Neoplasia lec2

RECALL: In the last lecture, we agreed that neoplasms are new growths with specific genetic mutations that allow them to grow autonomously. We also said that neoplasms can be benign or malignant

Characteristics of malignant neoplasms

- 1. Differentiation and anaplasia
- 2. Increased rate of growth
- 3. Local invasion
- 4. Metastasis

Differentiation

The extent to which neoplastic cells resemble the cells they originated from, both morphologically and functionally.

- The more the difference, the more the de-differentiation. Which means the worse the behaviour of the tumour

Benign tumors: well differentiated

- Benign tumors resemble their parent cells morphologically and functionally
- Example: Pituitary adenoma can look exactly like normal pituitary gland and can secrete hormones secreted from that gland

Malignant neoplasms: less differentiated or dedifferentiated

- Malignant neoplasms have a wide range of differentiation.
- Well differentiated tumours still have some similarity with their cell of origin.
- Moderately differentiated: less resemblance to cell of origin
- Poorly diff: almost no similarity to cell of origin
- These stages of differentiation are referred to as: tumour grades.

well is grade1, moderate is grade 2, poor is grade 3.

**A QUICK NOTE

For each tumour there is a grade and a stage.

• Grade: refers to the morphology: to what we see under the microscope

• Stage: refers to extent of tumour spread: presence of metastasis.

• Both grade and stage are important for prognosis. BUT stage is much more important.

• Tumour stage is the single most important prognostic factor.

Anaplasia

Lack of differentiation. So we have almost complete loss of differentiation.

• Anaplasia is a hallmark for cancer

<u>Features of anaplastic cells</u>

• Pleomorphism: variation in size and shape

• Hyperchromatic, dark nuclei

• Bizarre abnormal nuclei with coarse chromatin

• Large nuclei with high nucleo-cytoplasmic ratio (N/C ratio). Note: normal N/C ratio is 1:4 or 1:6

• Presence of large giant cells, with multiple nuclei

• Prominent nucleoli.

• Increased mitotic activity with abnormal appearance: tripolar (Mercedes sign) or quadripolar

• Cells abnormally oriented with loss of polarity (loss of normal organization)

Increased growth rate

• Most benign tumors: slow growing

• Most malignant: fast growing, more mitotically active

Local invasion

Benign neoplasms: remain localized and do not invade.

• This is because they are encapsulated: the capsule is derived from

1. Stroma of the host tissue and

2. Parenchymal cell atrophy under the pressure of the expanding tumor.

*parenchymal cells are cells that constitute most of the organs volume

• However, not all benign tumors are encapsulated but even the un-encapsulated ones have a line of cleavage in the majority of cases (e:g uterine leiomyoma)

Invasion In malignant tumors

• Cancer: progressive infiltration and invasion

• Usually no well-defined capsule. So must be removed with a wide margin

• Local invasion is the second most important feature to differentiate benign from malignant neoplasms; metastasis is the most important feature.

Metastasis

Secondary implants of the tumor which are discontinuous with the primary tumor and located in distant sites.

- Metastasis is the most important feature of malignancy.

Cancers differ in their ability to metastasize

• Basal cell carcinoma of skin doesn't metastasize

• CNS tumors rarely metastasize

• Bone =osteogenic sarcoma usually found to be metastasized before discovering the primary tumor

Routes of metastatic spread

• 1. Seeding within body cavities

Ex. Ovarian cancer, tumor cells move through the peritoneal cavity and fill it with metastatic deposits.

• 2. Lymphatic spread

More in carcinoma, rare in sarcoma

• Pattern of lymph nodes affected depends on the site of primary tumor

• Tumors metastasize to regional lymph nodes first, however skip metastases can occur.

• 3. Hematogenous spread

• Sarcomas spread mainly by hematogenous route

• Carcinomas also spread by this route but they metastasize to lymph nodes first (via lymphatic route)

• Liver and lungs are the most common sites of spread (most common recipients), because they receive a large amount of blood so metastatic deposits can colonize these sites.

Benign vs. malignant neoplasms

	benign	Malignant
genetics	Few mutations, clonal but genetically more stable	Genetically un stable
Macroscopic appearance	Soft, mobile, encapsulated	Hard, fixed, infiltrative
differentiation	Well differentiated	Well or poor Anaplastic
mitosis	low	High and abnormal
Local invasion	localized	Invasive
metastasis	no	yes

Two important terms: dysplasia and carcinoma in situ.

• These two are precancerous lesions, occurring mainly on mucosal surfaces.

They are preneoplastic and with time they can progress to neoplasia.

Dysplasia

Ground info

• Normal epithelium is well organized.

• It is composed of layers of cells that mature as we go up: towards the surface.

• Epithelial tissue regenerates all the time, so cells originate from the base of the epithelium and grow upwards.

• During this growth they mature and when they reach the surface they spend the rest of their lifespan as fully mature cells then they die by apoptosis

• There is an intact, non-invaded, basement membrane.

Definition

•Disordered but non-neoplastic proliferation confined to the mucosa without affecting the underlying tissue. (because dysplasia is confined to the epithelium, It doesn't disrupt the basement membrane)

•Loss of uniformity of individual cells and in their architectural orientation, tissue loses its organization.

•Expansion of immature cells

•Seen mainly in epithelial lesions

Histologic features of dysplasia

•Loss of orientation

•Pleomorphism

•Large cells

•Hyperchromatic nuclei

•More mitoses than normal

•Mitosis in an abnormal location (normal location is at the basal layers of epithelium… abnormal: mitosis seen in more superficial layers)

NOTE: many of these features are similar to those we discussed in anaplasia. But here these changes are seen only within the epithelium without invading the basement membrane that separates the epithelium from the underlying tissue.

Grades of dysplasia

• Dysplasia is divided into mild, moderate and severe

• This depends on the extent of epithelial involvement.

• If only the lower third of the epithelium affected: mild

• Two thirds: moderate

• Full thickness: severe

In situ carcinoma: severe dysplasia involving the whole thickness of the epithelium Again: basement membrane intact. That's why it is "in situ"

Micro invasive carcinoma: there is dysplasia but it is invading the basement membrane

Behavior of dysplasia

•Although non neoplastic, dysplastic cells can accumulate mutations and transform to malignant lesions. But not always and not commonly.

•Dysplasia is a precursor of malignancy.

•However, mild and even moderate dysplasia can regress if initial insult removed

Summary

• There are certain changes that can affect epithelial tissue before it gets fully carcinomatous.

• Abnormal organization of abnormal cells confined to the mucosa; this is dysplasia

• Dysplasia can be divided to three grades: mild, moderate and severe.

• Mild dysplasia affects the lower third of the epithelium

• Moderate: affects the lower two thirds

• Severe: involves almost the full thickness.

• Carcinoma in site is the worst, severest form of dysplasia. It involves the entire thickness, and the individual cells are very pleomorphic and anaplastic.

• The basement membrane is intact in all these stages

• If the abnormal cells invade the basement membrane, then the lesion has transformed to micro-invasive carcinoma.

• Microinvasive carcinoma can spread further to become an invasive carcinoma

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Benign tumors tend to be well differentiated, encapsulated, non-invasive, slowly growing and they do not metastasize.

Malignant tumours are anaplastic, rapidly growing, invading masses and they do metastasize. .

Metastasis occurs via three routes: 1. lymphatic spread where the tumour cells invade lymphatics and colonize lymph nodes. Carcinomas spread first by this route. Sarcomas rarely spread by lymphatics.

2. Hematogenous : tumour cells invade blood vessels and reach distant organs. Sarcomas spread by this route. Carcinomas also use it.

3. Peritoneal seeding: occurs when a tumour in a site in close proximity to a peritoneal surface, usually the ovary or appendix, seeds the surface.

• Dysplasia means disorganized growth confined to a mucosal surface. It is not neoplastic but can progress to neoplasia.

• Carcinoma in situ is full thickness atypia not invading the underlying tissue.

• Microinvasive carcinoma occurs when the carcinoma in situ cells penetrate the basement membrane