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Case report on atezolizumab-associated encephalitis in metastatic lung adenocarcinoma

P Thenmozhi[1*], Dinesh Kumawat[2]
[1] Department of Medical Surgical Nursing, Saveetha College of Nursing, SIMATS, Thandalam, Chennai, India
[2] M. Sc (NPCC) II Yr, Saveetha College of Nursing, SIMATS, Thandalam, Chennai, India

Abstract
Background: Nowadays immune checkpoint inhibitors have been used as a therapy in malignant tumor. Immune checkpoint inhibitors can cause various autoimmune side effects. Encephalitis associated with Atezolizumab has been rarely reported as an immune related effect.
Case Description: A 56 years old man with lung cancer that has been previously treated with surgery and chemotherapy was admitted with high fever, consciousness disorder, and motor aphasia. MRI report had shown no abnormalities. CSF shown cell count 20/l, protein 166 mg/dl, glucose 73mg/dl, and interleukin 6 82.9 pg/ml. It is diagnosed as Atezolizumab induced encephalitis.
Conclusion: Clinicians should be aware of the possibility of encephalitis after initiation of immune checkpoint inhibitors, because these types of case are very few, further investigation will be required to provide effective management for such life threatening conditions.

Keywords: atezolizumab, associated encephalitis and metastatic lung adenocarcinoma

Introduction
Atezolizumab is a monoclonal antibody that used to death ligant-1. Use of this drug can cause immune related adverse effect. The most common side effects are GI symptoms, fatigue, rash. Encephalopathy is a rare case of Atezolizumab associated.

Case Descreption
A 56 years old man with lung cancer that has been previously treated with surgery and chemotherapy was admitted with high fever, consciousness disorder, and motor aphasia. MRI report had shown no abnormalities. CSF shown cell count 20/l, protein 166 mg/dl, glucose 73mg/dl, and interleukin 6 82.9 pg/ml. It is diagnosed as Atezolizumab induced encephalitis. His clinical condition improved after use of steroid pulse therapy. Following steroid pulse therapy, Oral Prednisolone 30 mg was started. The CSF findings normalized on day 14 and he was discharged on day 16 without neurological imbalance. After discharge, he was treated with combination chemotherapy with a regimen of Docetaxel plus Remucirumab for lung adenocarcinoma without replace of encephalitis.

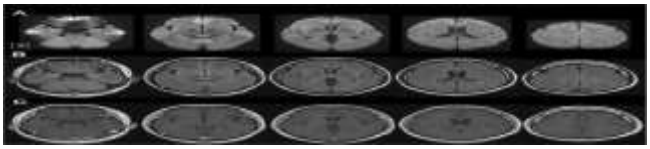

Fig 1: Brain magnetic resonance imaging on admission. There are no abnormal findings on (a) diffusion-weighted images, (b) fluid-attenuated inversion recovery, and (c) T1-weighted images with gadolinium enhancement.

Discussion
A case of encephalitis that occurred after treatment with Atezolizumab was presented. Early diagnosis and initiation of steroid pulse therapy were successful. Encephalitis associated with Atezolizumab has been rarely reported. These patients developed encephalitis about 2 weeks after treatment with Atezolizumab and showed fever and consciousness disorder. Some potential mechanisms include increased T-cell activity against antigens that are present in tumors and healthy tissue, increased levels of pre-existing autoantibodies, increased levels of inflammatory cytokines, and enhanced complement-mediated inflammation due to direct binding of an antibody against cytotoxic T-lymphocyte antigen 4 (CTLA-4) with CTLA-4 expressed on normal tissue. In the present case, the level of IL-6 in CSF was elevated in acute phase and normalized after steroid therapy. Because IL-6 in the CSF is a representative cytokine reflecting inflammation in the central nervous system, excessive production of inflammatory cytokines was likely the cause for developing encephalitis in this case.

Conclusion
A case of encephalitis associated with Atezolizumab was presented. Early diagnosis and steroid pulse therapy had shown successful response. The CSF level of IL-6 reflected the severity of the encephalitis. Clinicians should be aware of the possibility of encephalitis after initiation of immune checkpoint inhibitors, because these types of case are very few, further investigation will be required to provide effective management for such life threatening conditions.

Conflict of interest
None

Funding:
None

Consent for publication
Informed consent was obtained from the patients to publish this case in medical journal.

Ethical approval
Ethical approval is not required at our institution for publishing a case report in medical journal.

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