Dexamethasone Treatment Increases Immunosuppressive Myeloid Populations Within Immunocompetent Models Of GBM

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Disclosures

• I DO NOT have any financial or organizational relationships with commercial interests or other entities
Introduction

• Dexamethasone is the mainstay of therapy to control vasogenic edema surrounding GBM and thereby ameliorate symptoms. However, dexamethasone does not influence survival in patients, and in the current era of adjunct immunotherapies, may lead to worse outcomes due to reduced efficacy of immune-modulating agents. Furthermore, the effects of dexamethasone on immune populations within the systemic circulation as well as in the peri-tumoral GBM microenvironment have been incompletely characterized.
Methods

• Immunocompetent C57Bl/6 mice were stereotactically injected with syngeneic murine GBM cell lines, and subsequently treated with dexamethasone. Bone marrow and peripheral blood was isolated when mice developed tumors, and was analyzed for myeloid populations by flow cytometry.

• A murine resection model to mimic standard of care therapy in GBM was developed and implemented to analyze immune populations in response to current GBM treatments. Immunocompetent C57Bl/6 mice were stereotactically injected with syngeneic murine GBM cell lines, and subsequently treated with dexamethasone. The primary tumors of the mice were resected, and the immune populations were analyzed by flow cytometry.
Results (1)

A. Survival of GL261 Implanted mice

B. Post resection survival of GL261 Implanted mice

A) Mice were stereotactically implanted with intracranial syngeneic glioma cell lines and subsequently treated with dexamethasone (4 ug daily). B) Mice were stereotactically implanted with intracranial syngeneic glioma cell lines, and their tumors were resected on post implantation day 7, after which they were treated with dexamethasone (4 ug daily). Dexamethasone did not increase survival in either unresected or resected recurrent syngeneic models of glioma.
Mice harboring syngeneic intracranial tumors were given vehicle or dexamethasone (4ug) daily for 2 weeks after which their peripheral blood was isolated and the myeloid populations were analyzed. Dexamethasone treatment led to an increase in circulating monocytic myeloid derived suppressor cells while other myeloid populations were unchanged. This difference was not recapitulated in naïve mice treated with dexamethasone. ** p<.01
Results (3)

Mice harboring syngeneic intracranial tumors were given vehicle or dexamethasone (4ug) daily for 2 weeks after which their tumors and tumor bearing hemispheres were isolated and the myeloid populations were analyzed. Dexamethasone treatment led to no increases in immunosuppressive myeloid populations within the recurrent tumors of mice.
Discussion

- Dexamethasone treatment does not influence time to development of symptoms or survival in immunocompetent murine models of GBM, but leads to increases in immunosuppressive populations within the systemic circulation. This highlights the concerns over the use of steroids in the management of edema in GBM, and underscores the importance of monitoring immune system reactions to administered therapies.
Summary Points

• Dexamethasone does not increase survival in immunocompetent mouse surgical resection models of glioma
• Dexamethasone treatment in the setting of gliomas increases circulating monocytic myeloid derived suppressor populations
• Dexamethasone treatment does not increase immunosuppressive myeloid populations within the tumor microenvironment of recurrent mouse gliomas