalent glioma kind and grade (45%), with a median survival of roughly 15 months. There has been no substantial improvement in Glioma treatment for more than ten years, and the lack of effective treatment for glioma can be explained by the multiple ways that cancer cells utilize to elude the immune system (Obembe et al., 2015).

Immunotherapy is an immunological treatment in which cancer cells are recognized and eliminated by the host's immune system. Indeed, this form of therapy has been demonstrated to be fairly successful against several types of cancer, particularly when inhibitory immunological checkpoint molecules are blocked. These immunological checkpoints regulate T-cell interactions with cancer cells by inhibiting or activating T cells. This process happens in response to the demands of the organism and the tumor's activities. Furthermore, immunotherapy, which works by blocking immune checkpoint inhibitors, has increased patient survival in several forms of cancer (Olusegun et al., 2019). This novel cancer therapy promise remains one of the most promising ways for successful antitumor immune activation. These discoveries have piqued the interest of researchers who have developed a keen interest in immune checkpoint blocking in glioblastoma in recent years. Previous research has showed that combining anti-PD-1 and anti-CTLA-4 blocking antibodies did not increase overall survival. Furthermore, there was no evident advantage of neoadjuvant nivolumab with resectable glioblastoma (GBM), and the median overall survival was just 7.3 months. Similarly, a phase III trial comparing nivolumab (anti-PD-1 blocking Ab) to bevacizumab (anti-VEGF blocking Ab) in patients with recurrent GBM found no advantage for nivolumab and found a comparable median overall survival (mOS, 9.8 vs 10.0 months). The purpose of this study is to describe the immune response within the glioma microenvironment and to explore the role of several immune checkpoint inhibitor compounds employed by glioma cells to avoid the immunological response. It will also report on certain possible therapeutic approaches that include the blocking of immunological checkpoints (Hend et al., 2014).

Only 2% of all cancers are primary central nervous system malignancies. Despite their modest prevalence, they are extremely common in small children, adolescents, and young adults, with significant mortality and morbidity. Gliomas are the most frequent primary central nervous system (CNS) tumors and are graded by the World Health Organization (WHO) from I to IV. Thus, gliomas are classified into two types based on their malignancy: low-grade gliomas (grades I and II), which develop slowly, and high-grade gliomas (III and IV), which invade the brain parenchyma. Glioblastoma is now the most aggressive and lethal glioma. Even with modern therapies, including as surgical resection, radiation, and chemotherapy, it is still an incurable illness with a 12- to 15-month survival rate. In a lethal symbiotic relationship, GBM manages to evade the immune system. Furthermore, it can arise from a variety of cell types other than glial cells (Nwangwa et al., 2016). It primarily affects people aged 64 and older, although it can also affect youngsters, with males being more affected than women. Gliomas are classified as either primary (precursor) or secondary (when a low-grade glioma transforms). According to research, people with an isocitrate dehydrogenase (IDH) mutation live longer and respond better to chemotherapy and radiation than those who do not have the mutation. Tumor-infiltrating immune cells are cells that have entered the tumor microenvironment after leaving the circulation. Depending on the kind of cell and their functional relationships, their function may vary as the tumor progresses. Indeed, immune cells may play an important role in tumor suppression or tumor growth support, with implications for patient behaviour (Morteza et al., 2013).

CONCLUSION

Due to the presence of the blood-brain barrier (BBB), treating brain tumors presents unique and significant obstacles. The blood-brain barrier (BBB) is a highly selective semipermeable barrier that separates blood from the brain but also prevents medication entry. Surgery (if feasible and safe) is the primary therapy for brain tumors, and maximum resection is substantially associated with a prolonged OS. As a supplement, patients are frequently given radiation and chemotherapy. As a primary or postoperative treatment, radiotherapy with a total dosage of 60 Gy enhanced OS and progression-free survival (PFS). In newly diagnosed GBM patients, concomitant use of the oral alkylating drug temozolomide dramatically improved OS. Although radiation and temozolomide increase survival, tumor growth and recurrence are mainly caused by temozolomide resistance. New medicines such as molecular targeted therapy, alternating electric field therapy, ultrasound focusing, and nanotherapy have made significant progress in recent years, yet the prognosis of patients with glioblastoma has not improved significantly. This lack of progress might be attributed to the fact that the complicated pathological process of glioma has yet to be fully understood, and reliable biomarkers for accurate diagnosis and molecular targeted treatment are missing. However, the discovery of novel immunotherapy targeted at rousing the anti-tumor immune response has greatly improved the prognosis of patients with different advanced hematological disorders and solid malignant tumors. Immune checkpoint inhibitors, such as anti-PD-1 and anti-CTLA4 treatment, boost T

cell activation while suppressing immunosuppression in the TME. Some indicators, such as mutant IDH, MGMT promoter methylation, epidermal growth factor receptor amplification, and p53 mutation, have predictive and diagnostic value in gliomas. As a result, we must develop more effective medicines to increase the survival rate of these individuals. Some genes and transcription factors have been implicated in the emergence, development, and evolution of gliomas. Improving our understanding of glioma development and recognizing critical molecular markers will aid in improving glioma diagnostic accuracy and identifying new therapy targets to attain improved clinical outcomes.

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