CANCER EDUCATION DAY

Acute and Chronic Toxicities: Systemic Treatment

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WINDSOR REGIONAL HOSPITAL
OUTSTANDING CARE – NO EXCEPTIONS!

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Systemic Treatment

1. Chemotherapy toxicity
2. Immune Checkpoint Inhibitor (ICI) Therapy Toxicity

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Chemotherapy toxicity

- **Chemotherapy Regimens**: Side effects are not unique to H&N cancer patients
- **General Side Effects**: Myelosuppression/nausea/vomiting etc
- Platinum based Chemotherapy (Cisplatin/carboplatin)
- Taxanes (Paclitaxel/docetaxel)
- 5 F-U (fluorouracil)
- Cetuximab

Chemotherapy Regimens

- **Platinum**: Nephrotoxicity, ototoxicity, Peripheral neuropathy
- **Taxanes**: Allergic reactions, neurotoxicity
- **Fluorouracil**: Mucositis, cardiotoxicity, Hand-Foot syndrome
- **Cetuximab**: Hypersensitivity reactions, exacerbated radiation-induced mucositis and radiation-induced skin reactions.

Cisplatin Toxicity

- **Peripheral Neuropathy**: Dose limiting,~ 30%, partially reversible
- **Clinical manifestations:**
  - Bilateral Numbness, paresthesia and occasional pain initially affects toes and fingertips
  - Decreased vibration and loss of ankle reflex
  - NCS reveal sensory axonal damage

Prevention and Treatment

- **Risk factors**: Increased age at diagnosis, smoking, excessive alcohol use
- Most patients recover over time but not fully
- No effective preventive strategies
- **RX**:no effective therapy, Symptomatic, Duloxetine/tricyclic antidepressants, opioids etc

Cisplatin Toxicity

- **Ototoxicity**: often irreversible (~ 20%)
- Bilateral high frequency sensorineural loss, usually, associated with tinnitus
- Often permanent
- **Risk factors**: age, cumulative dose, concomitant ototoxic drugs, synergistic effect of radiation
- **Monitoring**: audiometry
- **Treatment**: no specific RX
- STS (Sodium thiosulphate), Amifostine, intratympanic steroids
  - Insufficient data

Cisplatin Toxicity

- **Nephrotoxicity**: ~ 30%, dose limiting
- **Risk factors**: higher cumulative doses, prior kidney disease, eGFR <50, older age, dehydration, concomitant nephrotoxic medication
- **Clinical manifestations**: acute (within days to weeks), partially reversible
- Rise in serum creatinine, electrolyte abnormalities, polyurea due to impaired concentrating ability

Prevention and Treatment

- Isotonic normal saline with electrolytes, promotes diuresis and dilution of cisplatin
- Avoid nephrotoxins like NSAIDS, aminoglucosides, amphotericin B, etc.
- No established role of drugs like STS, amifostine etc.,
  - Not cost effective
- Chemotherapy dose modification or use of alternative chemotherapy like carboplatin
- **AKI**: full or partial recovery within weeks if adequately treated

Immune Checkpoint inhibitor (ICI) Therapy

- Immune therapy like Pembrolizumab/Nivolumab enhance the immune response of the body by activating T-cells (PD1/PDL1, CTL4A)
- Toxicities from immune activation and not direct cytotoxicity like chemotherapy
- May occur any time, even after stopping therapy.
- Often reversible if recognized early.

Common Toxicities

- **Skin**: ~ 20-40% (Rash, pruritus etc.)
- **GI:** ~ 20% (diarrhea/colitis)
- **Pneumonitis**: ~5 % (cough/dyspnea/hypoxia)
- **Endocrinopathy**: ~ 10-20%(thyroid)
- **Other rare**: (cardiac/neurologic)
- **Systemic Adverse Effects**: mild fatigue, fever, infusion reactions

Management

- **Grade 1**: Con't ICI, monitor
- **Grade 2**: Hold ICI, oral steroids
- **Grade 3**: Admit, High dose steroids
- **Grade 4**: Permanently discontinue therapy, steroid taper 4-6 weeks

Thank you!

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