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IMMU-13. TUMOR INFLAMMATION-ASSOCIATED NEUROTOXICITY (TIAN): A TOXICITY SYNDROME IN PATIENTS TREATED WITH IMMUNOTHERAPY FOR CENTRAL NERVOUS SYSTEM TUMORS

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BACKGROUND: Immunotheapies are increasingly being explored as potential therapeutic modalities for the treatment of central nervous system (CNS) tumors and have unique toxicity profiles. Toxicity syndromes such as cytokine release syndrome (CRS) and immune effector-cell associated neurotoxicity (ICANS) were identified through experiences with chimeric antigen receptor (CAR) T-cell therapies for B cell malignancies; the creation of grading scales for these toxicities standardized the reporting and enabled management. METHODS: From our collective experiences in treating patients with immunotherapies for CNS tumors, we have identified a localized neurotoxicity syndrome, distinct from the systemic toxicities of CRS and ICANS, termed tumor inflammation-associated neurotoxicity (TIAN). RESULTS: TIAN develops secondary to localized inflammation at the tumor site. From a mechanistic perspective, we identified two types of TIAN: 1) type 1 TIAN arises in the setting of mechanical space constraints when peritumoral edema results in tissue shifts and increased intracranial pressure, which if untreated, can lead to a life-threatening herniation syndrome and 2) type 2 TIAN occurs when local neuronal dysfunction causes transient worsening/new neurological deficits. Whereas type 1 TIAN encompasses the concept of “pseudoprogression,” type 2 TIAN can occur in the absence of edema when inflammatory-cell interactions disrupt local neural function. Patients can have both type 1 and type 2 TIAN simultaneously; understanding the type of TIAN can inform management. To facilitate the uniform reporting and management of TIAN, we created a TIAN grading scale that applies to both types of TIAN. Although, type 1 TIAN is generally associated with higher-grade toxicity, high-grade type 2 TIAN can occur when local inflammation compromises respiratory or autonomic functions. CONCLUSIONS: Recognizing TIAN as a distinct, local neurotoxicity syndrome is critical to guiding clinical management and prognosis in patients with CNS tumors with immunotherapies.

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