CHAPTER:4
PRINCIPLES OF CANCER TREATMENT

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INTRODUCTION

- Cancer is a group of more than 100 different diseases that are characterized by uncontrolled cellular growth, local tissue invasion, and distant metastases

- Many tumor and patient specific factors must be considered in the decision-making process for an individual patient.
- We will discuss the basic principles of cancer growth and treatment
- Treatment with drugs is the main focus of the pharmacist

Pathology of cancer: *tumor origin*

- Tumors may arise from any of four basic tissue types
  - epithelial tissue,
  - connective tissue (i.e., muscle, bone, and cartilage)
  - Lymphoid tissue
  - nerve tissue

Pathology of cancer: *tumor origin*

- Malignant cells are divided into those of epithelial origin or the other tissue types.
- Carcinomas are malignant growths arising from epithelial cells.
- sarcomas are malignant growths of muscle or connective tissue.
- Adenocarcinoma is a malignant tumor arising from glandular tissue.

Tumor characteristics

- invade and destroy the surrounding tissue.
- The cells are genetically unstable
- loss of normal cell architecture results in cells that are atypical of their origin.
- lose the ability to perform their usual functions.
- metastasize, and consequently, recurrences are common after removal or destruction of the primary tumor.

Invasion and metastasis

- Metastasis is the spread of neoplastic cells from the primary tumor site to distant sites.
- many patients have detectable metastatic disease at diagnosis.
- Once clinically evident distant metastases are present, cancers are seldom curable
- microscopic cancer metastases

Invasion and metastasis

- two primary pathways of metastasis hematogenous and lymphatic.
- Not all of the shed cancer cells result in a metastatic lesion.
- The "seed" must first find the appropriate "soil," or an environment suitable for growth

Metastasis

- This process is illustrated in the diverse patterns of metastasis that are characteristic of individual types of cancer
- E.g. colorectal cancer metastasizes to the liver and prostrates cancer to the bone

Metastasis

- Used to refer to solid tumor only
- The concept of tumor spread is not relevant to hematological malignancies because cancer cells circulate in the blood early in the course of the disease

Metastasis

- 30% of patients will have metastatic tumor > 1 cm at the time of diagnosis
- Another 30% will have microscopic metastases that are too small to be detected (the proof is they have cancer recurrence even when the 1ry tumor has been removed or destroyed)

Staging and workup

- tumors should be staged to determine the extent of disease before any definitive treatment is initiated.
- Staging provides information on prognosis and guides treatment selection.
- After treatment, the staging is usually repeated to evaluate the effectiveness.

Staging and workup

- Some cancers produce tumor markers
- Often nonspecific,
- more useful for monitoring response and detecting recurrence than as diagnostic tools.

Goals of cancer treatment

1- **Primary goal**

- Cure the patient
- Render him clinically and pathologically free of disease and return their life expectancy to that of healthy individuals of the same age and sex.
- Current therapies do not offer cures for all patients

Goals of cancer treatment

2- The best alternative goal

- To prolong survival while maintaining the patient's functional status and quality of life.

3- The 3rd goal

- Relive symptoms such as pain for patients in whom the likehood of cure or prolonged survival is very low

Modalities of cancer treatment

The Major Modalities

- Surgery
- Radiation
- Chemotherapy
- Biological therapy

Modalities of cancer treatment

The most appropriate type of therapy for each individual patient is determined by

- Type and extent of tumor involvement
- Treatment goals
- Performance status
- Age
- Concomitant disease
- Many patient receive 2 or 3 of these modalities together

Surgery

- The oldest cancer treatment
- The most invasive method
- Requires patient be able to tolerate physical challenges of surgery
- Was only method that could produce cures
- Still provides the best chance of cure for most patients with solid tumors.

Surgery

- **Uses**
  - Treat the primary cancer
  - To remove isolated metastatic masses
  - To make other methods of treatment possible e.g. providing access for chemotherapy delivery (implanted infusion pumps)

Surgery

- Diagnosis and Staging
- Reconstruct anatomical defects to improve function, cosmetic appearance, and quality of life
- Prevention
  - Permitting the removal of precancerous lesions such as abnormal moles or colon polyps.

Surgery

- Treat complication
  - Hemorrhage
  - Perforation
  - Bowel obstruction
  - Spinal cord compression

Chemotherapy

- refers to the use of conventional cytotoxic drugs in addition to hormonal and endocrine therapy.
- Originally started in 1941, when Goodman and Gilman first administered nitrogen mustard to patients with lymphoma

Chemotherapy

- Now there are > 50 conventional cytotoxic agents and > 15 hormonal agents for cancer treatment

Chemotherapy

Cancer chemotherapy may be

- Primary
- Palliative
- Adjuvant
- neoadjuvant

Chemotherapy used alone with curative intent	
Acute lymphocytic leukemia	Acute myelogenous leukemia
Chemotherapy used as adjuvant therapy with curative intent	
Breast cancer	Colorectal cancer
Chemotherapy used as neoadjuvant therapy	
Anal carcinoma	Bladder cancer
Chemotherapy used to palliate symptoms in advanced disease	
Bladder cancer	Brain tumors
Chemotherapy has little or no effect on palliation	
Hepatocellular cancer	Renal cell carcinoma

Adjuvant therapy

- To eradicate any residual micro metastases and prevent them from growing into clinically evident disease.
- Usually systemic cytotoxic drugs, hormones, or biological agents after the 1ry solid tumor mass has been eliminated with surgery or radiation.
- It also can be administered after the 1ry disease has been eliminated by antineoplastic drugs

Neoadjuvant therapy

- A less conventional form
- Systemic chemo or biological therapy is given before surgery to debulk the tumor, reducing the extent and disfigurement of surgery
- may play a double role because may also eradicate micro metastases.
- Practically useful in head, neck, and bone tumors
- Hormones may be used for the management of locally advanced prostate cancer

Tumor burden

- a certain % of cancer cells will be killed with each course of chemotherapy.
- According to this hypothesis, the tumor burden will never reach zero.
- Tumors consisting of less than 10^4 cells are believed to be small enough for elimination by host factors, including immunologic mechanisms.

Tumor proliferation

- Both cancer cells and normal cells reproduce in a series of steps known as the cell cycle
- DNA synthesis occurs in S phase.
- %of cells in the S phase is an indicator of the rate of tumor-cell proliferation.
- Tumors with a high percentage of S-phase cells are aggressively growing

Tumor proliferation

- Most normal human cells exist in the G_0 phase
- Most cancer cells are not sensitive to the effects of chemotherapy when they are in this stage

III-Chemotherapy

Uses

A-Limited in case of primary localized cancer, since only a few solid tumors are sensitive enough to be treated with drugs alone.

B-chemotherapy is the main treatment in disseminated cancer, because drugs go almost everywhere in the body

Endocrine therapy

- Option for management of cancers from tissues whose growth is under gonadal hormonal control, especially breast, prostate, and endometrial cancers
- These cancers may regress if the "feeding" hormone is eliminated or antagonized.

Endocrine therapy

USES:

1-as adjuvant therapy

2- to treat disseminated disease

Endocrine therapy

- Corticosteroids
  - Play important role in managing hematological malignancies
  - Also in supportive care of patient with cancer
    - Corticosteroids are lymphocytotoxic
    - Useful in malignancies in which lymph tissue are involved such as lymphocyetic leukemia, lymphoma

Biological therapy

The immune system is an effective antitumor defense

- Malignant cells occasionally arise in healthy bodies as a result of mutations but Not all these cells give rise to clinically evident cancer
- There are rare cases of spontaneous remission from metastatic cancer
- An intact immune system can identify malignant cells and destroy them without negative effects on normal cells.

Biological therapy

Biological therapies boost the immune system, either directly or indirectly by

- making cancer cells more recognizable by the immune system, and more susceptible to destruction
- boosting the killing power of immune system cells
- changing the way cancer cells grow, so that they act more like healthy cells

Angiogenesis inhibitors for cancer treatment

What is angiogenesis?

- The formation of new blood vessels is a process controlled by certain chemicals produced in the body.
- may help in normal wound healing.
- becomes unregulated in several malignancies and can lead to tumor growth, invasion, and metastasis
- Angiogenesis provides cancer cells with oxygen and nutrients.

Angiogenesis inhibitors for cancer treatment

- This process is regulated by pro- and antiangiogenic growth factors.
- The best studied of the proangiogenic factors is VEGF, whose elevated levels have been associated with a poor prognosis and an increased risk of metastases in a variety of malignancies

Angiogenesis inhibitors for cancer treatment

Drugs can interfere with angiogenesis by

- targeting vascular growth factors
- the production and control of the endothelial cells that make up the vessel linings.
- Most drugs are cytostatic rather than cytotoxic,

Combination chemotherapy

- administration of multiple agents to overcome factors for decreased patient response
- Drugs that possess minimally overlapping mechanisms of action and toxicities are combined
- Combination of chemotherpay with bioligical therapy

Factors affecting response to chemotherapy

- tumor burden
- tumor-cell heterogeneity,
- drug resistance,
- dose intensity
- patient-specific factors.

The relationship between dose and response

- Dose is believed to be a critical factor in determining response for many types of cancers.
- *Dose intensity*
  - the dose delivered to the patient over a specified period of time. Determined by
  - the dose per course
  - the interval between doses
  - and the total cumulative dose.

Patient-specific factors

- performance status
- Comorbidities
- renal and hepatic function
- Pharmacogenomics
- tumor-specific factors (e.g., pathology, stage, and molecular profile)
- treatment goals (e.g., palliation and cure)