

Letter to Editor:

Steroids Use in Glioblastoma: Why Do We Persist?



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Dear Editor

Glioblastoma (GBM) is the most common malignant brain tumor and arises from glial cells. The condition was initially described ninety years ago. Despite intense research efforts, the prognosis for most patients remains woefully poor. Over the past few decades, our understanding of the pathologic processes implicated in GBM has improved, and we have a greater appreciation for the genetic and epigenetic aberrancies which drive disease progression and impact treatment response [1, 2]. We also have a clearer perspective of tumor-microenvironment interactions, hypoxia-induced cellular changes, and tumor-related cytokine dysregulation. Specifically, there is ample evidence that patients with GBM are immune-deficient; unfortunately, most conventional management strategies worsen this impairment.

There is a complex and well-established association between GBM and immune compromise. Over the past fifty years, various groups have described how these tumors impair the innate and adaptive immune response [3-5]. Studying the tumor microenvironment, various groups have discovered that the secretion of factors such as interleukin 1 (IL-1), Transforming Growth Factor B (TGF- β), prostaglandin E and Colony-Stimulating Factor 1 (CSF-1) lead to significant immune suppression [5, 6].

In addition to inducing aberrant cytokine production, glioblastomas benefit from a lymphopenia and a largely dysfunctional cellular immunity. For example, there is a preponderance of myeloid cells within these tumors but few tumor-infiltrating lymphocytes [7]. An effective cellular response is also handicapped by the T-cell senescence and anergy observed in patients [8]. Finally, a recent study from Duke University found that lymphocyte sequestration in the bone marrow contributes to significant lymphopenia [9].

Dexamethasone is a synthetic glucocorticoid that is ubiquitously used to manage the vasogenic edema caused by GBM. Its usual indication is in decreasing "mass effect" pre-operatively but it is also used to ameliorate the symptoms patients experience after radiation. Despite its clinical efficacy, dexamethasone has also several deleterious effects which should preclude its use once adequate alternatives have been found. These effects include inducing stem-like cellular changes and Epithelial-Mesenchymal Transition (EMT) as well as significant immune suppression [10-13].

Moreover, dexamethasone likely decreases chemotherapy penetration by stabilizing the Blood-Brain Barrier (BBB) and likely diminishes the therapeutic benefit of radiation [14, 15]. There is evidence that radiation induces pseudo-progression that is associated with im-

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proved prognosis, but the immune-suppressive effect of dexamethasone may blunt this benefit [16].

This perspective certainly concedes that vasogenic edema is a significant issue to be managed in patients with GBM. However, it is hoped to be a call-to-arms for the clinicians to explore better solutions to this issue. A simple (if imperfect) suggestion may be the use of agents such as the COX-2 inhibitor, Celecoxib [17, 18]. This medication has been shown to limit edema in patients with intracerebral hemorrhage or trauma [19]. It also has a smaller immune-compromising footprint than dexamethasone; and, in fact, it has been proposed to improve radiation response in GBM [20].

Despite its known flaws, surgeons and oncologists continue to prescribe dexamethasone. Our growing understanding of the molecular genetics of glioblastoma and its interactions with the immune system will allow us to rationally develop new therapeutic strategies. However, in the interim, we ought to maximize the benefits of existing adjuvant therapies and minimize iatrogenic immune-suppression.

Ethical Considerations

Compliance with ethical guidelines

As there is no animal or human research reported in this letter, there was no need for ethics board approval.

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Conflict of interest

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