AUTOIMMUNE MENINGOENCEPHALITIS INDUCED BY IMMUNE-CHECKPOINT INHIBITOR USE: A SINGLE CENTER EXPERIENCE

Shin Hye Yoo¹, Miso Kim¹, Soon-Tae Lee², Bhumsuk Keam¹

¹Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea;

²Department of Neurology, Seoul National University Hospital, Seoul, Korea;

INTRODUCTION

- Immune checkpoint inhibitors (ICIs) have emerged as promising class of anti-cancer treatment in several types of tumor, but immune-related adverse events are occasionally encountered during ICI treatment.
- Autoimmune meningoencephalitis is a rare but fatal adverse event. However, little has been known about the natural course and optimal strategies to manage immune-related meningoencephalitis (irME).

METHODS

Retrospective review of clinical characteristics and the natural course of **three urothelial carcinoma** of bladder patients who developed irME induced by ICI

RESULTS

Presenting symptoms

- The most common presenting symptoms were **fever** and **altered mentality**, with the median onset of 14 days.

Measurements

- Cerebrospinal fluid analyses revealed pleocytosis and elevated protein level, but **negative** results for infectious etiologies.
- Malignant cells were **not** detected in cerebrospinal fluid.
- Paraneoplastic antibody** was observed in one patient (**Case 1**).

Treatments

- As irME was highly suspected, the patients were given steroid.
- Case 1 was completely recovered with concurrent steroid plus immunoglobulin (IVIG).
- Case 2 received IVIG as he did not show improvement with steroid and responded transiently, but finally recurred.
- In case 3, steroid resolved her altered mentation, but weakness of bilateral extremities due to Guillain–Barré syndrome remained and was partially recovered with IVIG and intravenous rituximab.

Tumor response

- Tumor size was decreased in 2 patients (**Case 2, Case 3**).

No.	Age /Sex	Drug	Disease	PD-L1 expression by IHC (SP142*)	Time to onset	CSF WBC (/μL)	CSF protein (mg/dL)	Immunosuppressive Treatment (D: day from onset)	Time to recovery
1	42/M	Anti-PD-L1 antibody plus MEK inhibitor	Urothelial cell carcinoma of bladder (HER2-amplified)	Negative	14 days	65 (P 0 L 6 O 58)	133	Steroid (mPd 1g daily 5 days) (D3-7) IVIG (0.4 g/kg/day 5 days) (D3-7)	10 days
2	49/M	atezolizumab (TECENTRIQ®)	Urothelial cell carcinoma of bladder (HER2-amplified)	Positive 1% on TC 7% on IC	14 days	50 (P 17 L 7 O 76)	218.1	Steroid (mPd 1g daily 5 days) (D3-7) IVIG (0.4 g/kg/day 5 days) (D5-9; D44-48)	Death
3	70/F	atezolizumab (TECENTRIQ®)	Urothelial cell carcinoma of bladder	Positive 1% on TC 5% on IC	15 days	30 (P 6 L 6 O 18)	358	Steroid (mPd 1mg/kg daily, then tapering to 15mg daily) (D4-) IVIG (0.4 g/kg/day 5 days) (D6-10; D27-31; D52-56) Mycophenolate mofetil (500mg twice a day) (D49-) Rituximab (375mg/m2 IV) (D47, D71, D78, D88)	22 days 80 days (to partial recovery of GBS)

Abbreviation: M, male; F, female; PD-L1, programmed death-ligand 1; MEK, mitogen-activated protein kinase kinase; HER-2, human epidermal growth factor receptor-2; IHC, immunohistochemistry; TC, tumor cell; IC, immune cell; CSF, cerebrospinal fluid; WBC, white blood count; P, polymorphonuclear cell; L, lymphocyte; O, other cells; mPd, methylprednisolone; IVIG, intravenous immunoglobulin; GBS, Guillain–Barré syndrome;

* VENTANA PD-L1 (SP142) Assay (Ventana Medical Systems Inc., Tucson, AZ)

CONCLUSIONS

irME associated with ICI develops early after the first dose given within two weeks. The natural course varies and fatal. The **prompt use of high dose steroid and IVIG treatment** after exclusion of infectious cause might be essential for **neurologic recovery**.

Keywords: immune checkpoint inhibitor; meningoencephalitis; neurological adverse event; steroid; intravenous immunoglobulin;

Contact email: bhumsuk@snu.ac.kr