Treatment-Emergent Parkinsonism Associated with BCMA-Targeted Chimeric Antigen Receptor T-Cell Therapy in a Patient with Schizophrenia

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Background

•Chimeric antigen receptor (CAR) T-cell therapy was first approved for treatment of select hematologic malignancies in 2017
•T-cells are genetically modified to express antigen receptors targeting B-cell precursors
•Ciltacabtagene autoleucel is a CAR-T therapy which express two B-cell maturation antibodies (BCMA) and a CD3-ζ domain to increase lymphocyte activation

Case Report

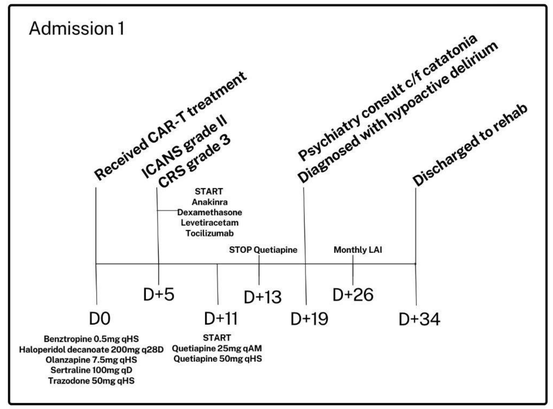
•69-year-old male with history of schizophrenia (complicated by medication-induced resting tremor) and multiple myeloma treated with Ciltacabtagene autoleucel T-cell therapy
•Post-treatment course was complicated by CRS (grade 3) and ICANS (grade 2); resolved with standard of care
•Post-infusion day 45 he developed right-sided Bell's palsy and new MNTs
•No improvement with changes to his antipsychotics
•Disordered movements returned to baseline with immunomodulatory therapy
•Cognitive changes persisted

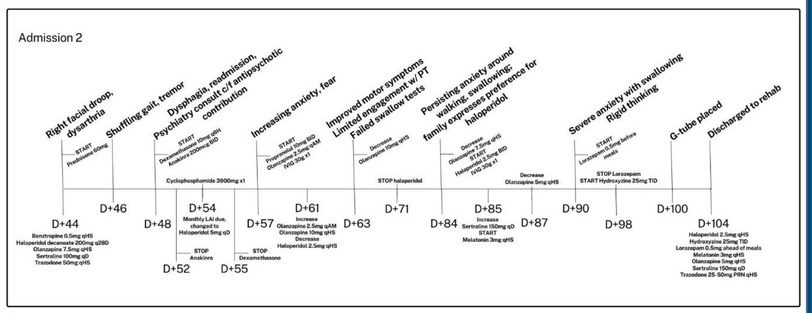
ICANS Consensus Grading[2]

Neurotoxicity Domain	Grade 1	Grade 2
Encephalopathy Score	7-9	3-6
Level of Consciousness	Awakens Spontaneously	Awakens to auditory stimuli
Seizure Activity	None	None
Motor Strength Findings	None	None
Elevated Intracranial Pressure; Cerebral Edema	None	None

CRS Consensus Grading[2]

Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever	T ≥ 38˚C	T ≥ 38˚C	T ≥ 38˚C	T ≥ 38˚C
		With		
Hypotension	None	No pressor requirement	Vasopressor +/- vasopressin	Multiple vasopressors
		And/Or		
Hypoxia	None	Low-flow Nasal Cannula	Highflow or Non-Rebreather	Positive Pressure





Common Neuropsychiatric CAR-T Side Effects[1]

Side Effect	Incidence	Timing
Cytokine Release Syndrome (CRS)	~95%	Median onset: 7 days Median duration: 4 days
Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)	~15%	Median onset: 8 days Median duration: 4 days
Movement and Neurocognitive Treatment-emergent Adverse Events (MNT)	~4%	Median onset: 26.5 days Median duration: 70 days

New Signs/Symptoms

- Right facial droop
- Dysarthria
- Dysphagia
- Masked facies
- Worsened BUE resting tremor
- New BUE postural, intention tremors
- Bradykinesia
- Shuffling gait
- Cognitive rigidity
- Worsened anxiety
- Auditory hallucinations newly benevolently

Discussion

•MNT incidence reported at 4%[1]
•Possible risk factors include high tumor burden, grade ≥2 CRS, ICANS, high CAR T-cell expansion and persistence
•Relative risk following exposure to dopaminergic antagonists remains unclear
•Only one published report of symptom remission with treatment[3]
•This patient's new parkinsonism resolved, however cognitive changes remained
•Available MNT reports focus on motor findings, little mention of cognitive symptoms
•May represent fertile area for future research and care

References

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