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LETTER TO THE EDITOR

A case of fatal Guillain–Barre syndrome from anti-PD1 monoclonal antibody use

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Editor,

A 68-year-old woman with stage III squamous cell carcinoma of the lung was treated with carboplatin, nab-paclitaxel, and concurrent radiation. A year later, she was diagnosed with brain metastases and nivolumab, an anti-PD1 monoclonal antibody, was initiated at a dose of 3 mg/kg given every 2 weeks. Three months later, she presented with fatigue and bilateral lower extremity weakness of 4 days duration. Her most recent dose of nivolumab was administered 9 days ago. Physical examination revealed decreased strength in both legs. A CT scan of the brain revealed partial response to nivolumab therapy. An MRI scan of the spine was normal. Twelve hours later, she reported tingling sensation in her feet and profound weakness in lower extremities. Soon, she experienced progressive loss of motor and sensory function in arms and legs. Physical examination revealed loss of deep tendon reflexes in all four extremities associated with complete lack of strength. Cerebrospinal fluid (CSF) analysis showed clear appearance, with no nucleated cells, normal glucose and elevated protein levels (85 mg/dL; normal range 15–45). CSF Gram stain test, microbiological cultures and herpes simplex virus (HSV) DNA test were negative. The clinical finding of acute areflexic paralysis and the CSF finding of albuminocytologic dissociation were consistent with a diagnosis of GBS. She was started on intravenous immunoglobulin (IVIG) and plasma exchange. Within 2 hours, she developed respiratory muscle paralysis, and was placed on ventilator support. Unfortunately, her clinical condition did not improve and she was extubated after 11 days. She expired in hospice care within a few hours.

Immune checkpoint inhibitors modulate the immune system and may cause immune-related adverse events (irAE) (Naidoo et al. 2015). Neurologic manifestations of irAE's are extremely rare. A few cases of ipilimumab-induced Guillain–Barré syndrome (GBS) have been reported in the literature (Gaudy-Marqueste et al. 2013; Wilgenhof and Neyns 2011). To our knowledge, this is the first case of nivolumab-induced GBS. Immune response directed against the myelin or axon of the peripheral nerve is implicated in the pathogenesis of GBS (Yuki and Hartung 2012). Nivolumab can cause disruption in normal immune checkpoint molecule function resulting in decreased peripheral tolerance to ganglioside-related epitopes and unchecked immune responses (Csurhes et al. 2005). With increasing use of nivolumab in advanced malignancies, physicians should be aware of rare adverse events like GBS, which can be effectively treated with rapid initiation of corticosteroids, IVIG or plasma exchange along with discontinuation of anti-PD1 antibody therapy.

Compliance with ethical standards

Conflict of interest None.

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