Biochemistry of Cancer and Tumor Markers

University Of Fallujah
College Of Medicine

Lecture : 9

Stage : Second 2nd

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Date:

ONCOFETAL PROTEINS

- These are proteins produced during fetal life.
- present in high concentrations in the sera of fetuses & decrease to low levels or disappear after birth.
- They reappear in individuals with cancer.
- This demonstrates that certain genes are reactivated as a result of the malignant transformation of cells.
- There are several oncofetal antigens as AFP & CEA

ALFA-FETO PROTEIN (AFP)

- AFP is a glycoprotein, is one of the major proteins in the fetal circulation
- The maternal AFP level increase from 12 weeks to peak during the third trimester
- It is a marker of hepatocellular carcinoma & nonseminomatous ca of testis
- Other causes of increased AFP due to non-malignant causes:- Pregnancy- Non- cancerous liver diseases : hepatitis & cirrhosis
- Except in pregnancy , AFP level greater than 1000ug/L indicates cancer
- Clinical Application of AFP: Screening, diagnosis, prognosis & monitoring of hepatocellular carcinoma(i.e. hepatoma).

- **CARCINOEMBRYONIC ANTIGEN (CEA)**
  - ▪It is the most widely used tumor marker for **colorectalcancer.**

- Plasma concentrations may also rise in non-malignantdisease of the gastrointestinal tract and in smokers.
  - The main clinical use of CEA is as a tumor marker incolorectal cancer for:
  - Prognosis
  - Post-surgery surveillance
  - Monitor response to chemotherapy

HORMONES AS TUMOR MARKER

- The production of hormone in cancer involves 2 separate routes:
- The endocrine tissue that normally produces the hormone can produce excessive amounts

- A hormone can be produced by nonendocrine tissue that normally does not produce the hormone (e.g. ectopic production of ACTH & PTH)

Human Chorionic Gonadotropin (hCG)

- hCG is a hormone normally secreted by trophoblasts in the placenta during pregnancy.
- It is a glycoprotein consisting of alfa and Beta subunits.
- And it is the most useful marker for detection ofgestational trophoblastic diseases (GTDs) that include:

✓ Hydatiform mole (vesicular mole)
✓ Choriocarcinoma
✓ It is also elevated in nonseminomatous tumors of the testis (with AFP).

ENZYMES AS TUMOR MARKERS:

- Generally, an increase in enzymes is not specific or sensitive to identify type of cancer.

Neuron-specific enolase (nse)

- NSE is the most abundant enzyme, enolase found in adult neurons and is thought to serve as a growth factorin neurons.
- It is elevated in tumors derived from these tissues, including neuroblastoma

CARCINO- ASSOCIATED PROTEINS

Prostate Specific Antigen (PSA)

- PSA is a glycoprotein produced only in the epithelial cells of the acini & ducts of the prostate.
- Levels of PSA increase with age, which is mainly due to the increasein the volume of the prostate that occurs.
- Prostate- specific antigen (PSA) is a marker for prostatic carcinoma, a common male tumor

- Its level is raised in benign prostatic hyperplasia (BPH) and prostatic carcinoma but also in prostate infection, for example **prostatitis, and after rectal examination.**
- The **PSA** is bound in the plasma to either a1 - antichymotrypsin or a2-macroglobulin .
- There are 2 major forms of PSA that are found in the blood (free and complexed) .
- The concentration of bound or complexed PSA is higher in prostate carcinoma, whereas that of free PSA is higher in BPH.
- The ratio of free to total PSA is lower in men with prostatic carcinoma.
- Total PSA is used in screening & in monitoring of prostate cancer

CARBOHYDRATE MARKER

Carbohydrate Antigen-125 (CA-125)

- **CA-125** concentration may be raised in the plasma of patients with ovarian carcinoma.
- It can also be raised In pregnancy, fibroids, liver and pancreatic disease, endometriosis and pelvic inflammatory disease.
- Additionally, it can also be raised in other malignant diseases such as lung, breast or colon carcinoma

- **CA15-3** : CA-15-3 concentration may be raised in the plasma of some patients with advanced breast carcinoma, although it can also be raised in cirrhosis, and with ovarian cysts.

- **CA-19-9** : Concentration may be raised in the plasma of patients with pancreatic or colorectal carcinoma and those with obstructive liver disease

TISSUE RECEPTORS.

- Tissue receptors, which are proteins associated with the cell membrane, are another type of tumor marker.
- These substances bind to hormones and growth factors, and therefore affect the rate of tumor growth.
- Some tissue receptors must be measured in tissue samples removed for a biopsy, while others are secreted into the extracellular fluid (fluid outside the cells) and may be measured in the blood.
- Some important receptor tumor markers are estrogen receptor, progesterone receptor

- **Estrogen receptor** : Measurement of the estrogen receptor (ER)is used specifically to evaluate breast cancers.
- It gives an indication of prognosis and responsiveness to therapy.
- Tissue from a biopsy is used to measure the estrogen receptor.
- Most breast cancers in post-menopausal women are ER-positive, meaning that they require estrogen to grow.
- These ER positive breast cancers are less aggressive than ER negative breast cancers.

GENETIC MARKERS

- Two classes are involved in the development of cancer Oncogenes: as HER-2/neu (Human Epidermal growth factor)
- Suppressor genes: as p53, BRCA1 , BRCA2...

- **ONCOGENES**. Some tumor markers are the product of oncogenes, which are genes that are active in fetal development and trigger the growth of tumors when they are activated in mature cells.

- **Her-2/neu** : HER-2/neu is an oncogenic growth factor receptor also known as c-erbB-2..
- The presence of HER- 2/neu is generally associated with a poorer prognosis for breast cancer.
- It can also help to determine treatment options, since newer drugs can block this protein and decrease cancer growth.

Tumor suppressor genes

- Tumor suppressor genes are genes that encode for proteins that are involved in normal protection of cells from unregulated growth
- If mutated may lead to cancer
- Examples of tumor suppressor genes:
- ✓ P53
- ✓ BRCA1 & BRCA2

P53 carcinogens causing mutations

- p53 (an example of tumor suppressor genes)
- Gene product (protein) normally result in cell cycle arrest & induces apoptosis.
- Upon mutation: loss of function mutation
- Cancer: Colon, Brain cancer, lung & liver Cancer

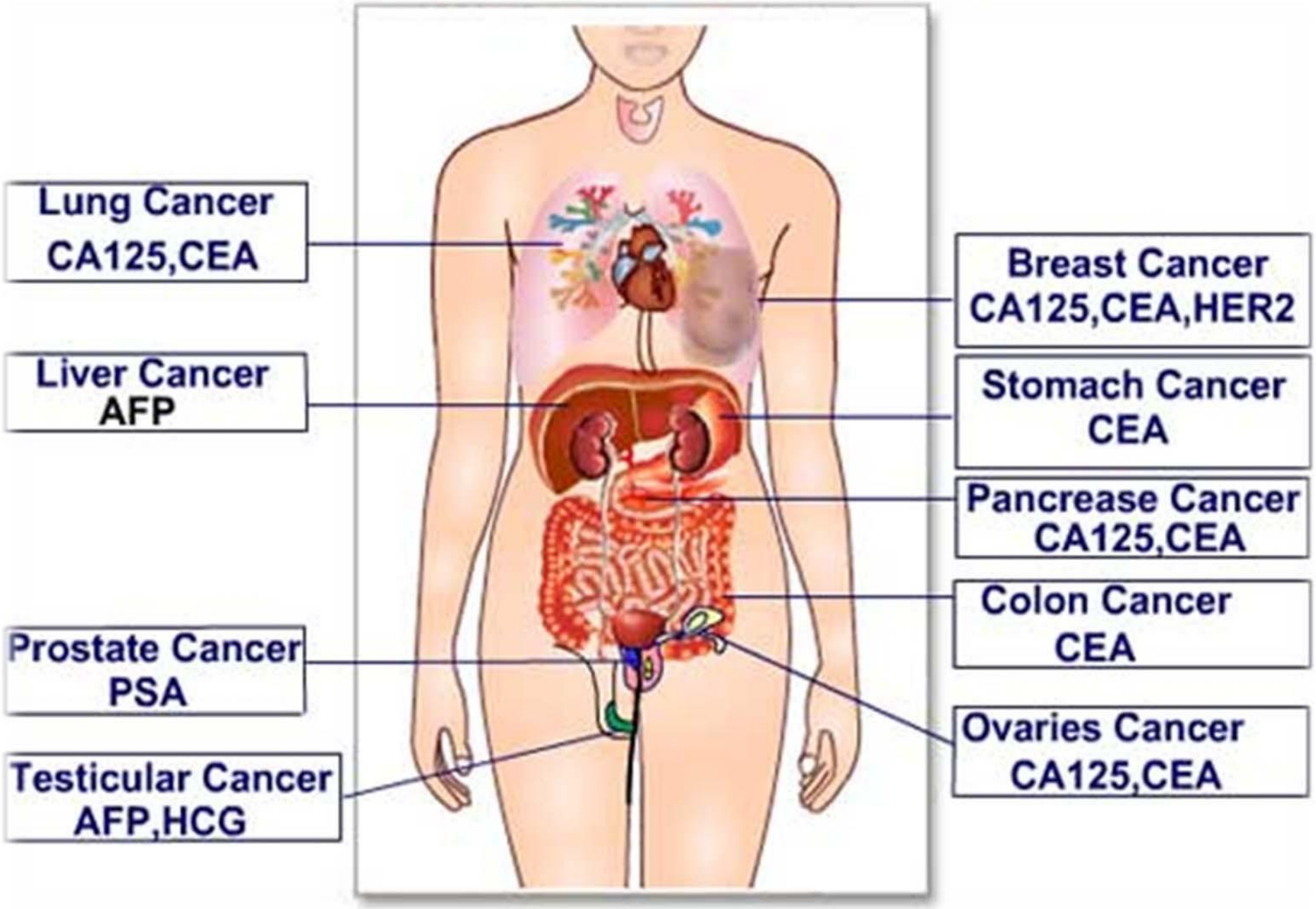
BRCA1 & BRCA2

- They are genes that are inherited as autosomal dominant trait.
- If these genes are mutated, cancer occur (mutation is inherited to off spring).
- Carriers of BRCA1 gene mutation have an 85% risk of developing breast cancer& 45%risk of developing ovarian cancer

DISCUSSION

- Tumor markers are generally best used for monitoring the progression of tumours with therapy (remission or relapse).
- Many are of little value in diagnosis or screening of disease.

- A tumor does not mean cancer - tumors can be benign (not cancerous), pre-malignant (pre-cancerous), or malignant (cancerous).


Lung Cancer
CA125,CEA
Liver Cancer
AFP
Prostate Cancer
PSA
Testicular Cancer
AFP,HCG
Breast Cancer
CA125,CEA,HER2
Stomach Cancer
CEA
Pancrease Cancer
CA125,CEA
Colon Cancer
CEA
Ovaries Cancer
CA125,CEA