4. Neoplasia

Terminology

- Neoplasm
  - a neoplasm is a mass of abnormal cells that grows autonomously
  - neoplasm may be benign or malignant
- Tumor
  - literally means a swelling (one of five signs of inflammation)
  - often used interchangeably with neoplasm
- Cancer
  - generally refers to a malignant neoplasm
  - derived from Greek word for “crab”

Benign neoplasms

- General characteristics of a benign neoplasm
  - well differentiated
  - slow rate of growth
    - few mitoses, no necrosis
  - no invasion
    - expansile growth, smooth border, encapsulated
  - no metastases

Malignant neoplasms

- General characteristics of malignant neoplasms
  - less well differentiated
    - anaplasia is total lack of differentiation
  - grow quickly
    - necrotic areas due to ischemic necrosis
  - locally invasive
    - irregular infiltrating border, no capsule
    - adequate removal requires rim of adjacent tissue (margin)
  - metastasize
    - metastasis is the transfer or spread of malignant cells from one site to another
    - invasion of lymphatics, blood vessels
Neoplasia

Nomenclature of epithelial neoplasms
• Benign epithelial neoplasms (-oma)
  • adenoma (gland formation)
  • papilloma (finger-like projections)
• Malignant epithelial neoplasms (carcinomas)
  • adenocarcinoma (gland formation or mucin production)
  • squamous cell carcinoma (intercellular bridges or keratin production)
  • transitional cell carcinoma (arises from transitional type epithelium)

Nomenclature of soft tissue neoplasms
• Benign soft tissue neoplasms (-oma)
  • fibroma
  • lipoma
  • chondroma
  • leiomyoma
• Malignant soft tissue neoplasms (sarcomas)
  • fibrosarcoma
  • liposarcoma
  • chondrosarcoma
  • leiomyosarcoma

Nomenclature of other neoplasms
• Melanoma is a malignant neoplasm of melanocytes
• Lymphoma is a malignant neoplasm of lymphocytes
• Leukemia is a malignant neoplasm of hematopoietic cells
• Carcinoid is a malignant neoplasm of neuroendocrine cells
• Teratoma is a neoplasm of germ cells containing different types of tissues, may be benign or malignant
• Mixed tumor is a neoplasm containing two neoplastic components usually epithelial and mesenchymal
Neoplasia

Predisposing factors

- Neoplasms are a heterogeneous group
- Interplay of environment and genetics
- Geographic factors
  - some malignancies more common in certain areas
  - gastric cancer in Japan
- Carcinogens
  - substance that may produce cancer (chemical, virus, radiation, etc)
  - some malignancies more common if exposed to carcinogens
    - asbestos and mesothelioma
- Age
  - most malignancies are more common in elderly
  - some malignancies are more common in children
    - leukemias, neuroblastoma, Wilms’ tumor, retinoblastoma
- Hereditary factors
  - Inherited cancer syndromes
    - inherit a mutant gene that increases risk of developing certain tumor
      - familial adenomatous polyposis
  - Familial cancers
    - familial clustering of specific forms of cancer
  - Syndromes of defective DNA repair
- Certain clinical conditions of chronic irritation are associated with increased risk of malignancies
  - liver cirrhosis and liver cancer
  - atrophic gastritis and stomach cancer
  - chronic ulcerative colitis and colon cancer
- Certain benign neoplasms are associated with increased risk of malignancies
  - villous adenomas of colon and colon cancer

Grade and stage of malignant neoplasms

- Grade
  - the grade of a malignant neoplasm is the degree of differentiation of the malignant cells
  - High grade tumors are poorly differentiated
  - Low grade tumors are well differentiated
- Stage
  - amount of malignant neoplasm in the body (“tumor burden”)
  - TNM system
    - T  Size of primary tumor
    - N  Amount of tumor in lymph nodes
    - M  Presence or absence of distant metastasis
  - Other staging systems exist for different organs
Neoplasia

Clinical features of neoplasms

• Local effects
  • neoplasms are space occupying lesions
  • expansion of the neoplasm causes physical compression of adjacent structures
  • benign neoplasms may be fatal (e.g. Meningioma)

• Systemic effects
  • cachexia state of general ill health and poor nutrition
  • weight loss
  • anorexia

• Paraneoplastic syndromes
  • syndrome of symptoms in patient with cancer not explained by local or distant effects of tumor itself
  • Hypercalcemia (increased serum calcium)
    • most common paraneoplastic syndrome
    • production of PTH-rp (protein)
  • Cushing’s syndrome
    • production of ACTH
  • Syndrome of inappropriate antidiuretic hormone
    • production of ADH

• Hormonal effects
  • some endocrine neoplasms make hormones

Chemical carcinogenesis

• Carcinogen is a cancer producing substance
• Chemical carcinogenesis is a multi-step process requiring initiation and promotion
• Initiation
  • chemical induces irreversible change in DNA of cells
• Promotion
  • promoter chemicals induce tumor formation in initiated cells
• Progression
  • acquisition of additional genetic changes
  • clonal expansion of various cell lines
• Pro-carcinogen is a chemical that must be modified in body to become a carcinogen
• Some carcinogens can initiate and promote, others just initiate
• Examples of chemical carcinogens
  • Alkylating agents used to treat cancer may cause other cancers
  • Aflatoxin is potent liver carcinogen produced by fungus
  • Polycyclic hydrocarbons are skin, lung carcinogens
  • Aniline dyes are bladder carcinogens
  • Nitrosamines and amides may induce gastric cancer
Neoplasia

Radiation carcinogenesis

- Ultraviolet radiation
  - UV light may be carcinogenic because it damages DNA
  - DNA damage is usually repaired enzymatically
  - Xeroderma pigmentosa
    - genetic defect in DNA enzymatic repair system
    - develop skin cancers at young age
  - long term exposure to UV results in increased skin cancers
    - basal cell carcinomas, squamous cell carcinomas, melanoma
- Ionizing radiation
  - electromagnetic radiation (x-rays) and particulate radiation are associated with increased cancer
  - increased thyroid cancers in children who receive radiation to the neck
  - leukemias may occur in individuals exposed to excessive radiation
    - Hiroshima

Viral carcinogenesis

- Viruses are implicated in some cancers
  - Papillomavirus (HPV)
    - infects squamous epithelial cells forming warts
    - HPV types 16, 18, and 33 associated with cervical cancer
    - HPV types 6, and 11 associated with benign cervical lesions
  - Epstein Barr virus (EBV)
    - infects B lymphocytes
    - association with Burkitt’s lymphoma, nasopharyngeal cancer
  - Hepatitis B virus
    - associated with increased incidence of liver cancer
  - Human T-cell leukemia virus
    - associated with rare form of T-cell leukemia

Oncogenes

- Oncogenes are mutated genes whose products are associated with formation of neoplasms
- Proto-oncogenes are the normal gene counterpart to oncogenes that code for important proteins which control cell growth
- Tumor suppressor genes
  - genes whose products suppress development of tumors
  - damaged tumor suppressor gene results in increased tumors
  - Retinoblastoma
    - hereditary retinoblastoma due to inherited defective TSG
    - sporadic retinoblastoma occur due to spontaneous mutation TSG
Neoplasia

Epidemiology

• Incidence of a cancer
  • number of new cancers of that type arising within a specified time
• Females
  • breast cancer most common
  • lung
  • colorectal
  • uterine
• Males
  • prostate cancer most common
  • lung
  • colorectal

• Mortality
  • number of deaths attributed to a cancer for a given period of time
• Females
  • lung cancer
  • breast cancer
  • colorectal cancer
• Males
  • lung cancer
  • prostate cancer
  • colorectal cancer

Immune response

• Immune system may recognize neoplasm as “foreign”
• Immune response initiated against the neoplasm
  • eliminate small neoplasms
  • spontaneous remissions do occur
  • immunosuppressed individuals may develop malignancies (AIDS)
• Immunotherapy
  • drugs to enhance immune destruction of tumor