Ipilimumab and Craniotomy in Patients with Melanoma and Brain Metastases: A Case Series

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Introduction

Ipilimumab, an anti-CTLA4 immunotherapy known to improve survival in patients with advanced systemic melanoma, has also demonstrated activity in patients with brain metastases, particularly when tumors are small, asymptomatic, and patients are not using corticosteroids. Through a case series review, we aimed to assess the value of surgical resection in the context of systemic therapy with ipilimumab, looking at changes in performance status, corticosteroid dose, and survival.

Methods

All patients with melanoma and brain metastases who received ipilimumab and underwent craniotomy for tumor resection between 2008 and 2012 at the Massachusetts General Hospital were identified through retrospective chart review. We restricted our final analysis to patients who underwent craniotomy within 3 months prior to initiation of therapy or up to 6 months after cessation of ipilimumab administration.

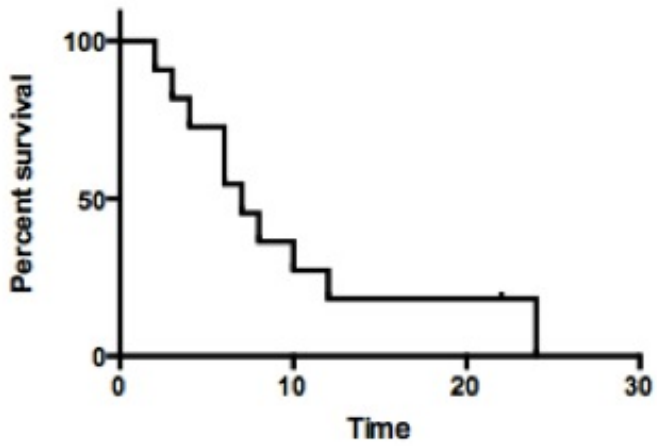
Results

Nineteen patients received ipilimumab and also underwent craniotomy for tumor. Of this group, 11 patients fit the inclusion criteria based on timing of therapy (median age 56, range 39 to 72; Table 1). Median number of metastases at time of craniotomy was two (range one to greater than 20). Median number of ipilimumab doses was four (range two to four). All courses of ipilimumab were stopped for disease progression. Eight of 11 patients had improvement in their performance status following craniotomy. The one patient who worsened had five additional brain metastases and the two other patients had an unchanged performance status. Of the four patients on corticosteroids prior to craniotomy, only one patient tolerated corticosteroid dose reduction after surgery. Patients unable to taper had three, four, and greater than 20 remaining tumors post-operatively. The one patient who tolerated taper did so after his third craniotomy for his remaining third metastasis. Ten of 11 patients had died by time of data collection, with the one living person lost to follow-up. Median survival after start of ipilimumab treatment was seven months (Figure 1).

Table 1- Timing of Ipilimumab and Surgery

Surgery Timing	Patient	Reason for surgery
Surgery BEFORE Ipi	Patient 1	Mass effect- R frontal
	Patient 2	Weakness
	Patient 3	Hemorrhage, weakness
	Patient 4	Hemorrhage
	Patient 5	Hemorrhage
Surgery DURING Ipi	Patient 6	Large cerebellar tumor
	Patient 7	Large cerebellar tumor
	Patient 8	Hemorrhage, weakness
	Patient 1	Speech problems, enlarging tumor
Surgery AFTER Ipi	Patient 9	Mass effect
	Patient 10	Solitary lesion, hemorrhage
	Patient 11	Solitary lesion
	Patient 2	Weakness, hemorrhage

Figure 1- Survival Plot for Patients Treated with Ipilimumab and Surgery



Kaplan Meier survival plot for 11 patients; time represented in months

Conclusions

The role of surgical resection of melanoma metastasis in combination with ipilimumab therapy has not yet been addressed in the literature. This is the first case series to document the characteristics of patients who underwent craniotomy for resection of brain metastases in close time proximity to receiving ipilimumab. While surgery improved performance status in the majority of cases, most patients on corticosteroids continued to require them post-operatively, and there did not appear to be impact on overall survival when compared to historical survival rates. Overall, even without intracranial response to ipilimumab, surgery for metastasis and multiple metastases, in general, may improve quality of life for a brief period. Ultimately, we need to continue to study predictive biomarkers to determine which patients will respond to ipilimumab, thereby determining who will get the greatest quality-of-life and survival benefit from surgery.

Learning Objectives

By the conclusion of this session, participants should be able to better understand the impact of ipilumumab and craniotomy for tumor resection in advanced melanoma.

References

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