NEET SS ANAESTHESIA
ONCOANAESTHESIA

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MODALITIES OF ANTICANCER TREATMENT AND PERIOPERATIVE IMPLICATIONS

Chemotherapy 00:00:40

Chemotherapy affects the following systems :

- Central nervous system.
- Cardiovascular system.
- Pulmonary system.
- Renal.
- Hepatic.
- Immunological system.
- Haematopoeitic system.

CNS toxicity :

- Common adverse effect : Limiting factor.
- Cumulative dose/dose intensity.

Risk factors :

- DM.
- Advanced age.
- Hereditary neuropathies.
- Previous treatment with neurotoxic agent.

Symptoms :

i. Peripheral neuropathy : Chemotherapy induced peripheral neuropathy (CIPN).
   - Pins and needle sensation.
   - Ants crawling sensation.

ii. Central (Autonomic) neuropathy
   - Reduced autonomic reflexes.
   - Large fluctuations in hemodynamics during postop.

Symptoms usually start during treatment and stabilise after that.
Implicated agents : Vince alkaloids, platins, paclitaxel and dorcetaxil.

Central neurotoxicity :

- Encephalopathy.
- Acute cerebellar syndrome.
- Posterior reversible encephalopathy syndrome.
- Aseptic meningitis.
- Cognitive deficits.
- Hemiparesis.
- Progressive dementia.

Peripheral neuropathy

- Predominantely affects sensory neurons.
- Autonomic dysregulation.
- Regional anaesthesia not contraindicated but pre-existing neurological abnormality should be documented.

Cardiovascular system :

- Cardiotoxicity → mechanism is not understood.
- Chemotherapy → Damage myocytes → Limited repair.

Plethora of symptoms :

- LV dysfunction.
- Arrhythymias.
- Heart failure (HF).
- myocardial ischemia.

Drugs implicated (CATAPAA) :

- Cytotoxic antibiotics.
- Arsenic Trioxide.
- Taxanes.
- Anthracyclines.
- Platinum compounds.
- Alkylating agents.
- Antimetabolites.

Drug class	Effect on CVS
Cytotoxic antibiotics (Pneumonic : C8M) (Bleomycin/Mitomycin)	Cardiomyopathy
Arsenic trioxide Taxanes (Docetaxel, Paclitaxel)	QT prolongation Ventricular arrhythymias Bradycardia AV Blocks
A- Antimetabolites Gemcitabine, Capecitabine, 5- Fluorouracil, Tioguanine, Fluoropyrimidines	Myocardial Ischemia Heart failure Atrial Fibrillation
P – Platinum Compounds Carboplatin, Cisplatin, Oxaliplatin	Heart failure Atrial fibrillation (12-33% Cisplatin) Torsades de pointes
A- Anthracyclines : Major group Irreversible Cardiotoxicity Incidence – 9-18%	ECG changes (Early signs). Nonspecific ST and T wave changes. Decreased QRS voltage. Prolongation of QT interval. Supraventricular arrhythmias (Atrial Fib : 2-10%). Transient LV dysfunction. Late – Decline in LVEF : Dilated cardiomyopathy.
A- Alkylating agents Cyclophosphamide, Ifosfamide, Mel- phalan, Treosulphan, Mitomycin C, Busulfan.	Myocardial Ischemia. Heart failure. Atrial Fibrillation.

Respiratory system :

Many CT agents

- Bleomycin (most commonly known).
- Alkylating agents.
- Antimetabolites.
- Mitomycin C.
- Gemcitabine.
- Paclitaxel/Docetaxel.

Bleomycin induced pulmonary toxicity :

- Most commonly known pulmonary toxicity.
- Interstitial pulmonary fibrosis (ITP).
- Concentration >400 IU/m^2.
- Incidence : 5-16%
- Life threatening.
- Lung injury within 6m.
- Lung injury progress to chronic pulmonary toxicity.
- Fractional inspired O2 concentration (FiO2).

- SpO2 – 88-92%
- Symptoms
  - Dry cough.
  - Rhales on auscultation.
- ILD – Restrictive lung disease.

Drug class	Pulmonary toxicity
Alkyating agents (Especially mitomycin C)	ARDS Bronchospasm Intersitial pneumonitis Diffuse Alveolar haemorrhage (DAH)
Antimetabolites	Interstitial pneumonitis DAH Capillary leak syndrome Pleural effusion
Platinum compounds (Carboplatin, Cisplatin & Oxaliplatin)	Interstitial pneumonitis
Gemcitabine	DAH Interstitial pneumonitis Capillary leak syndrome Non cardiogenic PE Pleural effusion
Taxanes (Pacilataxel, Docetaxel)	Interstitial pneumonitis Capillary leak syndrome Pulmonary toxicity occurs in days to weeks.

CT induced pulmonary toxicity :

- Course of pulmonary toxicity - weeks to months.
- Symptoms
  - Cough, dyspnoea, low grade fever.
  - Bibasal crackles.
- Investigations
- CXR – U/L or B/L reticular markings.
- ↓ DLCO.
- Spirometry : ↓ TLC and FVC.

Renal system :

- CT agents : Renally excreted.
- Alkylating agents, antimetabolites, platins.
- Chemotherapy induced acute kidney injury (AKI).
- AKI : Presents as prximal tubular injury.
- Proteinuria.
- Phosphate wasting.
- Fanconi syndrome : Hypophosphataemia, hypokalemia, glycosuria, proteinuria (HHGP).
- magnesium wasting.

Cisplatin induced renal toxicity :

- Cisplatin : Notorious due to AKI.
- HIPEC surgeries : U/O monitored carefully.
- ↓GFR.
- ↓ Sr magnesium (Due to ↑ magnesium wasting)/potassium/calcium.
- Deranged KFT.
- Dose related.
- Reversible.
- W/F signs and symptoms of Hypomagnesemia.

CT induced renal toxicity :

Ifosfamide (Alkylating agent)

- Proximal Tubular injury.
- Fanconi Syndrome.
- Nephrogenic diabetes insipidus .

methotrexate

- Intratubular precipitation.

mitomycin C

- Microangiopathic hemolytic anaemia.
- Renal failure.

Hepatic system :

- CT agents : metabolized in liver.
- Risk : ↑ preexisting liver dysfunction.

Clinically

- Usually, asymptomatic.
- Only increase in liver enzymes.
- Inflammatory hepatitis.
- Cholestasis.
- Steatosis.
- End stage liver disease.

Drug class	Pulmonary toxicity
Alkylating agents/platinum compounds	Hepatic Sinusoidal injury Sinusoidal obstruction syndrome Centrilobular hepatocyte necrosis
Antimetabolites	Steatosis Steatosis : Increased risk of intra-operative blood loss and postoperative complications
Topoisomerase (Irinotecan, topotecan)	Increase in enzymes (Transaminases) Steatosis Critical Hepatocellular injury
Vinca alkaloids (Vincristine)	Transient increase in transaminases

Grading of severity : WHO/ National Cancer Institute grading of severity for CT induced liver toxicity.

Haematological system :

- Alkylating agents, anthracyclines.
- Antimetabolites, arsenic trioxide.
- Cytotoxic antibodies, platinum compounds.
- Vinca alkaloids.

Clinical features

- Bone marrow suppression.
- Increased risk of thrombosis.

Immune response and CT :

- Affects innate & acquired immune system.
- Innate – myelosuppression.
- Myelosuppression – CT induced neutropenia (CIN).
- Febrile (>38.5oC) neutropenia on two occasions.
- 50% : Solid tumors.
- 80% : Hematological malignancies.

Pancytopenia (↓ erythrocytes, leucocytes, & platelets).

- Perioperative period → Hemorrhage → ↓ O2 Carrying capacity.
- Complicated by preexisting anemia.
- WBC (ANC) : Infection rates ↑
- Bm recovery : Take upto 6 weeks.

Adaptive immune system : Immunosuppression

- Lymphopenia.
- Depends on the CT agent used, malignancy type.
- Alkylating agents/Protein Kinase Inhibitors : Impaired function of peripheral "T" cells.
- Platinum compounds : Enhance "T" cell activation by dendritic cells.

CT and thrombosis :

- Cancer and Neo-adjuvant CT (NACT).
- Both conditions
  - ↑ inflammatory response (↓ antithrombin, protein C).
  - ↑ Procoagulant response (↑ TF expression).
  - ↑ Antifibrinolytic response.
  - ↑ Pro-aggregative response.
- Increased risk of thrombosis – persists upto 6months.
- Extended thromoprophylaxis for 4 weeks after surgery.
- Increased perioperative risk of thrombosis.
- Patients can be on Anticoagulants.
- Timing of neuraxial block : ASRA guidelines.

Cancer immunotherapies :

- Manipulate host's immune system.
- Reactivate the antitumor immune response.

Different immunotherapies :

- Interferon.
- Immune checkpoint inhibitors (ICIs).
- Chimeric antigen receptor T Cells.

Toxicity of immunotherapy :

Immunotherapy (Toxicity)

- Endocrine.
- Cardiac.
- Pulmonary.
- Hepatic.
- Miscellaneous S/E : Fever, fatigue, nausea, diarrhoea, thrombopenia and leukopenia.

Immune checkpoint inhibitors (ICIs)

Endocrinopathies

- Hypophysitis (Inflamed pitutary gland).
- Hypothyroidism/Hyperthyroidsm.
- Adrenal insufficiency.
- Hypongonadism.
- Diabetes Insipidus.
- IDDM.

Cardiac toxicity of immunotherapy :

Cardiac toxicity (Overall < 1%).

Myocarditis most common (1.14%).

- ↑ Ipilimumab + Nivolumab (0.27%).
- Nivolumab alone : 0.06%
- Median onset time : 17 days.
- Grade : 1 (Asymptomatic).
- Grade 2 Mild.
- Grade 3 Completely symptomatic.

Symptoms and Signs :

- Fatigue.
- Dyspnoea.
- Chest pain.

Investigations : Raised BNP, Troponin, ECG abnormalities.

Management :

- High dose glucocorticoids.
- Alternatively immunosuppressants.

Other effects :

- Cardiac fibrosis
- Pericarditis
- Arrhythymias
- Heart Failure
- Cardiomyopathy

Pulmonary toxicity of immunotherapy :

Pneumonitis (most common)

- PD-1 inhibitors : Incidence 3-7%
- PDL1 incidence 1.3%
- Life threatening.

Symptoms

- Pneumonitis : Non specific symptoms.
- Cough.
- Chest pain.
- Wheezing.
- SOB.
- Respiratory failure/hypoxemia.
- CT : Ground glass opacities with peripheral consolidations.

Gastrointestinal toxicity of Immunotherapy :

- most common S/E.
- Diarrhoea.
- Gastritis.
- Enterocolitis (most common).
- Incidence 20-30%

Hepatitis (5-10%) :

- Anti PD 1, hepatitis (5%).
- Ipilimumab + Nivolumab : 30%
- Screening for Immune hepatitis – done before starting of therapy.
- Grade 3 hepatitis (AST/ALT > 5x).

Monoclonal antibodies

00:41:22

Drug class (Monoclonal Antibodies)	Indication
Transtuzumab (Her2/neu inhibitor)	Breast Cancer
Bevacizumab (VEGF- inhibitor)	Colorectal cancer
Imatinib	GIST
Panitumumab	Colorectal cancer
Sorafenib (multikinase inhibitors)	Renal cell Carcinoma
Sunitinib	Renal Cell Carcinoma

Systemic effects of monoclonal antibodies :

Drug class	Toxicity
Sorafenib	Rash, diarrhoea, hand and foot syndrome
Sunitinib	Fatigue, nausea, diarrhoea, hypertension, myelosuppression, Hand and foot syndrome
Transtuzumab	Cardiac dysfunction, Decrease in LVEF
Bevacizumab	Hypertension, proteinuria, bleeding, poor wound healing, visceral perforation
Imatinib	Fluid retention

Drug class	Hepatic system effects
HER – 2 inhibitors • Transtuzumab • Lapatinib	Elevated LFTs Sinusoidal obstruction syndrome, hepatitis
Small molecule TKIs & VEGF inhibitors • Imatinib • Vemurafenib • Erlotinib • Geftinib • Crizotinib • Sorafenib	Elevated LFT's Hepatitis Cholestatic Hepatitis Granulomatous Hepatitis Hepatocellular liver injury Acute liver failure
Check –point inhibitors • Nivolumab • Pembrolizumab • Atezolizumab • Darvalumab	Eevated LFTS Hepatitis Cholestatic Liver injury Hepatocellular Liver injury

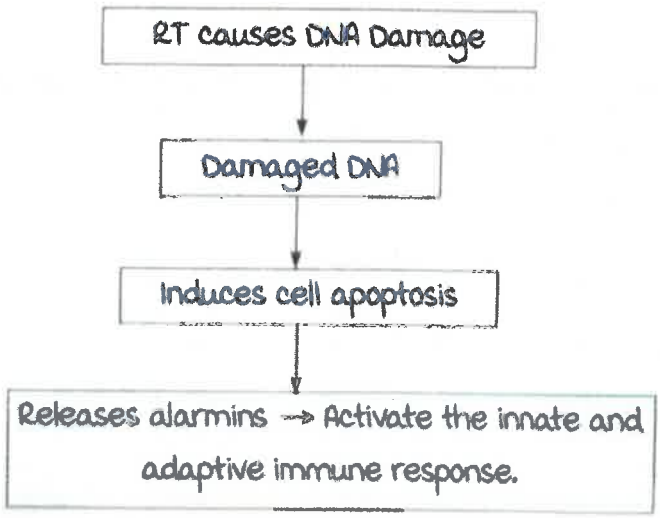
Radiotherapy

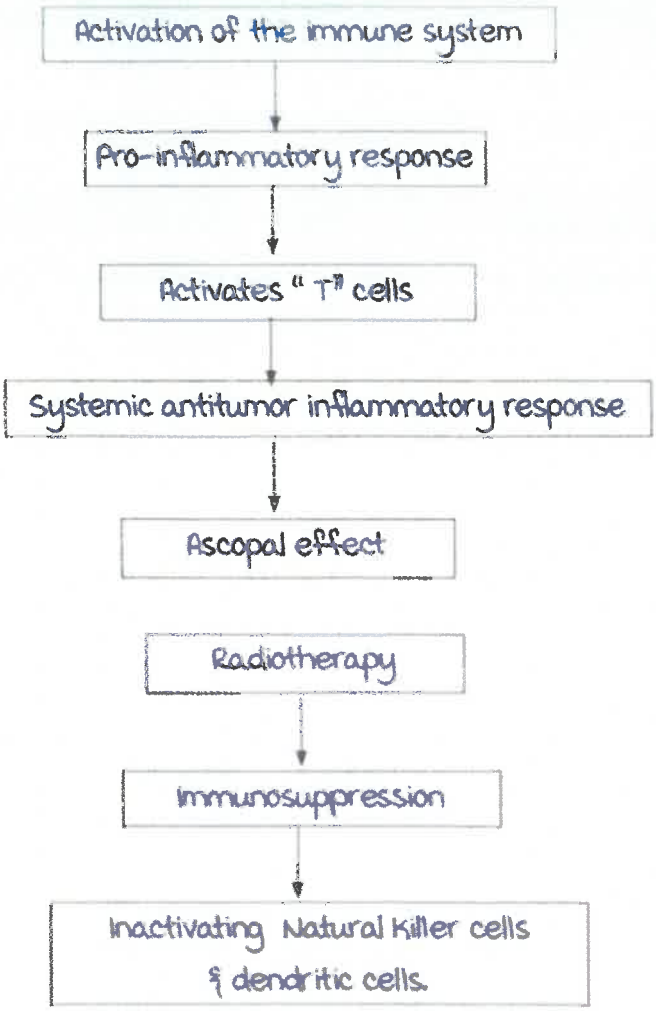
00:46:08

Affects the following systems

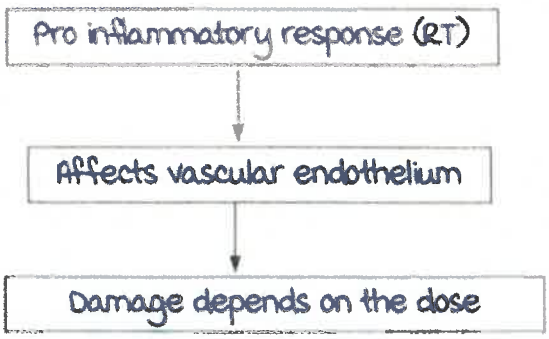
i. Immune system.
ii. Cardiovascular.
iii. Pulmonary.
iv. Head and neck.
v. Skin.
vi. Mucosa.

Effect of RT on Immune system :





RT induced vascular thrombosis :



- mild dose (5-10 Gy per fraction) → Damage is mild.
- Doses > 10 Gy → more damage → ↑ Vascular permeability.
- Can lead to thrombosis.

Cardiac toxicity of RT :

- Thoracic RT (Hodgkin's lymphoma, Ca breast).
- Cardiac toxicity : endothelial damage + Oxidative stress + inflammation + DNA damage.

Can damage any cardiac component

- Pericardium.
- myocardium.
- Heart valves.
- Conduction system.
- Coronary arteries.

Pericardium

- Exudative Pericarditis.
- Pericardial effusion.

Exudative Pericarditis :

- Develops early.
- Hemodynamic instability.
- Self limiting.

Conduction abnormalities :

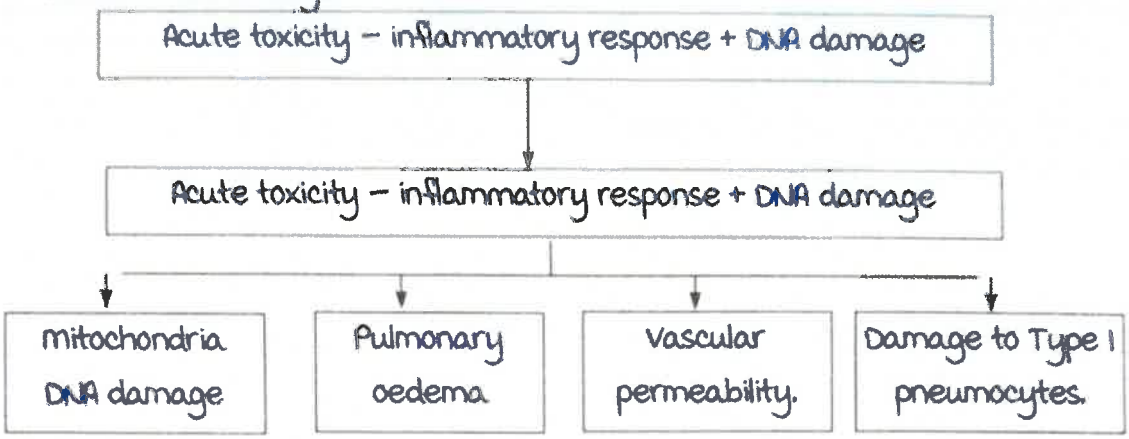
- Early complication.
- Self limiting within 12 m.
- AV block/ QTc prolongation.
- Supraventricular arrhythmia /ventricular Tachycardia.

Late complication : CAD.

Restrictive cardiomyopathy due to fibrosis.

Pulmonary toxicity of RT :

- Lung injury – three phases.
  a. Acute
  b. Subacute
  c. Late
- Acute – hours/ days.



Acute → Chronic (2-6m post RT) → Pneumonitis

Side effects :

- Mean lung dose.
- Proportion of lung dose > 20 Gy.
- Underlying comorbidities.
- CT scan – Asymptomatic ↑ density.

Clinically : s/o sterile pneumonitis

- Low grade fever.
- Dysnoea.
- Non-productive cough.
- Severe symptoms – Mx with steroids.
- Sx : Happens in subcaute phase .
- Not at ↑ risk of PPCs.

Late pulmonary toxicity

- Occurs 9-12 months.
- Irreversible remodeling of lung parenchyma.
- Increased stiffness.
- Fibrosis and thickening.

RT of Head & Neck :

- Head and neck : most important concern.
- Anticipated difficult airway.
- Acute.
  - Mucositis/Fistulae.
  - Osteonecrosis.
  - Lack of dentition.

  } Difficult BMV
- Later : Fibrosis of neck → ↓ Neck Extension.
- Fibrosis : (Floor of mouth/facial muscles).
- TMJ fibrosis → Trismus.

  } Limited MO
- Glottic/ epiglottic edema.
- Swollen oral mucosa.
- Glossomegaly.

  } Difficult laryngoscopy and intubtion.
- Fibrosis & oedema → Suprahyoid region → Limited neck mobility.
- Mobility of larynx compromised externally.
- Oral mucositis : Bleeds on dlscopy.
- RT administered to neck → Thyroid abnormalities.
- Hypothyroidsm should be ruled out.

External Beam Radiation therapy (EBRT) :

- Preoperatively : Carcinoma Rectum/Ca Cervix.
- Tissues adherant/ tissue fibrosis/obstructred lymphatics.
- ↑blood loss.
- ↑surgical duration.
- ↑surgical stress.

Anaesthetic implications

00:56:32

Organ system	Preoperative considerations	Intraoperative Considerations
Cardiac	• 12 lead ECG • QT interval • 2D ECHO • Lab tests – Plasma troponin NT-pro BNP	• Invasive monitoring as per patient's status • 5 lead ECG • Stress dose glucocorticoids as needed • Avoid QT prolonging drugs (Ketamine, Etomidate, isoflurane, sevoflurane, desflurane, succinylcholine, 5HT3 antagonists, Antidepressants, β-blockers, antifungals) LA (Toxic dose) • Avoid hypothermia • Fluid management

Organ system	Preoperative considerations	Intraoperative Considerations
Pulmonary	• Room air SpO2 • CXR • BHT • PFT • DLCO • CT scan	• Room air SpO2 • CXR • BHT • PFT • DLCO • CT scan
Hepatic	• Lab test • Hepatic transaminases • INR	• Avoid hepatotoxic drugs
Renal	• Labs - Urea/Cr • GFR	• Fluid management • Electrolyte correction (Mg^{2+}, K^{+}, Ca^{2+}) • Avoid nephrotoxic drugs
Endocrinopathy (Immunotherapy)	• TSH, Free T4 • HbAIC, ACTH, cortisol, electrolytes • Cardiac troponins at 6 weeks after treatment	• Stress dose steroids • Balanced fluid management • Electrolyte monitoring • Interaction with antidepressants and antiemetics
Central and Peripheral neuropathy	• Detailed assessment and documentation of any baseline neurological deficit	• Autonomic neuropathy - abnormal hemodynamic response to laryngoscopy & intubation, surgical stress and blood loss • Aspiration prophylaxis and RSI
Haematopoetic System	• Rule out Pancytopenia	• Increased risk of postoperative infections with low TLC / ANC count • Thrombocytopenia - • Gen surgery > 50,000 • Closed cavity Sx > 1,00,000 • RA > 75000-80,000
Head and neck (RT)	• Assessment and Counselling for DA	• Difficult Airway management • Consider Viscope/Awake FOB

Time to surgery after these therapies :

- Time to surgery (TTS) after neoadjuvant therapy.
- Weeks : Cytotoxic effects to recover.
- Optimally 4-6 weeks.
- This window allows for prehabilitation.