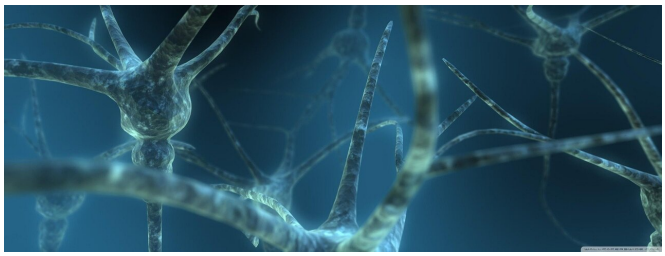
Immunotherapy for brain metastases: Where are we now?

27 April 2021



Credit: Pixabay/CC0 Public Domain

Brain metastases are the most common type of brain tumors, affecting nearly 200,000 people in the United States each year. Once diagnosed, patients have a median survival of sic months. Immunotherapy, a type of cancer treatment that helps your immune system fight cancer, is on the rise and have already shown potential in several cancers. Yet, brain metastases are known to possess extraordinary genetic variability and special features that allow them to impede immunotherapy.

On 24 April 2021, a study was published in the journal *Brain*, exploring the emerging principles of immunotherapy in brain metastases.

"Brain metastatic cells are famous for their ability to manipulate immune responses," said lead author of the study Jawad Fares, MD, Postdoctoral Scholar at Northwestern University. While this ability might be helpful in limiting inflammation in the brain, it can restrict immune cells that can fight metastatic cancer cells.

Brain metastases escape anti-tumor immune responses to promote their survival and resistance to therapy. Metastatic cells interact with a variety of immune cells, such as microglia and monocytes, and neuronal cells, such as astrocytes, in the brain to decrease anti-cancer immunity.

"Unfortunately, patients with brain metastases continue to be excluded from clinical trials due to their dismal outcomes and poor prognoses," said Fares. Immunotherapy has not yet been brought to the brain metastasis space in patients with breast cancer, despite reported efficacy in patients with brain metastases from melanoma and lung. "Preclinical studies in metastatic breast cancer have shown a lower immune content in brain metastases," said Fares. "Basic science and immunology research is needed to understand the mechanism behind this and what role other immune cells, such as B cells, and brain cells are playing in the tumor microenvironment."

Combining immunotherapy with other forms of chemotherapy, radiotherapy, and/or surgery may potentiate their effect in the setting of brain metastases. "Randomized controlled trials are needed to fully understand the exact clinical benefit of immunotherapy as monotherapy or in combination," said Fares. "At the moment, there are a number of clinical trials that are trying to combine immunotherapeutic agents with other forms of therapy to try to achieve a breakthrough." While some have succeeded, others continue to try to achieve clinical benefit.

"Future research should be directed to understand the biological mechanisms of immunity in brain metastases," Fares concluded. "In addition, developing appropriate preclinical models that recapitulate the immune system in the setting of brain metastases is important to advance new, effective therapies that can be translated to patient settings."

More information: Jawad Fares et al. Emerging principles of brain immunology and immune checkpoint blockade in brain metastases, *Brain* (2021). DOI: 10.1093/brain/awab012

Provided by Northwestern University