# Perilesional edema in brain metastases

Perilesional edema in brain metastases:

Little is known about tumor-associated vasogenic edema in brain metastases, yet it causes significant morbidity and mortality. Our purpose was to characterize edema in patients treated with anti-PD-1 and to study potential causes of vessel leakage in humans and in pre-clinical models.

Methods: We analyzed tumor and edema volume in 18 non-small cell lung (NSCLC) and 18 melanoma patients with untreated brain metastases treated with pembrolizumab on a phase II clinical trial. Melanoma brain metastases were stained with anti-CD34 to assess vessel density and its association with edema. We employed an in vitro model of the blood-brain barrier using short-term cultures from melanoma brain and extracranial metastases to determine tight junction resistance as a measure of vessel leakiness.

Results: Edema volumes are similar in NSCLC and melanoma brain metastases. While larger tumors tended to have more edema, the correlation was weak (R2 = 0.30). Patients responding to pembrolizumab had concurrent shrinkage of edema volume and vice versa (R2 = 0.81). Vessel density was independent of the degree of edema (R2 = 0.037). Melanoma brain metastases cells in culture caused loss of tight junction resistance in an in vitro blood-brain barrier model system in some cases, whereas extracerebral cell cultures did not.

Conclusions: Edema itself should not preclude using anti-PD-1 with caution, as sensitive tumors have resultant decreases in edema, and anti-PD-1 itself does not exacerbate edema in sensitive tumors. Additional factors aside from tumor mass effect and vessel density cause perilesional edema. Melanoma cells themselves can cause decline in tight junction resistance in a system void of immune cells, suggesting they secrete factors that cause leakiness, which might be harnessed for pharmacologic targeting in patients with significant perilesional edema [1)].

1)
Tran TT, Mahajan A, Chiang VL, Goldberg SB, Nguyen DX, Jilaveanu LB, Kluger HM. Perilesional edema in brain metastases: potential causes and implications for treatment with immune therapy. J Immunother Cancer. 2019 Jul 30;7(1):200. doi: 10.1186/s40425-019-0684-z. PMID: 31362777; PMCID: PMC6668163.

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