NEOPLASIA

Essay.

Define. metastasis. mode of spread of malignant tumor / metastasis.

Metastases — definition.

are secondary implants of a tumor that are discontinuous with the primary tumor and located in remote tissue (distant tissue).

This process is known as metastasis ★ and the secondary deposits are called metastases

- The most important attribute that identifies a neoplasm as malignant is the ppty of metastasis.

SIGNIFICANCE

(1) metastases clearly identify a tumor as malignant as benign neoplasms never metastasize.
- Exception → BCC of skin, Glioma } locally invasive but rarely metastasise.

(2) - metastases strongly reduce possibility of cure of cancer.

(3) metastatic spread is the most common cause of Cancer death.

Factors favouring metastasis.

(1) poorly differentiated tumor (anaplasia)
(2) size of primary tumor - large.
(3) rapidly growing tumor.

MORPHOLOGY

- It should resemble primary tumor microscopically.
- but if highly anaplastic → undistinguished, unrecognisable.

MODE OF SPREAD OF METASTASIS

- Lymphatics
- hematogenous
- spread along body cavities (seeding)
- direct transplantation
- Rarely → along epithelial lining.

I. Lymphatic spread

most common pathway of spread of.
→ Carcinomas ★

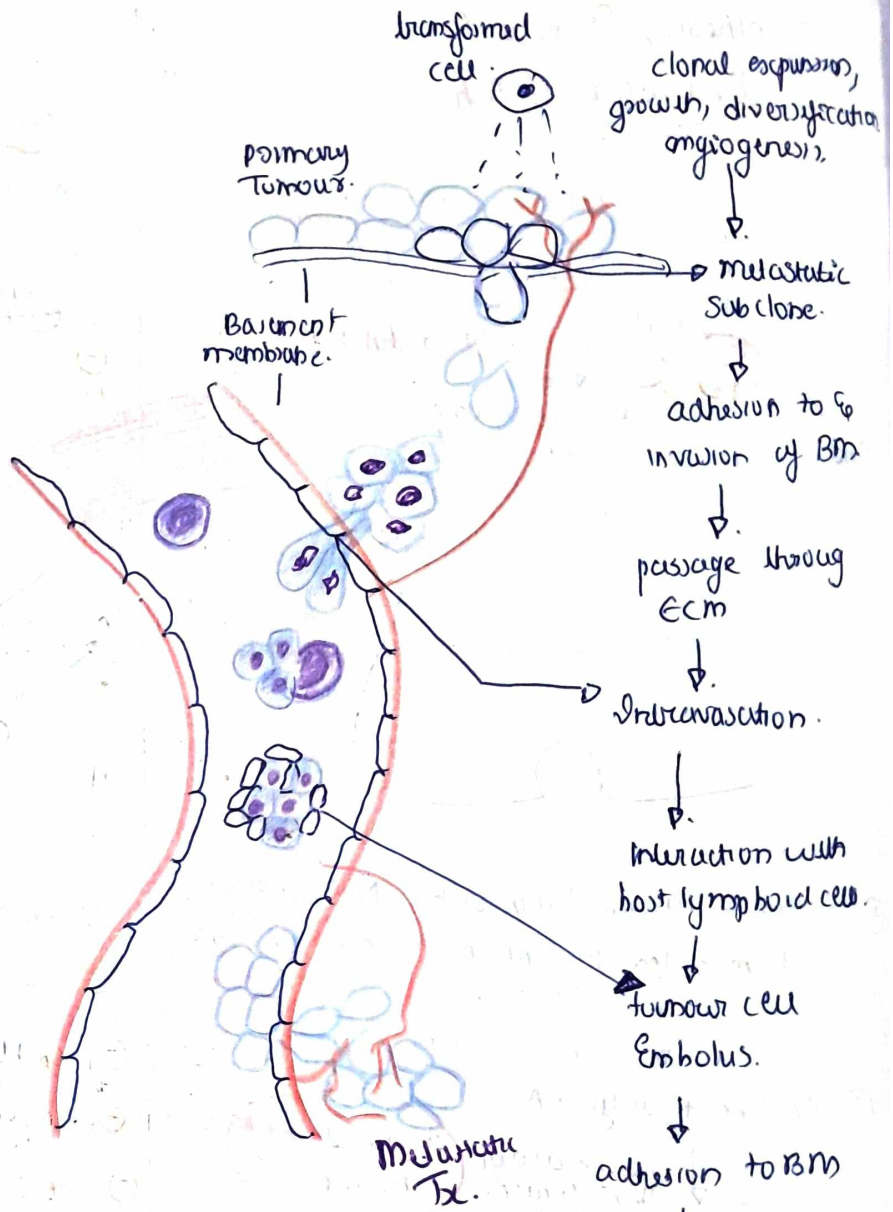
Regional node involvement

- wall of lymphatics ~~in regio of tumor~~.
↓
invaded by cancer cell.
↓
continuous growth within lymphatic channels (lymphatic permeation).
↓
detach → tumor emboli
↓
Carried to regional draining lymph nodes
↓
grow in subcapsular sinus - subsequently entire lymph node.

Cholinoceptors.

- muscarinic & nicotinic.
  - $M_1 - M_5$
  - Nm
  - NN.

Location, action table from tex ✓



Robbins: metastasis is defined by the spread of a tumour to sites that are physically discontinuous with the primary tumours, and unequivocally marks a tx as malignant, as by definition benign neoplasms do not metastasize.

Skip metastasis?

- Here, local lymph nodes are bypassed and metastases develop in lymph nodes distant from site of 1° tumor.

↓

eg: Abdominal Cancers

↓

Supraclavicular lymph node.

↓

Virchows lymph node.

- Retrograde → spread against lymphatic flow.

eg: Carcinoma prostate

↓

Supraclavicular lymph node.

Sentinal lymph node.

- first node in a regional lymphatic basin that receives lymph flow from the 1° tumor.

Examples

Breast → upper outer quadrant → axillary lymph nodes
→ inner quadrants → nodes along internal mammary artery.

- Lung → perihilar tracheobronchial mediastinal.

II. Hematogenous Spread.

- Usual → Sarcoma.

Vessels invaded →

- easily invade capillaries and venules.
- arterioles and arteries ↓ relatively resistant.

m/c

Pattern → venous invasion ↓ pattern of metastases follows the venous flow.

Tumors with affinity for venous invasion

① Renal cell carcinoma.
↓ invade renal vein.
↓ grows in snake like fashion up the IVC
↓ Sometimes reach right side of heart.

② Hepatocellular Carcinoma.
↓ Invade branches of portal & hepatic vein.

Target Organ for metastasis by hematogenous.

① Liver and Lungs - most frequently involved

Liver → all portal area drains into liver.

Lungs → all caval blood flows to lungs

② vertebral column.

carcinoma of thyroid, prostate.
↓ paravertebral plexus
↓ vertebral column.

③ Bone.

- prostate, lung, thyroid breast*, liver etc.

④ Brain

lung cancer (common) kidney adrenal).

Organs relatively resistant

- spleen
- skeletal muscle.

Morphology

Gross

multiple round nodules of varying size found throughout the organ.

mc

generally resemble primary tumor.

Seeding of Body Cavities & Surfaces.

① Transcoelomic spread.

~~occurs when~~ malignant tumor arising in organs adjacent to body cavities.
↓ may.
seed body cavities.
↓
peritoneal (most common).
pleural
pericardial.
joint space.
subarachnoid space.

* peritoneal cavity.
- Ovarian tumors.
- GI tract tumors.
↓
ascites.

* pleural cavity.
peripherally situated lung tumors → pleural effusions

Subarachnoid space.
Ependymoblastoma.
↓ through CSF.
to spinal cord.

- Pseudomyxoma peritonei - from appendiceal mucinous Carcinoma.

② spread along epithelial lined space.

* Carcinoma endometrium. ↔ via fallopian tube. ovary

* Kidney
↓ via ureters.
lower urinary tract

Direct Transplantation.

Direct transplantation
- Surgical instruments.
- direct contact.
↓
spread from lower lip to upper lip.

Figure.

Invasion - metastatic Cascade

2 phase → Invasion of ECM.
→ ~~metastasis~~. Vascular dissemination. Homing of TC cells, colonization.

Invasion of ECM.

① Loosening of tumor cell.
loss of E-cadherin
↓
loosening of tumor cells.
↓
cells get detached from primary tumor.

2. Focal degradation/ proteolysis of basement membrane and Interstitial Connective tissue.
↓
due to secretion of degrading enzyme by tumor cells and stromal cells in cancer.
↓
matrix metalloproteins
MMP; U-PA, C.
↓ cathepsin.
degradation.

3. Attachment of tumor cell to ECM proteins
focal degradation of BM.
↓
new and strong site
↓
receptors on tumor cells (eg: integrin).
↓
attach to the new site
↓
(4) tumor cell migration.

(4) locomotion / migration.
↓
drives tumor cell forward through degraded BM & zones of proteolysis in Interstitial Connective tissue matrix
↓

↓

involves many receptors and signaling proteins.

↓

potentiated by autocrine motility factor, which is a tumor cell derived cytokine.

↓

tumor cell traverse through the interstitial connective tissue and ultimately reach nearby bloody lymphatic vessel.

↓

penetrate basement membrane of vessels

↓

access to circulation.

Metastasis ✓ figure.

(vascular dissemination and Homing of Tumor cells).

① Penetration of vascular/lymphatic channels.

↓

by penetrating their basement membrane

↓

access to circulation.

"Intravasation into tumor vessels

② Interaction of tumor cells with host → lymphoid cells, mechanical stress, apoptosis).

↓

Survived tumor cells Clumps with platelets → platelet-tumor aggregates

↓

bind with coagulation factor.

↓

Tx. emboli.

③ Transit through circulation

④ Arrest, → at distant location away from 1° tumor

↓

at site of arrest.

tumor cell adhere to endothelial cell

⑤ Exit from circulation into a new tissue site.

↓

by Extravasation of tumor cells at metastatic site.

↓

micro metastasis : prostate → bone
Neuroblastoma - liver, bone

↓

Angiogenesis

↓

metastatic tumor.