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Neoplasia*:*

Introduction:

Neoplasia means "**new growth**," and the new growth is a "**neoplasm"**.

The term **tumor** was originally applied to the swelling caused by inflammation.

Oncology (Greek oncos=tumor) is the study of tumors or neoplasms.

Definition :

"A neoplasm is an abnormal mass of tissue, the autonomous growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after stop of the stimuli which evoked the change."

The tumor cells competes with normal cells and tissues for energy supplies and nutritional substrate, neoplasms ultimately depend on the host for their nutrition and vascular supply; still many forms of neoplasia require an endocrine support.

Classification of tumors:

Tumors divided into two main types (benign and malignant), this classification depend on the following parameters:

(1) differentiation and anaplasia, (2) rate of growth, (3) local invasion, and (4) metastasis.

1- Differentiation and Anaplasia

Differentiation refers to the extent to which tumor cells resemble comparable normal cells, both morphologically and functionally. Well-differentiated tumors are thus composed of cells resembling the mature normal cells of the tissue of origin to that neoplasm. Poorly differentiated or undifferentiated tumors have primitive-appearing, unspecialized cells. In general, benign tumors are well differentiated. The neoplastic cell in a benign smooth muscle tumor--a leiomyoma--so closely resembles the normal myomatrial cells as to make it impossible to recognize it as a tumor cell on high-power examination.

Malignant neoplasms, in contrast, range from (well differentiated, moderately differentiated, poorly differentiated reaching to undifferentiated types). Lack of differentiation, or anaplasia, is marked by a number of morphologic and functional changes.

Following parameters are important in grading of tumors.

1- Both the cells and the nuclei characteristically display "**pleomorphism**" variation in size and shape, cells may be found that are many times larger than their neighbors, and other cells may be extremely small and primitive appearing.

2- Characteristically the nuclei contain an abundance of DNA and are extremely dark staining (**hyperchromatic**).

3- The nuclei are disproportionately large for the cell, and the nuclear-to-cytoplasmic ratio (**N/C ratio**) may approach 1:1 instead of the normal 1:4 or 1:6.

4- The nuclei show large **prominent nucleoli**.

5- Malignant cells usually possess **high numbers of mitoses**, reflecting the higher proliferative activity of these cells and also presence of **atypical, bizarre mitotic figures** sometimes producing tripolar, quadripolar, or multipolar spindles.

6- loss of orientation and disarray of tissue architecture.

2-Rate of Growth

The generalization can be made that most benign tumors grow slowly over a period of years, whereas most cancers grow rapidly, Such an oversimplification, moreover, the rate of growth of benign as well as malignant neoplasms may not be constant over time. Factors such as hormone dependence, adequacy of blood supply, and likely unknown influences may affect their growth. For example, leiomyomas (benign smooth muscle tumors) of the uterus are common. Not infrequently, repeated clinical examination of women bearing such neoplasms over the span of decades discloses no significant increase in size. After the menopause, the neoplasm may atrophy and later be found to be replaced largely by collagenous, sometimes calcified, tissue. Leiomyomas frequently enter a growth spurt during pregnancy. These neoplasms to some extent depend on the circulating levels of steroid hormones, particularly estrogens.

3-Local Invasion

Nearly all benign tumors grow as cohesive masses that remain localized to their site of origin and do not have the capacity to infiltrate or invade surrounding tissue , as do malignant tumors. Because they grow and expand slowly, they usually develop a rim of compressed connective tissue, sometimes called a fibrous capsule, that separates them from the host tissue.

Most malignant tumors are obviously invasive and can be expected to penetrate the wall of the colon or uterus, for example, or fungate through the surface of the skin. Such invasiveness makes their surgical resection difficult, and even if the tumor appears well circumscribed, it is necessary to remove a considerable margin of apparently normal tissues about the infiltrative neoplasm.

4-Metastases:

Metastases are tumor implants discontinuous with the primary tumor. Metastasis unequivocally marks a tumor as malignant because benign neoplasms do not metastasize. The invasiveness of cancers permits them to penetrate into blood vessels, lymphatic, and body cavities, providing the opportunity for spread. With few exceptions, all cancers can metastasize.

In general, the more aggressive, the more rapidly growing, and the larger the primary neoplasm, the greater the likelihood that it will metastasize or already has metastasized.

Approximately 30% of newly diagnosed patients with solid tumors present with metastases. Metastatic spread strongly reduces the possibility of cure, and associated with bad prognosis.

<u>Pathways of metastatic spread</u>

1- Lymphatic Spread:

Transport through lymphatic is the most common pathway for the initial dissemination of carcinomas, The pattern of lymph node involvement follows the natural routes of drainage. Because carcinomas of the breast usually arise in the upper outer quadrants, they generally disseminate first to the axillary lymph nodes. Cancers of the inner quadrant may drain through lymphatic to the nodes within the chest along the internal mammary arteries.

2- Hematogenous spread :

It is typical of sarcomas but is also used by carcinomas. Arteries, with their thicker walls, are less readily penetrated than are veins, so the veins are the most vessels that responsible for hematogenous spread, With venous invasion, the blood-borne cells follow the venous flow, draining the site of the neoplasm. Understandably the liver and lungs are most frequently involved secondarily in such hematogenous dissemination All portal area drainage flows to the liver, and all caval blood flows to the lungs.

3- Body Cavities and Surfaces.

Seeding of body cavities and surfaces may occur whenever a malignant neoplasm penetrates into a natural "open field." Most often involved is the peritoneal cavity, and pleural cavity, such seeding is particularly characteristic of carcinomas arising in the ovaries, when the peritoneal surfaces become involved by malignant implants.

Benign versus malignant tumors:

Feature	Benign	Malignant
Rate of growth	Progressive but slow. Mitoses few and normal	Variable. Mitoses more frequent and may be abnormal
Differentiation	Well differentiated	Some degree of anaplasia
LOCAL INVASION	Cohesive growth. Capsule & regular borders	Poorly cohesive and infiltrative
Metastasis	Absent	May occur

NOMENCLATURE

All tumors, benign and malignant, have two basic components:
(1) proliferating neoplastic cells that constitute their parenchyma.
(2) supportive stroma made up of connective tissue and blood vessels. The nomenclature of tumors is based on the parenchymal component.

Benign Tumors.

In general, benign tumors are designated by attaching the suffix -oma to the cell of origin. Tumors of mesenchymal cells generally follow this rule. For example, a benign tumor arising from fibroblastic cells is called a fibroma, from adipose tissue (lipid) called Lipoma, and a tumor of osteoblasts is an osteoma.
In contrast, nomenclature of benign epithelial tumors is more complex. They are variously classified, depending on their cells of origin, and also on microscopic architecture, and gross appearance .
Adenoma is the term applied to the benign epithelial neoplasm that forms glandular patterns or a tumor derived from glands but not necessarily reproducing glandular patterns. On this basis, a benign epithelial neoplasm that arises from renal tubular cells growing in the form of small glands would be termed an adenoma, as would a heterogeneous mass of adrenal cortical cells growing in no distinctive pattern.
Benign epithelial neoplasms producing microscopically or macroscopically visible finger-like or warty projections from epithelial surfaces are referred to as papillomas.
Those that form large cystic masses, as in the ovary, are referred to as cystadenomas. Some tumors produce papillary patterns that protrude into cystic spaces and are called papillary cystadenomas.

Malignant Tumors.

The nomenclature of malignant tumors essentially follows the same schema used for benign neoplasm, with certain additions.
Malignant tumors arising in mesenchymal tissue are usually called sarcomas (Greek sar = fleshy) because they have little connective tissue stroma and so are fleshy (e.g., fibrosarcoma, liposarcoma, and leiomyosarcoma).
Malignant neoplasms of epithelial cell origin, are called carcinomas. Carcinomas may be further qualified, one with a glandular growth pattern microscopically is termed an adenocarcinoma, and one producing recognizable squamous cells arising in any epithelium of the body is termed a squamous cell carcinoma. It is further common practice to specify, when possible, the organ of origin (e.g., a renal cell adenocarcinoma or bronchogenic squamous cell carcinoma). Not infrequently, however, a cancer is composed of undifferentiated cells and must be designated merely as a poorly differentiated or undifferentiated malignant tumor .
The great majority of neoplasms are composed of cells representative of a single germ layer. The teratoma, in contrast, is made up of a variety of parenchyma cell

types representative of more than one germ layer, usually all three. They arise from cells differentiate along various germ lines, producing, for example, tissues that can be identified as skin, muscle, fat, gut epithelium, tooth structures, and, indeed, any tissue of the body. A particularly common pattern is seen in the ovarian cystic teratoma (dermoid cyst), which differentiates principally along ectodermal lines to create a cystic tumor lined by skin replete with hair, sebaceous glands, and tooth structures .

Others do no fellow the roles like, carcinomas of melanocytes have been called melanomas, although correctly they should be referred to as melanocarcinomas, and carcinomas of testicular origin are called seminomas.