22nd INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM

Nursing Perspective on Managing Neurotoxicity – What Tools Do We Have?

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Disclosures

Speaker for Pfizer, Inc.

Immune Related Adverse Events

Manageable and reversible but can be fatal

Requires timely recognition and early intervention

2 most common adverse events are

- Cytokine Release Syndrome (CRS)
- Neurotoxicity
  - Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

What Are Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and CRS?

- Definition of ICANS
  - “ICANS is a clinical neuropsychiatric syndrome that occurs in patients treated with immunotherapy”
- Not clearly understood but surmised that cytokines cross the blood-brain barrier which causes inflammatory cascade

- Definition of CRS
  - An inflammatory syndrome that can occur after immunotherapy and cellular treatments

Therapies with toxicities related to immune activation

- Immune Effector Cell (IEC) Therapy
  - Chimeric Antigen Receptor T-Cell (CAR T-Cell)
  - Tumor Infiltrating Lymphocyte (TIL)
  - Chimeric Antigen Receptor Natural Killer Cell (CAR-NK cell)
  - T Cell Receptor (TCR)

- BiSpecific Antibodies (BsAbs) Therapy

Risk Factors and Mitigation

CAR T-cells

Risk factors

- Tumor burden
- Cell dose
- Concurrent infections

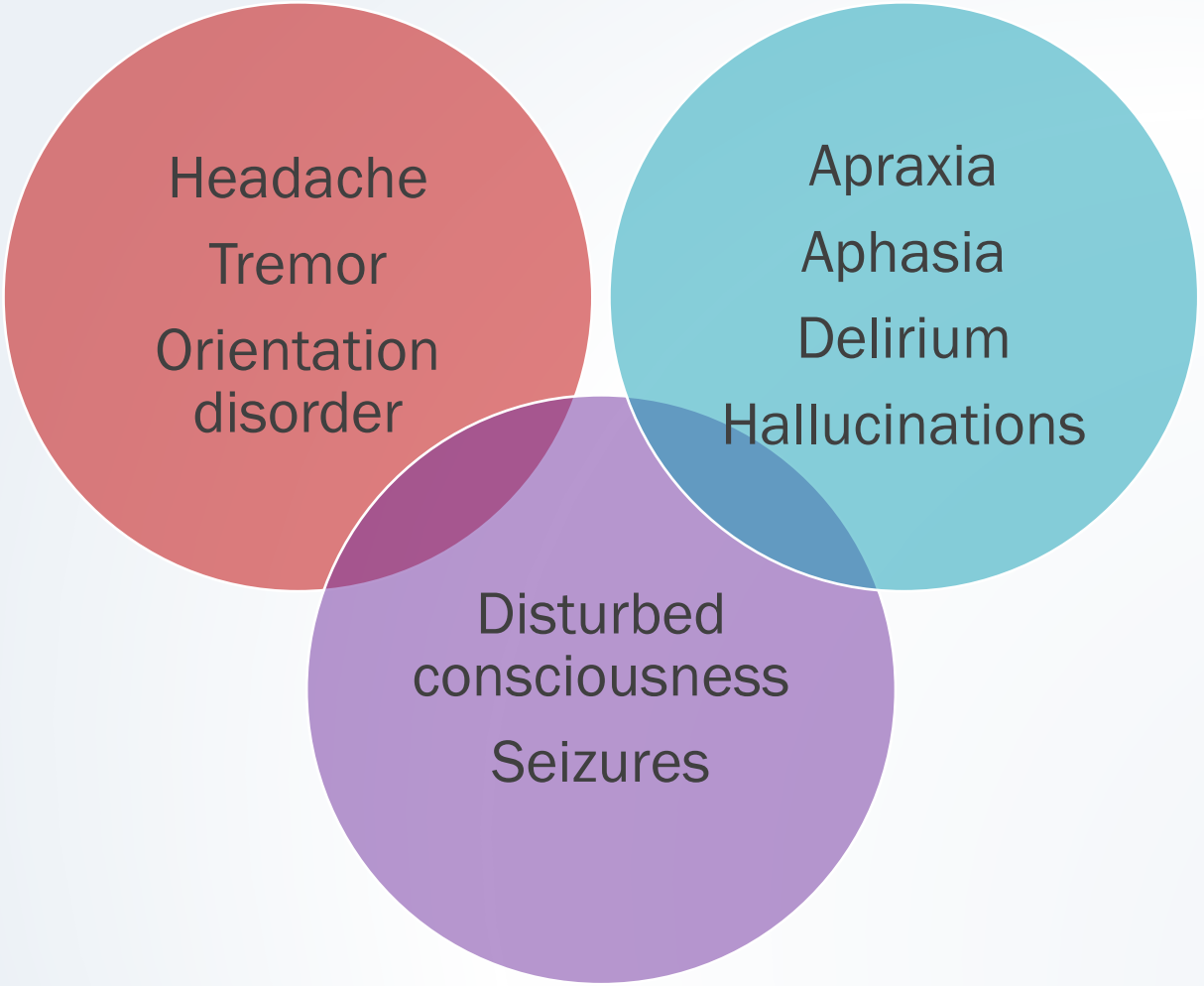
Mitigation measures

- Cytoreductive chemotherapy
- Early intervention
- Rule out/treat infection

Bispecific antibodies

- **Risk factors**
  - Tumor burden
- **Mitigation measure**
  - Step-up dosing
  - SQ vs. IV
  - Use of pre-medications
  - Cytoreductive chemotherapy
  - Early intervention

Signs and Symptoms of ICANS



Nursing Management - Tools

ICE scoring

- Effective tool in identifying CRS/Neurotoxicity

– 5 sections with point scoring:

1. Orientation (4 points): Orientation to year, month, city, hospital
2. Naming (3 points): Name 3 objects – point to pen, clock, computer etc
3. Following Commands (1 point): Ex: show me 2 fingers, close your eyes and stick out your tongue
4. Writing (1 point): Ability to write a standard sentence (eg Our national bird is the bald eagle)
5. Count backwards from 100 by 10 (1 point)

- Score of 10 = no impairment
- Score of 7-9 = Grade 1 neurotoxicity
- Score 3-6 = Grade 2 neurotoxicity
- Score 0-2 = Grade 3 neurotoxicity
- Score of 0 = Grade 4 – medical emergency

ICE Tool (Immune Effector Cell-Associated Encephalopathy)	
Orientation to year, month, city, hospital: 4 points	
Name 3 objects (e.g., point to clock, pen, button): 3 points	
Following Commands: (e.g. Show me 2 fingers or Close your eyes and stick out y…	
Writing: Ability to write a standard sentence: (e.g. Our national bird is the bald eag…	
Count backwards from 100 by ten: 1 point	
Total Score	
CAPD (Pediatric Neurotoxicity Grading if unable to complete ICE)	
Does the child make eye contact with the caregive?	
Are the child's actions purposeful?	
Is the child aware of his/her surroundings?	
Does the child communicate needs and wants?	
Is the child restless?	
Is the child inconsolable?	
Is the child underactive-very little movement while awake?	
Does it take the child a long time to respond to interactions?	
CAPD Score	
Cytokine Release Syndrome (CRS) Symptoms	
Temp	36.6 (97.9)
Hypotension Noted	
Hypoxia Noted	
ASTCT CRS Consensus Grade	
Treatment Type in Progress for CRS	

Neurotoxicity Grade (a.)	Tocilizumab (b.)	Steroids (b.)
Grade 1: ICE score 7 to 9 Mild drowsiness, confusion, limiting ADLs, dysphagia	**Concurrent CRS:** Manage by grade **No CRS:** Do not give tocilizumab	Supportive Care
Grade 2: ICE score 3 to 6, Moderate drowsiness, confusion, disorientation, limiting ADLs, dysphagia limiting communication	**Concurrent CRS:** Manage by grade **No CRS:** Do not give tocilizumab	Consider dexamethasone 10mg as needed
Grade 3: ICE Score 0 too 2, awakens to tactile stimuli only, focal/rapid seizure	**Concurrent CRS:** Manage by grade **No CRS:** Do not give tocilizumab	Dexamethasone 10mg every 4 to 24 hours
Grade 4: ICE Score 0, requires vigorous stimuli to arouse, coma, prolonged seizure (> 5 minutes)	**Concurrent CRS:** Manage by grade **No CRS:** Do not give tocilizumab	Methylprednisolone 1g IV x 3/days

CRS Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever	Temperature ≥ 38 °C	Temperature ≥ 38 °C	Temperature ≥ 38°C	Temperature ≥ 38 °C
			With	
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
			And/or	
Hypoxia	None	Requiring low-flow nasal cannula or blow-by	Requiring high-flow nasal cannula, facemask, nonrebreather mask or Venturi mask	Requiring positive pressure (eg, CPAP, BiPAP, intubation and mechanical ventilation)

Nursing Intervention and Treatment

- Treatment is dependent upon the severity
- Focus is mainly supportive
- Full sepsis workup
- Frequent vital signs
- Symptom control
- ICU screening for Grades greater than or equal to 3

Nursing Intervention and Treatment

- More frequent neurologic assessment
- Mainstay is supportive care
- Aspiration and seizure precautions
- Imaging – MRI, CT Brain
- Lumbar Puncture
- Electroencephalogram (EEG)
- ICU screening – may require intubation for airway protection

Medications Used to Treat Neurotoxicity

- Prophylactic anti-seizure
- Corticosteroids
- Anakinra
- Tocilizumab not given unless concurrent CRS

Management at Home

- Nurses play a vital role in ensuring patients know what to look out for at home:
  - Fever – especially 100.4°F
  - Symptoms of hypoxia and hypotension if pulse oximetry and blood pressure cuff is unavailable
    - SOB, lethargy, weakness, diaphoresis

- Remain within 2 hours (optimally 30 minutes)
- Self-monitoring – temperature, change in speech, hand tremors, trouble writing, change in consciousness
- No Driving (BsAb only if symptomatic)
- Stay hydrated

Patient and Family Factors

- May affect whether or not patient is a candidate for cellular therapy or bispecifics
  - Distance to hospital or office
  - Transportation for frequent visits
  - Support system at home
    - Monitoring for side effects at home

Conclusion:

- Nursing interventions play a large role in the management of neurotoxicity
  - Patient and family education
  - Pharmacological management and knowledge
  - Symptom identification

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THANK-YOU!

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