Treatment Modalities

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Agenda

Surgery
Chemotherapy
Targeted & Biotherapy
Radiation Therapy
Blood & Bone Marrow Transplantation

Surgery

Oldest and most investigated therapy for cancer
Varied roles of cancer-related surgery
Diagnostic – obtain tissue for diagnosis and staging
- Biopsies
  - Fine-needle aspiration
  - Core needle
  - Open
- Incisional biopsy – remove a portion of the mass
- Excisional biopsy – remove the entire mass
Surgical Roles

Preventive – to reduce the risk of cancer developing in high-risk patients
  ▪ Bilateral mastectomy for BRCA mutations

Curative – to remove entire tumor with negative margins

Palliative – to enhance comfort, not cure
  ▪ Cytoreduction – remove bulk of disease
  ▪ Decompression/diversion
  ▪ Stent placement
  ▪ Colostomy

Rehabilitation or reconstruction – improve the function and appearance of a surgical site
  ▪ Depend on anatomic site
  ▪ Breast reconstruction

Treatment access
  ▪ Intravascular catheter placement

Treatment of oncologic emergencies
  ▪ To relieve spinal cord compression, cardiac tamponade

Multimodality treatment
  ▪ Chemotherapy
  ▪ Radiation therapy
  ▪ Interventional radiology
    ▪ Preoperative
    ▪ Intraoperative
    ▪ Postoperative

Local excision – removal of cancer and small margin of surrounding tissue

Wide excision – removal of cancer and some adjacent tissue and lymph nodes

En bloc resection – removal of bulky cancer with contiguous tissues

Debulking – remove significant part of tumor
  ▪ Decrease overall tumor burden
  ▪ Greater chemosensitivity of remaining tumor
Surgical Approaches

Traditional open approach – large incision to completely expose target organs and other structures

Minimally invasive approaches
- Laparoscopic
- Robotic
- Natural orifice transluminal endoscopic surgery (NOTES)
- Laser
- Percutaneous

Surgery Techniques

Adjuncts to surgical resection
- Ablation – use of thermal energy to destroy tumor
  - Cryoablation – liquid nitrogen destroy malignant tissue & provide local control
  - Radiofrequency ablation – high frequency radio waves local destruction of tumor
- Control of metastatic liver disease

Pre-operative Considerations

Patient history
- Allergies, current medications
- Previous surgeries
- Current medications

Physical examination
- Cardiovascular, Pulmonary
- Hematologic
- GI/GU
- Endocrine
- Integumentary

Psychosocial evaluation
- Stressor/coping mechanisms
- Caregiver access and readiness

Safety Measures

General safety interventions
- Informed consent
- Surgical safety checklist
- Asepsis
- Patient positioning
- Electrical safety
- Equipment availability
Post-operative considerations

Hemodynamic & cardiopulmonary stability
Pain management
Pulmonary toilet
Venous thromboembolism
Wound healing
Nutrition
Bowel function
Tubes & drains
Patient/caregiver education

Discharge Planning

Psychosocial options
- Safe discharge destination
- Caregivers
Level of care options
- Durable medical equipment
- Care supplies
Insurance limitations
Rehabilitation needs

References

Itano, J (2016). Core Curriculum for Oncology Nursing. St. Louis, MO. Elsevier
Chemotherapy

An integral component of systemic therapy

Based on concepts of
- Cellular kinetics
- Cell cycle
- Time
- Growth fraction
- Tumor burden

The Cell Cycle

- 5-stage cellular reproduction process
- Cycle occurs in all cells.
- Cycle phase times differ per cell.
  - Gap 0 (G0) = resting phase
  - Gap 1 (G1) = post-mitotic phase
  - Synthesis (S) = DNA synthesis occurs
  - Gap 2 (G2) = pre-mitotic
  - Mitosis (M)
    - Prophase
    - Metaphase
    - Anaphase
    - Telephase

Approaches to Chemotherapy

Single agent
- Commonly used in recurrence

Combination chemotherapy
- Increase # of cells exposed
- Decrease drug resistance
- Effective in large tumors
Approaches to Chemotherapy
Regional chemotherapy
- Delivering dose of chemotherapy to specific sites
- Decreases intensity of systemic toxicity
High-dose chemotherapy
- Administered with supportive therapy

Factors that influence response
Characteristics of the tumor
- Size or tumor burden
- Growth rate/fraction
- Genotype
Characteristics of the patient
- Physical status
- Performance status
- Age
- Comorbidities

Chemotherapy Treatment
Administration or schedule
- Combination vs single agent
- Dose density
- Dose intensity
Routes of administration
- Oral
- Intravenous
- Intraperitoneal
- Intra-arterial

Role of Chemotherapy
- Prevention
- Cure
- Control
- Palliation
## Classification of Antineoplastic Agents

Classified according to:
- Phase of action during the cell cycle
  - Cell cycle-specific
    - Major effects on cells actively dividing
    - Schedule dependent
  - Cell cycle-nonspecific
    - Major effects on cells at any phase including G0
    - Dose-dependent
- Mechanism of action, biochemical structure or physiological action

### Alkylating agents
- Interfere with DNA replication
- Most agents cell cycle non-specific

**Major toxicities**
- Hematopoietic, GI/GU, Neurologic, Reproductive systems

**Agents**
- Cyclophosphamide, Platinos, Busulfan, Ifosfamide

### Antimetabolites
- Inhibit protein synthesis
- Most agents cell cycle-specific

**Major toxicities**
- Hematopoietic, GI

**Agents**
- Azacytidine, Cytarabine, Fludarabine, SFU, Gemcitabine, Methotrexate

### Antitumor antibiotics/anthracyclines
- Inhibit DNA and RNA synthesis
- Most agents cell cycle non-specific
- Topoisomerase II

**Major toxicities**
- Hematopoietic, GI, Organ, cutaneous

**Agents**
- Bleomycin, Dactinomycin, Mitoxantrone
- Rubicin family
## Classification of Antineoplastic Agents

### Miscellaneous agents
- Mechanism of action poorly understood
- Most agents cell cycle non-specific

### Major toxicities
- Hematopoietic, GI, Neurologic

### Agents
- Arsenic trioxide, Asparaginase, Ixabepilone

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## Classification of Antineoplastic Agents

### Nitrosureas
- Interfere with DNA replication
- Cross the blood brain barrier
- Long nadir 4-6 weeks

### Major toxicities
- Hematopoietic, GI

### Agents
- Carmustine, Lomustine

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## Classification of Antineoplastic Agents

### Topoisomerase targeting agents
- Topoisomerase I
  - Prevent DNA realignment
  - Cell cycle specific

### Major toxicities
- Hematopoietic, GI

### Agents
- Camptosar

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## Classification of Antineoplastic Agents

### Plant Alkaloids
- Variety of mechanisms
  - Topoisomerase II, Mitotic spindle poison
  - Cell cycle specific

### Major Toxicities
- Hematopoietic, Neurotoxicity, Hypersensitivity

### Agents
- Epipodophyllotoxins – Etoposide
- Taxanes – Docetaxel, Paclitaxel
- Plant alkaloids – Vinblastine, Vincristine
Safe Handling

Many drugs considered hazardous
  - Carcinogenic, teratogenic, genotoxic
Potential risks for exposure
  - Increased risk for malignancies, embryofetal toxicities, chromosomal damage
Routes of exposure
  - Absorption, Inhalation, Ingestion, Injection

Mixing/compounding
  - Guidelines and recommendations
    - ONS, OSHA, ASHP, NIOSH
  - All preparations should take place in a primary engineering control (PEC) setting
  - Use of closed system transfer devices
  - Double gloving
  - Luer-lock fittings

Chemotherapy Administration

Review orders
  - References, drug protocol
  - Regimen specific, pre-printed electronic
  - Verbal orders not allowed
  - Complete orders
Determine drug dose
  - Actual height and weight
  - BSA, AUC

Chemotherapy Administration

Review drugs
  - Potential side effect
Current laboratory values
Informed consent
Patient assessment
  - Previous experience
  - Toxicities
  - Patient/family education
Chemotherapy Administration

Double verification
- Order, dose calculation lab values

PPE
- Gloves, gowns
- Respirators – NIOSH approved
- Eye and face protection

Peripheral IVs
- Distal then proximal
- Condition of veins
- Avoid sites where damage to tendons or nerves is possible

Just prior to administration verify
- Order, drugs, routes and sequence

Monitor sites for
- Blood return
- IVs infiltration

Administer pre-chemo medications
- 5 Rights

Immediate complications

Extravasation
- Irritants – local inflammatory reaction
- Vesicants – potential to cause cellular damage/tissue destruction

Prevention is key
- Observe infusion site for
  - Redness, swelling, lack of blood return
  - Instruct patient to report pain, burning
  - Use larger veins
  - Assess patency
    - Every 2-3 ml for IV push
    - Every 5 min for IVPB

If extravasation suspected
- STOP infusion
- Aspirate
- Remove IV
- Assess

Treatment
- For most medications
  - Non-pharmacologic treatment
  - Avoid pressure
  - Administer antedote
    - Heat or cool initially
    - Rubicin family – Dexrazoxane
    - Vinca Alkaloids - Haploprostau
Radiation Therapy

More than 60% of patients with cancer will receive radiation therapy.

Ionizing radiation – a form of energy when used in a controlled way to destroy cancer

Forms of ionizing radiation
- Electromagnetic – energy waves
  - (x-rays, gamma rays)
- Particulate – subatomic particles
  - Electrons, protons, neutrons, alpha/beta particles

Radiobiology
- Physical, chemical and biologic changes

Cellular targets
- DNA most important target
  - Double strand breaks
  - Creates free radicals
- Biologic response affected by
  - Oxygen effect
  - Tumor cell sensitivity
Radiation Therapy

Normal tissue and tumor are both affected by ionizing radiation.

Biologic effect of fractionation on tumors depend on:
- Repair
- Redistribution
- Repopulation
- Reoxygenation

Radiosensitivity
- All cells are vulnerable
- Cells will vary in sensitivity
  - Rapidly dividing cell will be most sensitive or radiosensitive
  - Non-dividing /slowly dividing less sensitive or radioresistant

Principles behind radiation therapy
- Deliver dose high enough to destroy tumor while not exceeding tolerance of normal tissue
- Side effects generally the result of the effect of RT on normal tissue

Side effects
- Early side effects – occur during RT or immediately after
- Acute responding tissue
  - Rapidly dividing cells affected first
- Subacute responding tissue – weeks to months after RT
- Late responding tissue – months to years after RT
- Combined treatment modality
  - Increases risk of late effects on normal tissue
Radiation Therapy

Tissue response to fractionation
- External beam – total dose tolerated by tissues and the RT field is prescribed and fractionated
- High dose per fractionation + large total doses – increased severity of late effects
- Radioactive source therapy – total dose tolerated by the tissues is prescribed
  - May be given over several days – continuous
  - In single or several doses – over several minutes

Radiation Therapy

Clinical uses for radiation therapy
- Cure
  - Definitive treatment
  - Neoadjuvant treatment
- Adjuvant treatment
- Prophylaxis
- Control
- Palliation

Radiation Therapy

Methods of delivery
- Local treatment
  - External beam
  - Linear accelerator (treat with x-rays, electrons or both)
  - Cobalt-60 – gamma rays
  - Radioactive source – brachytherapy
    - Beta particles and gamma rays
    - Sealed sources
- Systemic therapy
  - Radioactive source –
  - Radiopharmaceuticals
  - Unsealed

Radiation Therapy

Technologic advances
- Allow more precise planning and delivery of external beam radiation therapy
  - Intensity modulated RT
  - Image guided RT
  - Allows difficult tumors to be treated
  - Minimizes dose administered to healthy tissue
  - Cyber knife
  - Proton therapy
Radiation Therapy

Internal radiation therapy – radioactive source therapy
- Brachytherapy – sealed sources
  - Seeds, ribbons, plaques, or rods
  - Placed close to the tumor
  - Radiation dose emitted
    - Low dose rate
    - High dose rate

Treatment techniques
- Interstitial – placement of seeds
- Intracavitary – rigid applicator next to the tumor
- Intraluminal – seeds in a lumen
- Superficial – plaque or mold on a body surface

Can effectively deliver a high dose of radiation to the tumor while sparing surrounding normal tissue

Radiopharmaceutical therapy
- Unsealed sources
  - Ingested, injected, or instilled into a body cavity
  - Characteristics that determine where they will concentrate
  - Conjugated to monoclonal antibodies

Radiation safety and protection
- Dose limitation – dose limits applied to all individuals
  - ALARA (as low as reasonably achievable)
  - Should be continual monitored and controlled
- Radiation monitoring
  - Film badge – read and exchanged monthly
  - Dosimeter – x-ray, beta, gamma
  - Survey meters – Geiger counter
Radiation Therapy

Radiation safety
- Essential considerations
  - Time
  - Distance
  - Shielding

Radiation Therapy

Nursing implications
- Assessment
- Education
- Symptom management
- Emotional support/counseling
- Physical care
- Coordination of care

References
Biotherapy and Targeted Therapy

Biotherapy – helps the immune system fight cancer

GOAL
- Enhance the body’s natural defense and its ability to fight cancer
- Stop or slow the growth of cancer cells
- Easier for the immune system to destroy cancer cells
- Prevent cancer from spreading to other parts of the body

Immune system – two basic types of defense mechanisms
- Natural immunity – first line of defense, non-specific response
- Adaptive immunity – recognizes invaders, remembers what they look like

Immune system cells
- Lymphocytes
  - T-cells – directly attack foreign cells
  - B-cells – secrete antibodies
  - Natural killer (NK)
- Monocytes – White blood cells
  - Macrophages – engulf and digest invaders

Cytokines
- Messengers of the immune system
  - Upregulate or downregulate other molecule of the immune system
  - Regulate cells involved in innate and acquired immunity
- Agents
  - Interleukins, interferons
  - Tumor necrosis factor
  - Colony stimulating factors
Biotherapy and Targeted Therapy

Hematopoietic growth factors
- Natural occurring proteins
- Hematopoietic stem cells
- G-CSF - Neupogen, neulasta
- GM-CSF multi lineage growth factor - Leukine
  - Granulocyte, erythrocyte, macrophage, megakaryocyte (CFU-GEMM)
- Erythropoietin – regulator of erythropoiesis
  - Epogen, Procrit, Darbopoetin

Biotherapy and Targeted Therapy

Interferons – secrets substance that interferes with viral replication
- 5 different types
  - Alpha, beta, gamma, omega, tau
  - Alpha – most application in cancer therapy
    - Hairy cell leukemia, melanoma, kaposi sarcoma

Biotherapy and Targeted Therapy

Interleukins (ILs) “between leukocytes” – responsible for signaling and communication among cells of the immune system

Agents
- IL-2 – renal cell carcinoma

Biotherapy and Targeted Therapy

Monoclonal antibodies
- Target the extracellular receptors
  - Overexpressed or mutated
- Two groups
  - Unconjugated – naked work by themselves
  - Conjugated – attached to something else
    - Chemotherapy, radioactive particle, toxin
Biotherapy and Targeted Therapy

Monoclonal antibody types
- Dependent on amount of mouse antibody

Small molecule – Tyrosine Kinase Inhibitors
- Block receptor binding sites intracellularly
  - Bind at the ATP binding site to prevent cellular instructions to specific pathways
  - Numerous signaling pathways that interact with one another
- Administered orally
  - Many metabolized by cytochrome P450

Proteasome inhibitors
- Enzymes that breakdown proteins no longer needed
  - Bortezomib

Immunomodulatory agents
- Regulate/modify the immune system
  - Antiangiogenic properties
    - Thalidomide, Lenalidomide
Biotherapy and Targeted Therapy

Vaccines
- Condition immune system

Types of vaccines
- Preventive – Recombivax, Gardasil
- Whole Cell
- Peptide
- Dendritic – sipuleucel-T (Provenge)
- Vector-based
- Heat shock proteins
- DNA & RNA
- Oncolytic – Imlygic

Biotherapy and Targeted Therapy

Adverse events of targeted therapies
- Drug-drug and food interactions
  - Most oral medications metabolized by the liver CYP450
- Infusion reactions
  - Monoclonal antibodies
  - Will depend on the amount of mouse protein
  - Usually seen with the first 1-2 infusions
- Cardiac Toxicity
  - Arterial hypertension, decreased LVEF, arrhythmias (QTc prolongation)

Biotherapy and Targeted Therapy

Adverse events of targeted therapy
- Diarrhea
- HER1/EGFR inhibitors
- Metabolic disorders
  - Hypomagnesemia, hypercholesterolemia, hyperglycemia, hypothyroidism
- Dermatologic reactions
  - EGFR – papulopustular eruptions

Biotherapy and Targeted Therapy

Adverse events of targeted therapy
- GI perforation
- Bevacizumab, sorafenib
- Venous thromboembolism
- Bevacizumab, sunitinib, temsirolimus
- Wound healing
- Capillary leak syndrome
- Stomatitis
- Everolimus

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Biotherapy and Targeted Therapy

Nursing implications
- Assessment
- History
- Medications
- Diagnostics
  - MUGA, lab work, ECG
- Psychosocial
  - Coping, support
  - Ability to perform self care, adherence
- Financial status

References

Itano, J (2016). Core Curriculum for Oncology Nursing. St. Louis, MO. Elsevier


Blood and bone marrow transplantation
Blood and Marrow Transplantation

Hematopoietic stem cell transplantation (HSCT) infusion of healthy stem cells in someone whose stem cells have been destroyed or are diseased.

In patients with cancer HSCT allows
- Administration of high dose chemotherapy or radiation therapy

Transplant Terminology

- Related – donor is related to the recipient
- Unrelated – donor is not related to the recipient
- HLA typing
- Myeloablative therapy
- Nonmyeloablative transplant

How Stem Cell are Obtained

- Peripheral blood (PBSC)
- Umbilical cord blood (UCB)
- Bone marrow harvest

Major types of HSCT

- Autologous
  - Patients own bone marrow or peripheral blood stem cells (PBSCs)
  - In older patients > 50 may be more desirable
  - Treatment of Multiple Myeloma and Lymphomas
  - PBSC most commonly used
  - Benefits – Minimal risk of GVHD
  - Risks – potential for relapse
### Major types of HSCT

**Allogeneic**
- Bone marrow or PBSCs from healthy related or unrelated donor
- Umbilical cord blood (UCB)

**Benefits** – no disease contamination
- Related donor/UCB – decreased risk of GVHD
- Shorter period to engraftment

Most commonly used for
- AML, ALL, MDS, and NHL

**Risks** – increased risk of GVHD
- Shorter period to engraftment (PBSC)

**Major types of HSCT**

**Syngeneic**
- A subtype of Allogeneic transplant
- Bone marrow or PBSCs from identical twin

**Benefits** – immunosuppression not needed

**Risks** – no graft verses tumor effect (GVT)
- Potential to transmit genetic defects

### Stages of Transplantation

- Pretransplant evaluation/donor matching
- Mobilization/collection of stem cells
- Conditioning
- Engraftment
Pre-transplant Phase

Pre-transplant evaluation
- Patient factors
- Medical history
- Prediagnostic studies
- Lab work
- Diagnostic studies – MUGA, PFTs
- Psychosocial evaluation
- Decision to proceed with transplant
- Understanding of treatment
- Coping mechanisms

Donor Matching (Allogeneic)

HLA Compatibility

Medical evaluation of donor
- CMV status
- ABO compatibility
- Age
- Weight
- Sex
- Race

Mobilization

Increasing number of stem cells in peripheral blood
- G-CSF or GM-CSF
- Combination of chemotherapy and growth factors
- Goal is WBC count of 20,000

Collection of Stem Cells

Central vascular catheter placed

Apheresis

Umbilical cord blood
- Cells harvested from UBC and placenta immediately following birth
Cell Processing and Storage

Quantifying # of CD34+ cells
- Minimum of $2.5 \times 10^6$ required for

Testing for:
- Tumor cells
- Contaminants
- Mononuclear cell counts
- Viability of cells

Cryopreservation

Conditioning

Treatment given prior to transplant to
- Eradicate the disease
- Suppress bone marrow function
- Provide immunosuppression to prevent rejection

Includes chemotherapy and/or radiation therapy

Conditioning regimens range from two to eight days prior to transplant

Intra-transplant Phase

Pre-medications
- Diphenhydramine
- Acetaminophen
- Corticosteroids
- Antiemetics

Verification of product

Cell preparation

Infusion of Cells

Autologous transplants
- Thawed cells may be drawn up in large syringes and given via IVP
- Cells may be hung and infused over a specified period of time

Allogeneic transplants
- Procedure resembles PRBC transfusions
- Unfiltered tubing must be used.
Patient Safety Measures
- Emergency equipment at bedside
- Physician present during procedure

Post-transplant Phase
- Acute complications—occur within the first 100 days
- Chronic complications—occur after 100 days
- Neutropenic period—1-4 weeks
- Time to engraftment—2-4 weeks
  - First sign is WBC production

Conditioning complications
- Nausea and vomiting
  - Antiemetics, distraction, relaxations, dietary modifications
- Pancytopenia
  - Blood products and anti-infective agents
- Mucositis
  - Oral care, pain management, nutritional support

Prevention of Infection
- G-CSF
- Anti-infective agents
- Environmental interventions
- No visitors with respiratory symptoms
- Assessment for infection
Acute Graft-Versus-Host Disease

Identify patient as risk
Assessment and management of target organ involvement
- Skin
- GI tract
- Liver
Immunosuppressive agents

Chronic Graft-Versus-Host Disease

Occurs 3-24 months after transplant
May involve skin, liver, eyes, mouth, upper respiratory tract, and esophagus
Erythematous skin rash is hallmark
Cyclosporine and corticosteroids

Graft Failure

Donor cell fail to regenerate in the bone marrow
- Use of growth factors
- Further treatment with second transplant

Survivor Issues

Symptom surveillance for complications related to immune impairment and organ toxicities
Education related to healthful lifestyle and behaviors
References


