Immunotherapy-Induced Encephalitis: A Case of a Rare but Serious Complication of Anti-PD-1 Treatment

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Introduction: Immune checkpoint inhibitors (ICIs) are a highly effective and widely used treatment for various solid tumor malignancies. While immune-related adverse events (irAEs), such as thyroiditis, colitis, and pneumonitis associated with ICIs have been well described, encephalitis related to immunotherapy is an extremely rare yet severe complication.

Case Description: A 71 year-old African-American male with PD-L1 positive metastatic adenocarcinoma of unknown primary, treated with 5 cycles of carboplatin/paclitaxel/ pembrolizumab initially achieving partial response, presents with concerns for oligoprogression. Hence treatment plan was to consider focal radiotherapy while continuing pembrolizumab monotherapy. Approximately 2 weeks following C1D1 maintenance pembrolizumab, patient presented to the hospital with altered mental status (AMS), fatigue and fever. He exhibited incoherent speech and inability to follow commands. MRI brain, EEG, infectious, and toxic metabolic workup were all unremarkable. LP was negative for viral etiology, with WBC of 1/ mm3 and protein of 44. After ruling out most other etiologies of acute encephalopathy, plasmapheresis (PLEX) and high-dose 1 mg/kg/day IV methylprednisolone were initiated for suspicion of ICI-related encephalitis. Shortly after steroids and the first PLEX session, mentation started to improve, returning to baseline by the completion of 5 total sessions of PLEX.

Discussion: The incidence of CNS irAEs following ICI treatment is estimated to range 2-6%, among which, encephalitis remains poorly understood due to its low incidence of 0.05%[1]. Literature surrounding immune encephalitis (IE) is limited to case reports/ series at this time. IE has been described after the use of various ICIs—nivolumab, ipilimumab, pembrolizumab, sentilimab, durvalumab, dostarlimab and atezolizumab[1-3]. Clinically, IE presents with acute onset of AMS with progressive decline in alertness. The most common neurological symptoms are confusion (78%), fever (45%) and cerebellar ataxia (33%)[2]. Median time from ICI use to symptom onset is 3 months, though can range from 4 days to 18 months[1]. In small studies, CSF analysis has demonstrated a median WBC count of 22/ mm3 (lymphocyte-predominant), median protein level of 1.55 g/L, and autoantibodies identified in half of the patients[1-2]. MRI brain was abnormal in less than half of patients. Recommended management includes prompt discontinuation of ICI and initiation of corticosteroids (1-2 mg/kg/day of prednisone). Treatment with rituximab, IVIG and plasma exchange has also been utilized in case reports, as a mechanism to target B cell receptor repertoire[1]. While prognosis is generally good with early identification resulting in improvement or resolution of symptoms in most, there are a few cases of deaths from IE[1-3].

Conclusion: Immune encephalitis is a rare but serious complication of ICIs that warrants prompt clinical/ diagnostic recognition and early treatment with corticosteroids +- PLEX.

References:

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