Atezolizumab/bevacizumab

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Severe encephalitis and immune-mediated polyradiculoneuropathy: case report

A 70-year-old woman developed severe encephalitis and immune-mediated polyradiculoneuropathy following treatment with atezolizumab and bevacizumab for advanced hepatocellular carcinoma [HCC; *routes not stated*].

The woman, who was diagnosed with multifocal HCC with macrovascular invasion into the right portal vein (March 2020). She also had hepatitis C-induced liver cirrhosis. Further investigations revealed lymph node invasion and stage-C BCLC tumour was confirmed. She started receiving fixed dose of atezolizumab 1200mg over 2 hours, in addition to bevacizumab 15 mg/kg over 90 minutes. Ten days later, she presented to the emergency department due to previous episodes of impaired cognition and language, somnolence, emesis, and dyspnoea, in addition to severe deterioration of general condition. Neurological investigations was unremarkable except for a blurred orientation to time. Laboratory workup was slightly elevated for the inflammatory markers. Other laboratory testing including blood, urine and sputum cultures were unremarkable. Tests for SARS-COV-2, influenza A and B were negative. Chest radiograph and cranial CT scan were unremarkable.

The woman started receiving treatment with methylprednisolone, in addition to ceftriaxone, amoxicillin and acyclovir. She was presumed to have atezolizumab-related hypophysitis, but further examinations ruled out the possibility of hypophysitis. Her condition worsened with recurrent fever episodes, adynamia, and somnolence. Three days later, CSF analysis showed an elevated leucocyte count and protein levels. CSF cytology was unremarkable. The diagnosis of encephalitis, it was associated with atezolizumab and bevacizumab therapy. Her condition worsened with respiratory failure on day 5. Pulmonary CT scan revealed aspiration pneumonia and she was transferred to the intensive care unit and kept on mechanical ventilation. She was treated with piperacillin and tazobactam. She undergone plasmapheresis. Her CK and myoglobin normalised after 3 sessions of the plasmapheresis. Dose of methylprednisolone was increased. CSF analysis on day 8 showed decreased cell count and protein levels. Her cognition was impaired severely. Thus, she started receiving steroidal pulse therapy with methylprednisolone, it led to further remission of clinical symptoms and CSF cell count. Neurological investigations demonstrated areflexia and a reduced tone in all 4 extremities. On day 10, electromyography showed a motor neuropathy with axonal and proximal demyelinating component, suggesting a critical illness myopathy possibly accompanied by immune-mediated polyradiculoneuropathy. Chest CT scan demonstrated resolution of infiltrations parallel to clinical improvement. On day 15, she underwent dilatative tracheostomy. She showed a significant inmprovement later on; however, she was unable to mobilize on her own. Motor investigations demonstrated a decreased tone, proximal and distal muscle weakness and areflexia. She was transferred to weaning rehabilitation clinic on day 21 of hospitalisation. Two months later, she started masticate and swallow. As she had severe critical illness neuropathy, mobilisation was not possible. Due to progression of HCC, her condition deteriorated. After 76 days of initial therpy with atezolizumab and bevacizumab, she died due to multi-organ failure.

Ozdirik B, et al. Atezolizumab and bevacizumab-induced encephalitis in advanced hepatocellular carcinoma: Case report and literature review. [Review]. Medicine 100: No. 24, 18 Jun 2021. Available from: URL: http://doi.org/10.1097/MD.0000000000026377

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