ZAPOROZHZHIAN STATE MEDICAL UNIVERSITY

The department of pathological anatomy and forensic medicine with basis of low

Introduction into morphology of tumors

Tumors from epithelium

Lecture on pathological anatomy for the 3-rd year students

Neoplasia (tumor, *neoplasm*) - it is the process of new uncontrolled growth, characterized by violation of cellular genome with the un-regulation reproduction of new cell populations and losing a capability for differentiation.

In modern usage, a tumor/neoplasm develops in the wrong shape, in the wrong place, and persists after the initiating stimulus is removed.

There are 3 types of tumors according to prognosis:

1. benign tumors – slowly growing, not threatening to patient life;
2. malignant – quick progress, threatening to patient life without medical treatment;
3. tumors of transitional type – they have an unforeseeable biological behavior

All tumors, benign and malignant, have two basic components:

1) proliferating neoplastic cells that constitute their *parenchyma*

2) supportive *stroma* - connective tissue and blood vessels

The nomenclature of tumors is based on the parenchymal component

Tumor Nomenclature

I. In general, benign tumors are designated by attaching the suffix -oma to the cell type from which the tumor arises. *A benign tumor arising in fibrous tissue is a* fibroma.

II. Malignant neoplasms arising in mesenchymal tissue or its derivatives are called sarcomas (sarcos = fleshy). *A malignant tumors of fibrous tissue origin is a* fibrosarcoma. Malignant neoplasms of epithelial cell origin are called carcinomas.

Tumor Nomenclature

III. If the tumor originated in glandular epithelium, use the root adeno- *(adenoma or adenocarcinoma)*.

If the tumor originated in squamous or transitional epithelium, is benign, and protrudes above the epithelial surface, use the root papillo- *(papiloma)*.

If the tumor originated in non-glandular epithelium and is malignant, name it for the cell of origin.

Examples: Squamous cell carcinoma (skin)
Basal cell carcinoma (skin)

Tumor Nomenclature

IV. You can add adjectives as appropriate.

- papillary
- well-differentiated
- keratinizing

V. A handful of tumors that are thoroughly malignant have "benign" names:

- lymphoma
- mesothelioma
- myeloma ("multiple", plasma cell)
- melanoma

VI. Some tumors arise in "totipotential cells" and contain a variety of different mature and/or immature tissues from different germ layers, and they are called teratomas ("monster").

Tumor Nomenclature

VII. A hamartoma is "not a tumor, but is a developmental anomaly" which contains the same tissues as the organ in which it is found, but in the wrong proportions.

VIII. A tumor which ends in blastoma is composed of cells that resemble those seen in a developing organ. Most blastomas are malignant.

Benign Tumors

The suffix "-oma" is added to denote benign tumors.

For example, a benign tumor arising from adipose cells is called a *lipoma,*

- a cartilaginous tumor is a *chondroma*
- a tumor of osteoblasts is an *osteoma*.

Characteristics of benign tumors:

1. Cells resemble normal cells and tumor architecture resembles that of the mature organ - homological by appearance, to architectonics, color, consistence.

2. Usually are spherical and compress the surrounding tissues (giving rise to the appearance of a "capsule") - expansive type of growth.

3. Grow slowly and have few mitotic figures – only tissue atypism.

4. Never give metastasis and relapses.

Characteristics of malignant tumors

1. Malignant tumors generally grow more rapidly than benign tumors.
2. Cells differ morphologically and functionally from normal cells, and tumor architecture is less organized than that of parent tissue - heterological.
3. Tumor cells are locally invasive; the tumor grows into the surrounding tissues and destroys them - infiltrative type of growth .
4. It is characterized by cellular and by tissue atypism.
5. The tumor will eventually metastasize, spreading to another site remote from the original tumor.
6. Secondary changes in tissue – necrosis and haemorrhage – are seen.

Beningh tumor	Malignant tumor
1. homological by appearance, to architectonics, color, consistencies	1. heterological by appearance, to architectonics, color, consistencies
2. by tissue athypism	2. cellular and by tissue athypism
3. expansive growth – clear borders and scopes of tumor	3. infiltrative growth – without borders and scopes
4. there are no metastases	4. always gives metastases
5. there are no recidives	5. as a rule, recidivate
	6. secondary changes in tissue – necrosis's and haemorrhage

Stages of malignant tumor

1. The before tumor changes of tissue – is dysplasia (duration of this period is from a few months to about 2-3 years)

2. Formation of tumor cells clone – un-invasion stage (the complete recovery is possible).

3. The Invasive stage – penetration of tumor in the neighbor tissues.

4. Stage of metastasis formation.

DYSPLASIA ("atypia", "pre-cancer"): It is abnormal epithelium with "loss of uniformity of the individual cells, as well as a loss of their architectural orientation".

This includes "atypical hyperplasia" and "atypical metaplasia".

“Hyperplasia" and "metaplasia" imply the tissue cells look normal. In dysplasia, they look distinctly abnormal, and the changes resemble those seen in cancer cells. These weird changes are called ANAPLASIA.

Dysplasia

This stage can be recognized only by microscopy of tissue or by the zoned authentication of DNA. This is rapid proliferation and slow differentiation.

Microscopically: great number of cells, without stratification of layers, polyploidy, hyper-chromasia of cytoplasm (cellular atypia).

Dysplasia really can reflect:

- initial stage of development of cancer
- the process of reparation of tissue through dysplasia
- dyshormonal alteration of cellular pool (generations).

Tactic of doctor:

medical treatment > repeated biopsy through month > final conclusion.

Dysplasia – it is facultative pre-cancer in

- Breast
- cervix of uterus
- endometrium
- bronchioles
- gastric ulcer
- mucous membrane of stomach at the chronic gastritis.

The stage of formation of tumor rudiment (non-invasive stage)

It is appearance of different clones of tumor cells, which form the small cellular association. Part of these cells perishes under action of immune cells, and the other part slips out and is divided further. This stage is recognized by chance – during biopsy.

Microscopically:

1. intensive proliferation of cells with the presence of pathological mitosis's
2. structural atypism (cellular and tissue):

a) cellular – difference of daughter's cells from maternal (cellular and nuclear pleomorphism, hyperchromatic nuclei, and tumor giant cells)

b) tissue – violation of normal correlation between parenchyma and stroma

The Invasive stage – migration of tumor cells into surrounding tissues. Tumor cells connects with fibronectin and leave its tumor association. Tumor cells synthesize the molecules of adhesion and enzymes which destroy surrounding tissues, that allows to migrate up to the eventual points of migration – lymphatic and blood vessels (it is revealed at microscopy).

Metastatical stage – tumor cells must grow up to the vessels. Cancer cells have the tropism to the lymphatic vessels (nodules).

Cells, that are growing up to the vessels, must penetrate into the vessel, where, the part of cells are destroyed by immune cells of the organism. And a part of tumor cells becomes enveloped by fibrin and migrates by blood or lymph. Surviving tumor cells get into the organ, where a lot of macrophages that possess the macrophagical activity.

Metastatic spread:

There are four routes:

1) Spreading by serous surfaces
2) Mechanical transplantation (rare, typically iatrogenic)
3) Via lymphatic vessels (carcinomas). Tumors spread first to regional lymph nodes, then to any lymph nodes or organs
4) Via blood vessels (sarcomas, because the tumor cells are in direct contact with blood vessels from the beginning)

The common sites for metastatic spread for many common cancers include:

lymph nodes, lung, liver, bone, and brain.

Features of metastatic stage

1. the first tumor cells are destroyed by macrophages
2. there is the program of the repeated migration through the vascular wall, further in parenchyma of organ.

In parenchyma of organ a process can go as:

- tumor cells are destroyed in parenchyma of organ by tissue macrophages;
- tumor cells slip out from the immunological supervision and secure the appearance of new tumor cells.

The Anatomy-histological classification

According to the appearance:

- cellular infiltrate in tissue
- nodules
- polypus
- ulcer
- cyst

According to the type of growth:

- unicentrical – from one tumor rudiment
- policentrical (in stomach)
- expansive growth – without destroying surrounding tissues
- infiltrating (invasive) - tumor cells invade an organ diffusely without changing its shape growth, destroying surrounding tissues
- exophytic ("fungating") growth – tumor grows as a lump
- endophytic - tumor grows as an ulcer

According to the degree of maturity tumors are devided:

- differentiate – characterized by the slow growth and late metastases (I-II grade)
- undifferentiated – have not functions, except for the division, hasty growth and early metastases (III-IV grade)

Grade and Stage:

Tumor grade: assigned by the pathologist to reflect the cancer's degree of differentiation.

Grade 0: benign tumor

Grade I: Well-differentiated, cells look like normal organ

Grade II: Not so well-differentiated

Grade III: Worse than that

Grade IV: Even worse

Grade V: Worst of all (most tumor types are graded I-III)

Grade and Stage:

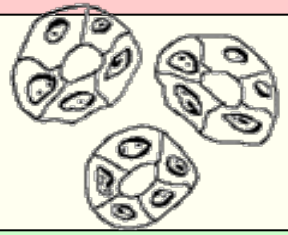
Tumor stage: assigned by the clinician on the basis of all available information on the extent of tumor spread.

Stage I might mean the tumor is smaller than 1 cm diameter, without metastases

Stage II might mean the tumor is larger than 1 cm and/or is symptomatic and/or there are metastases to the regional lymph nodes

Stage III might mean the tumor has infiltrated a non-resectable structure and/or there are distant metastases

Grading of Malignant Neoplasms

Grade	Definition
I	Well differentiated 
II	Moderately differentiated 
III	Poorly differentiated 
IV	Nearly anaplastic 

Alternative system: TNM

"T" for tumor:

- T1 might mean primary tumor is smaller than 1 cm in diameter
- T2 might mean primary tumor is larger than 1 cm in diameter
- T3 might mean primary tumor is invading something non-resectable
- Tx might mean primary tumor can't be found

"N" for regional lymph nodes:

- N0 would mean no tumor in regional lymph nodes
- N1 might mean tumor in a few nearby lymph nodes
- N2 might mean many nodes, or some nodes farther downstream, are involved
- Nx might mean unable founding tumor in lymph nodes

"M" for metastases:

- M0 would mean no distant metastases
- M1 would imply distant metastases, etc.
- Mx might mean unable founding of tumor metastases

Generally, tumors of high grade present at high stage, while tumors of low grade present at low stage

Benign epithelial tumors

Benign epithelial tumors are subdivided according to their origin from different types of epithelium into the tumors of integumentary epithelium (papillomas), tumors of glandular epithelium (adenomas).

Papillomas

It is broad-based superficial tumor of branching villous vascular stroma covered by neoplastic epithelium.

Papilloma has following features:

- Bening tumor.
- Origin from the skin and mucous membranes.
- It looks like a ledge or a bush of branching papillae.
- Exophytic tumor.
- Slow growth.

Adenomas

Benign epithelial tumor from the epithelium of the glands and glandular organs.

More often they can be found in the breast, thyroid gland, liver, ovaries, prostatic gland, gastrointestinal tract.

According to the histological composition adenoma may be tubular and alveolar.

Squamous cell carcinomas

These arise anywhere there is a stratified squamous epithelium, either healthy (skin, esophagus, mouth, many others) or metaplastic (endocervix, bronchi).

Look for any (or even all) of the following:

- keratin (will stain pink-red on H&E)
- pearls (i.e., whorls that mimic little hairs)
- desmosomes ("intercellular bridges", "prickles")
- tonofilaments (electron microscopy)
- single-cell apoptosis (they're at the top of the epidermis)

Adenocarcinomas

These arise anywhere there are glands, even single-celled glands (i.e., goblet cells)

Look for any (or even all) of the following:

- lumens (intercellular, intracellular)
- especially, glands-within-glands ("Swiss cheese")
- or even "inside-out" glands, with the malignant cells growing around a fibrous stalk ("papillary growth")
- mucin (intercellular "lakes", intracellular)
- other secretory products, depending on the gland of origin (immunostain may be required)
- cells forming cohesive nests, or at least sticking to one another
- signet-ring cells containing mucin, alone or in clusters
- microvilli

Nomenclature of Neoplasia
Based upon origin:

I. Maligant neoplasms arising from tissue embryologically derived from ectoderm or endoderm are usually carcinomas. Examples include:

- Squamous cell carcinoma of cervix
- Adenocarcinoma of stomach
- Hepatocellular carcinoma
- Renal cell carcinoma

II. Malignancies arising from mesoderm are usually sarcomas. Examples include:

- Leiomyosarcoma
- Chondrosarcoma
- Osteosarcoma
- Liposarcoma

Nomenclature of Neoplasia Based upon origin:

III. Neoplasms with more than one cell type but arising from only one germ layer are called "mixed tumors".
The best example is the benign mixed tumor of salivary gland.

IV. Neoplasms with more than one cell type and arising from more than one germ layer are called teratomas (in ovary)

Nomenclature of Neoplasia Based upon origin:

V. Neoplasms ending in "-blastoma" resemble primitive embryonic tissues.

Examples include:

- Retinoblastoma
- Neuroblastoma
- Hepatoblastoma
- Medulloblastoma

Nomenclature of Neoplasia
Based upon origin:

VI. Not all malignant neoplasms have benign counterparts:

Hematopoietic and lymphoid cells (as in bone marrow and lymph node) give rise to leukemias and lymphomas.
They have no benign counterpart.

Gliomas (astrocytomas, oligodengrogliomas, glioblastoma multiforme, etc) arise from glial cells in the CNS. They have no benign counterpart.