Management of Agitation Secondary to Immune Cell-Effector Associated Neurotoxicity Syndrome (ICANS) in a Pediatric Patient

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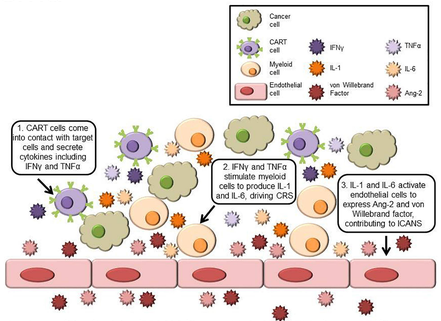
Background

Chimeric antigen T-cell therapy is an effective treatment for pediatric acute lymphoblastic leukemia

Immune cell-effector associated neurotoxicity syndrome (ICANS) is a potentially fatal side effect that can lead to cerebral edema[1]



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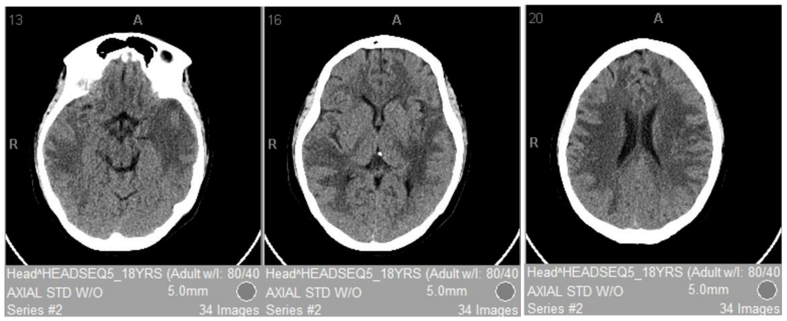
Case Presentation

18-year-old female with a past medical history of very high risk pre B-cell acute lymphoblastic leukemia s/p bone marrow transplant and CAR-T therapy presents with **decreased responsiveness and aphasia** one month after initiating CAR-T therapy

CT of head – multifocal confluent hypoattenuation of the supratentorial periventricular white matter with cortical involvement in the temporal lobes



Day 2 of admission
- Added two PRN medications for agitation
  1. Quetiapine
  2. Dexmedetomidine

Day 3 of admission
- Patient worsened clinically
- Transitioned to high dose IV methylprednisolone 1000mg qd

Psychiatry consulted for uncontrolled agitation and potential risk for self harm

Management

Day 6 (1)
- Psychiatry consulted for uncontrolled episodes of agitation
- Switched from quetiapine to olanzapine
- Started melatonin to help regulate patient's sleep cycle

Day 7 (2)
- Primary team added 24h 0.2mg clonidine patch
- Agitation plan updated:
1. dexmedetomidine bolus 0.5mcg/kg x2
2. olanzapine 2.5mg
3. diazepam 2mg

Day 8 (3)
- Increased nightly dose of olanzapine from 2.5mg to 5mg
- Scheduled a morning and afternoon dose of olanzapine 2.5mg for multiple episodes of agitation requiring multiple medications

Day 10 (4)
- Patient starts answering questions with slurred one word responses
- Agitation plan changed in preparation to discontinue dexmedetomidine
1. 179mcg clonidine
2. Up to two dexmedetomidine boluses of 0.5mcg/kg
3. diazepam 2mg

Day 12 (5)
- Discontinued dexmedetomidine
- Scheduled clonidine 50mcg q6h

Day 15 (6)
- Patient speaks in short phrases and asking simple questions
- No longer requiring PRN medications at night
- Stopped oral clonidine

Day 18 (7)
- Discontinued morning dose of olanzapine, followed by afternoon dose 48h later

Discussion

- The presentation and course of ICANS from CAR-T cell therapy are well-documented, but the concurrent psychiatric symptoms remain poorly understood[1]

Grade 1	Grade 2
Awakes spontaneously Fatigue	Awakens to voice Delirious/somnolent
Grade 3	**Grade 4**
Awakens to tactile stimulus Seizures that resolve with intervention Local edema on imaging	Comatose Motor weakness Life-threatening seizure Cerebral edema

- While quetiapine is an appropriate drug for initial management of agitation, adequate control was not observed
- We switched to scheduled olanzapine because it's been documented to alleviate the psychiatric symptoms associated with CAR-related encephalopathy syndrome (CRES)[2]
- Clonidine was added because of its known benefit in treating and controlling agitation[3]

Conclusion

- The combination of **scheduled olanzapine and clonidine** helped improve agitation and confusion and should be considered in other patients struggling with acute agitation secondary to ICANS

References

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