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NEOPLASIA

Neoplasia: abnormal mass of tissue, characterized by followings:

Incoordination, Autonomous, persistent growth and exceeding the growth of normal tissues. Neoplasia = tumors

Oncology: is the science that studies the tumors.

Oncology divided tumors according to their behavior into (**Benign & Malignant**.(

Naming of Tumors: All tumors (benign malignant) have two basic parts:

.1**Parenchyma Part**: formed by neoplastic cells.

✓ Parenchyma Part → Determine the clinical behavior of tumors.
→ Derived the name of tumors

.2**supporting part:** Made up of blood vessels &connective tissues

Naming of benign tumors: (Cell of origin of tumor+ Suffix oma) Like Fibroma)benign, tumor fibrous tissue), Chondroma (benign tumor of cartilage(

Important note: Lymphoma, melanoma, mesothelioma & meningioma although they are end with suffix oma, they are malignant tumors**.**

Naming malignant tumors:

-1Malignant neoplasm arising in mesenchymal tissue and its derivatives are called sarcoma e.g

.1Fibrosarcoma (malignant neoplasms of fibrous tissue(
.2Chondrosarcoma (malignant neoplasm of cartilage(
.3Osteosarcoma (malignant neoplasm of bone(

-2Malignant neoplasms of epithelial cells origin are called carcinoma. Sometime the type of malignant epithelia gives the name of malignant tumor, like

.1squamous cell carcinoma: tumor cells resemble stratified squamous epithelium.

.2Adenocarcinoma: tumor cells grow in glandular pattern.

- **Sometime the tissue of origin** can identify by the name of tumor, like

.1Renal cell carcinoma

.2Hepatocellular carcinoma.

❖ **Tumor like lesion:**

.1Hamartoma is a malformation that present as a mass of disorganized tissue not same tissue indigenous to the particular site. e.g, Hamartoma of lung.

.2Choristoma is a congenital anomaly it is heterotopic from the rest cells eg small nodule of pancreatic tissue may be found in the submucosa stomach, duodenum & small intestine.

Characteristics of benign & malignant tumors

Characteristics of differentiation between benign & malignant tumors are:

.1Differentiation and anaplasia

.2Rate of growth

.3Local invasion

.4Metastasis

.1**Differentiation and anaplasia**

Parenchymal part of tumor is responsible on important for differentiation and anaplasia of tumors while the stromal part of tumors is important on growth tumor because it contains blood supply of tumors.

Differentiation of parenchymal cells refers to the extent to which the tumor cell match to their normal original tissue morphologically and function

Anaplasia: mean loss structural and differentiation of normal cells

Characteristics of anaplastic cells:

.1 Pleomorphism (variation in the size & shape of cells.(
.2 Large hyperchromatic nuclei.
.3 Increase Nucleus/cytoplasm (N/cy ratio 1-1 (1:4 or 1:6 in normal.(
.4 Variation in the size of nucleus and poikilonucleosis (variation in the shape of nucleus(
.5 Chromatin is coarse, large prominent nucleolus.
.6 Numerous atypical mitosis Loss normal orientation of cells.

According to degree of differentiation: three grade of differentiation of malignant tumors:

.1Well differentiated malignancy (like normal tissue(

.2Moderately differentiated malignancy.

.3Poor differentiated, undifferentiated anaplastic malignancy.

***Benign tumors:** composed of well differentiated cells (closely resemble their normal counterpart e.g. Lipoma (consist of mature adipose cells), Chondroma (consist of mature chondrocytes(

- ❖ **Important not:** Usually benign & well differentiated cancer have functional capacity eg, like well differentiated malignancy of endocrine glands secrete hormones resemble the normal endocrine cells.

Dysplasia:

It is non neoplastic growth disorder; mainly occur in epithelia. It is a loss of uniformity of the individual cells & a loss in their architectural orientation.

Characteristics of dysplasia cell

.1 Pleomorphism.
.2 Large hyperchromatic cells
.3 Mitosis more than normal (mitosis not restricted to the basal layer .(
.4 Loss of normal maturation of cell e.g loss of maturation of squamous epithelium.

- ❖ When dysplastic changes involve the entire thickness of the epithelium, they are called carcinoma in situ or preinvasive stage of cancer.
- ❖ Dysplasia does not necessarily progress to cancer, & dysplasia not involve full thickness may be reversible.

-2Rate of growth

Most benign tumors grow slowly, and most of cancers (malignant) grow faster, in some exception of some benign tumors grow more rapidly than some cancer e.g leiomyoma (uterine fibroid), which is benign smooth muscle tumor influence by estrogen.

-3Local invasion:

Benign tumors are:

a(localized at the site of origin
b(not invade the surrounding tissue
c(not metastasized

d) Most (not all) of benign tumors have surrounding capsule (derived from the original normal tissue) e.g leiomyoma of uterus.

Malignant tumors are:

a(Rapid progressive growth
b(Infiltration invasion and penetration of the surrounding tissue .
c(Malignant tumors do not form well-developed capsules.
d(Always metastasis

Local invasion is the second most reliable feature (after metastasis) that distinguishes malignant from benign tumors

-4Metastasisis

It means development of secondary implant discontinuous with primary tumor possibly in remote tissues. Metastasis is the most important characteristic of malignancy.

- **Not all** cancers have ability of development metastasis e.g Basal cell carcinoma of skin & most of CNS malignancies are highly locally invasive but rarely metastasis, while osteosarcoma is usually metastasize to lung at the time of initial diagnosis.

Pathway of metastasis:

-1Seeding with in body cavities:

These occur, when cancers invade the (pleura, peritoneum, pericardium, meninges in CNS tumorsc). e.g carcinoma in colon and stomach invade the peritoneal cavity in female extend to both ovaries (krukenberg tumors), carcinoma of lung invade the pleura.

-2Lymphatic spread:

This is characteristically seen in carcinoma while sarcomas are more spread vascular system. It should be remembered, that lymph nodes enlargement with cancers not always means cancerous nodal involvement it may be due to necrotic debris of the cancers and tumor antigens, which may induce nodal enlargement

-3**Hematogenous spread**:

Is the most feared consequence cancer spread pathway, it is the favored pathway for sarcomas. Arteries are penetrated less readily than veins because of the wall thickness

are more in arteries.The liver & lungs are the most frequently secondary sites in such hematogenous spread

Characteristics	Benign	Malignant
Differentiation/ anaplasia	Well differentiated structure may be typical of tissue of origin	Some lack of differentiation with anaplasia, structure often is atypical.
Rate of growth	Usually progressive & slow; may come to a standstill or regress. abnormal Mitotic figures are rare &normal	Erratic may be slow to rapid: mitotic figures are numerous &abnormal
Local invasion	Well demarcated masses that do not invade or infiltrate the surrounding normal tissue.	Locally invasive, infiltrating the surrounding normal tissue.
Metastasis	Absent	Frequently present

Etiology cancer: many factors may play a role in etiology of cancer:

1. **Geographical & environmental factors: e** g (cancer of breast more in USA than JAPAN, while cancer of stomach is more in Japan than USA) All these geographical differences are due to environmental causes rather than genetic causes.

Examples an Environmental occupation factors & associated cancer are:

- Arsenic caused Carcinoma of lung carcinoma & skin
- Benzene caused leukemia lymphoma
- Nickle caused tumors of Nose, lung
- Vinyl chloride caused liver malignant
- Other environmental factors that have role in development of cancer: Alcohol consumption, smoking.

.2**Age**:

- Frequency cancer increase with Age (most death of cancer between 55-75 years ،(this is could be due to accumulation of somatic mutations & change in immunity with increase age.
- Cancer causes 10% of all death among children below 15 years). Major lethal Cancer in children is leukemia, CNS tumors, lymphoma & soft tissue sarcoma.

.3**Hereditary factor:** Hereditary forms of cancers can be divided into:

1- inherited cancer syndromes : These syndromes characterized by:

a. There is inheritance of a single mutant gene increase the risk

b. Mode of inheritance is Autosomal dominant.

eg, Familial retinoblastoma, Multiple endocrine Neoplasia, Neurofibromatosis type 1 type 2

-2**Familial cancer: Virtually all type of cancer can be occurd in familial pattern: e.g. Carcinoma of colon, carcinoma of breast, CNS tumors.**
characteristics or Familial cancer:

- Early Age of onset
- Tumor arising in two or more close relatives of patient.
- Multiple or bilateral
- Mode of transmission

-3**Autosomal recessive syndrome possibly linked to defective in DNA repair :**
A small group of autosomal recessive disorders is collectively characterized by DNA instability g.e xeroderma pigmentosum, ataxia telangiectasia.

.4Acquired preneoplastic dis:

- Chronic skin fistula or long stand unhealed skin wound (eg, chronic osteomyelitis predisposing to develop squamous cell carcinoma of skin
- Bronchial metaplasia & dysplasia can cause carcinoma of lung (smokers(
- Chronic atrophic gastritis can predispose to carcinoma of stomach.
- Chronic ulcerative colitis, predispose to carcinoma of colon.
- Leukoplakia of oral cavity (squamous cell carcinoma.(
- Villous adenoma of colon, increase risk of carcinoma of colon.

Molecular basis of Cancer (carcinogenesis:(

Principles of genetic basis of cancer:

A.Nonlethal genetic damage e lies at the heart of carcinogenesis:

This damage may be acquired by the action of environmental agents like (chemicals, radiation, viruses, or may be due to genetic cause.(

B.Three class of normal regulation genes (control the growth cancers:(

i. Growth promoting called proto oncogenes (dominant genes, present in normal cells, which in case of cancers covert into oncogenes.(
ii. Growth inhibiting called cancers suppressor genes (antioncogenes) (recessive genes, most Important one is p53, ApC "Adenomatous polyposis coli") these genes are lost in case of cancer.(
iii. Genes that regulate the apoptosis (these Genes are lost in case of cancer.(

C. **DNA repair gene:** disability of DNA repair genes can predispose to widespread mutation neoplastic transformation

Steps of Carcinogenesis: can be divided into three steps

A. Initiation steps: in which there is DNA damage (lies at the heart of tumor(usually due to (chemicals, viruses & radiation), these are called Initiator

B. Promotion step maintained the damage of DNA (hormones, drugs & phenols ‘(these are called promoters which augment replication of cells with DNA damage.

C. Tumor progression local increase in the size of tumor, local invasion& ‘ metastasis

Important notes of these steps of carcinogenesis:

.1 Application of promoters before the initiators will not result. In completion of carcinogenesis

.2 Same carcinogens can act as Initiators, promoters, this is called complete carcinogens

.3 Not all carcinogens induced DNA damage will not necessary result in initiation cancer

.4 Initiators are mutagenic but are not induce cells proliferation. While promoters are nonmutagenic but can induce cells proliferation.

Effect of tumors on the host

Cancers are more threatening to the host than benign tumors. Both benign and malignant affect the host by the followings:

.1 Location of tumors (benign & malignant) & their effects on adjacent tissue, even small size benign tumor can cause problem to the host like pituitary adenoma less than 1cm can cause compression of adjacent tissue.

.2 Effects on functional activity of the host:

Both benign and well differentiated malignant tumors arising in endocrine glands caused increased functional capacity e.g adenoma increase level steroid hormone that has effects on the host.

.3 Producing bleeding & secondary infection, these occur when the cancer lesion ulcerated through adjacent tissues (one of important causes of death malignant tumors (

.4 Many malignant tumor produce cachexia & Paraneoplastic syndrome.

Cancer cachexia

It referring to progressive loss of body fat, lean body mass, accompanied by profound weakness, anemia, & anorexia. There is correlation between the size and spread of cancer with severity of cachexia, small size malignant tumor not produce cachexia .

Paraneoplastic syndrome

Complex of symptoms other than cachexia that occur in patient with cancer symptoms that occur at sites distant from a tumor or its metastasis. Although the pathogenesis remains unclear, these symptoms may be secondary to substances secreted by the tumor or may be a result of antibodies directed against tumors that cross-react with other tissue

The grading and staging of cancer:

Are attempts to establish the aggressiveness or level of malignancy based on the cytologic differentiation of tumor cells and number of mitosis cell with in the tumor.

Staging of cancers: (team work) is based on clinical and radiographic examination)computed tomography and magnetic resonance imaging) and in some cases surgical exploration based on the size of the primary lesion. In addition its extent of spread to regional lymph nodes and the presence or absence of metastases.