HUDDLE CARD
IMMUNE EFFECTOR CELL ASSOCIATED NEUROTOXICITY SYNDROME

Definition
Immune effector cell associated neurotoxicity syndrome (ICANS) is a potentially life-threatening neurotoxicity associated with immune effector cell therapies (e.g., CAR T-cell, tumor-infiltrating lymphocyte (TIL), bispecific T cell engager (BiTE) therapies). While the pathophysiology of ICANS is less understood, neurotoxicity is commonly associated with signs of increased trafficking of cells and proteins across the blood brain barrier. It is a common acute toxicity observed in over 50% of patients receiving CAR T-cells. ICANS is generally reversible and may occur concurrently, after, or independently of cytokine release syndrome (CRS).

Risk Factors
- Cytokine release syndrome (CRS)
- Pre-existing neurologic comorbidities
- Younger age
- High disease burden or ALL as underlying disease
- High intensity lymphodepleting therapy (e.g., fludarabine, cyclophosphamide, etc.)
- High number of administered CAR T-cells
- Pre-treatment elevated LDH, decreased platelet or endothelial growth factor, and high levels of ferritin concentration on day 3 post administration.

Clinical Manifestations
- Typically presents within 5 days after immune effector cell therapies are administered, but delayed ICANs can occur 3-4 weeks post treatment.
- Early signs include changes in handwriting, impaired attention or confusion, and mild issues with language expression and understanding.
- Can progress to decreased level of consciousness, seizures, coma, motor weakness, and cerebral edema.
- Fatal neurotoxicities were caused by cerebral edema and all were associated with CRS.
- Severe CRS is associated with severe ICANS.

Diagnostic Assessment
- ICANS grading scales (e.g., immune effector cell-associated encephalopathy (ICE) score)
- Work-up to rule out other etiologies.
    - E.g., infection, malignancy, stroke, or hemorrhage
- EEG, neuroimaging, lumbar puncture (LP)
- EEG commonly shows a diffuse slowing in critically ill patients (a non-specific indicator of encephalopathy)
- Imaging may be normal even with neurotoxicity
- LP may show elevated protein concentration and lymphocytes including CAR T-cells.

HUDDLE CARD
IMMUNE EFFECTOR CELL ASSOCIATED NEUROTOXICITY SYNDROME

Interventions

- The neurology team should be consulted if the patient is symptomatic.
- Steroids (e.g., dexamethasone and methylprednisolone) are first-line therapy and dosing varies based on neurologic symptoms.
- Tocilizumab should be administered only if ICANS is concurrent with CRS.
- For Grade 3 and 4 ICANS toxicities, ICU treatment is recommended including the consideration of airway protection through intubation and mechanical ventilation.
    - Consider seizure control with anti-epileptics.
    - High dose corticosteroids- e.g., Methylprednisolone 1000mg/day
    - Lower intracranial pressure through elevating the head, hyperventilation, and hyperosmolar therapy.

Nursing Considerations

- Routine assessment and monitoring and prompt detection of toxicities are necessary for patient safety.
- Accurate interventions with supportive therapy and steroid management
- Provide emotional support and education to patients and family.

References

Dietrich, J., & Frigualt, M. (2023). Immune effector cell-associated neurotoxicity syndrome (ICANS). UpToDate. Retrieved September 26, 2023 from https://www.uptodate.com/contents/immune-effector-cell-associated-neurotoxicity-syndrome-icans

Lee, D.W., Santomasso, B.D., Locke, F.L., Ghobadi, A., Turtle, C.J., Brudno, J.N…Neelapu, S.S. (2019). ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biology of Blood and Marrow Transplantation, 25*(4), 625-638. https://doi.org/10.1016/j.bbmt.2018.12.758

Robert, C. S., & Rosalie, M. S. (2022). Immune effector cell associated neurotoxicity syndrome in chimeric antigen receptor-t cell therapy, 13. https://doi.org/10.3389/fimmu.2022.879608

Schubert, M.-L., Schmitt, M., Wang, L., Ramos, C. A., Jordan, K., Müller-Tidow, C., & Dreger, P. (2021). Side-effect management of chimeric antigen receptor (car) t-cell therapy, 32(1), 34–48. https://doi.org/10.1016/j.annonc.2020.10.478

October 2023