Tumor Marker

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Tumor Marker

- A tumor marker is a substance produced by a tumor or by the host in response to a tumor, which is used to differentiate a tumor from normal tissue, or to detect the presence of a tumor based on measurements in the blood or secretions. Such substances are found in cells, tissues, or body fluids and are measured qualitatively or quantitatively by chemical, immunologic, or molecular biological methods.

TUMOUR MARKERS

- For the measurement of a tumor marker to be clinically useful, the result should clearly separate those patients with from those without a tumor.
- Therefore (although in practice this is not the case), a tumor marker should ideally be:
- 100 per cent *sensitive*: levels should be raised if the tumour is present,
- 100 per cent *specific*: levels should *not* be raised if the tumour is *not* present.

- Tumour markers may be used for the following:

1. To screen for disease Very few markers are sufficiently sensitive or specific to be used to screen for the presence of a tumour.

2.To diagnose a tumour If a patient presents with clinical signs or symptoms, the measurement of a marker in plasma or urine may very occasionally be used to confirm a diagnosis.

3. To determine the prognosis In some cases the concentration of a specific marker is related to the mass or spread of the tumour.

4.To monitor the response to treatment If a tumour marker is present, the rate of its decrease in concentration may be used to assess the response to treatment such as surgery, chemotherapy or radiotherapy.

5. To identify the recurrence of a tumour If the concentration of the marker was previously raised, intermittent measurement during remission may sometimes be used to identify recurrence.

Some examples of tumour markers

- Prostate-specific antigen
- Prostate-specific antigen (PSA) is a marker for prostatic carcinoma, a common male tumour, and is a 33-kDa protein and is homologous with the protease kallikrein family; it has a plasma half-life of about 3 days.
- One of its probable functions is to help liquidize semen.
- Its level is raised in benign prostatic hyperplasia (BPH) and prostatic carcinoma but also in prostate infection, for example prostatitis, and after rectal examination.
- Levels of PSA increase with age, which is mainly due to the increase in the volume of the prostate that occurs. Therefore age-adjusted reference ranges should be used. There may also be a place for expressing plasma PSA in terms of prostate volume as found on ultrasound examination.

- Plasma PSA concentrations greater than 10 µg/L are strongly suggestive of carcinoma, although carcinoma may be present even if values fall within the reference range.
- A PSA above 20 µg/L is suggestive of prostatic carcinoma that has spread beyond the prostate gland.
- Plasma PSA assays in conjunction with digital rectal examination may be used as part of a screening programme for prostatic carcinoma in at-risk males.

Alkaline phosphatase

- Alkaline phosphatase may arise from liver, bone, or placenta. The alkaline phosphatase in the sera of normal adults comes primarily from the liver or biliary tract. Elevated alkaline phosphatase is seen in primary or secondary liver cancer.
- Quantification may be helpful in evaluating metastatic cancer with bone or liver involvement. Greatest elevations are seen in patients with osteoblastic lesions, such as in those with prostatic cancer with bone metastases. Minimal elevations are seen in patients with osteolytic lesions, such as those with breast cancer with bone metastases.

Carcinoembryonic antigen

- Carcinoembryonic antigen may be produced by some malignant tumours, especially colorectal carcinomas.
- If the initial plasma concentration is raised, serial plasma CEA estimations may sometimes help to monitor the effectiveness of, or recurrence after, treatment .
- Plasma concentrations correlate poorly with tumour mass, but a very high concentration usually indicates a bad prognosis. Plasma concentrations may also rise in non-malignant disease of the gastrointestinal tract and in smokers.
- Thus, the test is non-specific and thus lacks value in diagnosis.

a-Fetoprotein

- a-Fetoprotein (AFP) is an oncofetal protein, the synthesis of which is suppressed as the fetus matures.
- Concentrations may be very high in the plasma of patients with certain tumours such as hepatocellular carcinoma (primary hepatomas and hepatoblastomas) and teratoma.
- Moderately raised concentrations may be due to non-malignant liver disease.

Human chorionic gonadotrophin

- Human chorionic gonadotrophin (hCG) is normally produced by the placenta, but also by trophoblastic cells of gonadal and extragonadal germ cell tumours.
- Ectopic secretion has been observed in some bronchial carcinomas.
- The measurement of hCG can be used to screen for choriocarcinoma in women who have had a hydatidiform mole.
- Plasma concentrations may be raised in patients with malignancy of the gonads such as seminomas, and hCG may be used to monitor the response to treatment and tumour recurrence.

Carbohydrate antigens

- Carbohydrate antigens (CAs) are a group of tumour markers, raised plasma concentrations of which may be used to monitor the response to treatment and the recurrence of certain tumours.

1. 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. If plasma CA-125 is 35 kU/L or more, an ultrasound scan of the abdomen and pelvis has been proposed as a means of screening for ovarian carcinoma.

2.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.

3.CA-19-9 concentration may be raised in the plasma of patients with pancreatic or colorectal carcinoma and those with obstructive liver disease.

Other tumour markers

- Serum paraprotein and urinary Bence Jones protein used for diagnosis of multiple myeloma.
- Plasma lactate dehydrogenase (LDH): the activity can be raised in certain haematological tumours such as lymphomas.
- Placental alkaline phosphatase: true placental alkaline phosphatase and placental-like isoenzyme levels are raised in seminoma and dysgerminoma. Levels are not usually raised in teratomata.
- In conjunction with AFP and hCG, it is useful in the diagnosis and monitoring of extragonadal and gonadal germ cell tumours. However, plasma levels are also elevated in smokers.

- Thyroglobulin: this high-molecular-weight protein is produced in the follicular cells of the thyroid.
- Its concentration is raised in follicular or papillary carcinoma of the thyroid. Spuriously low levels may be found in the presence of thyroglobulin antibodies, which interfere with the assay.
- Neuronal-specific enolase: plasma levels may be raised in small cell lung carcinoma and neuroblastoma; it is derived from neurodectal tissue.
- Inhibin: this is secreted by the granulosa cells of the ovary and by the Sertoli cells of the testis. It can be used as a plasma tumour marker of ovarian granulosa cell tumours and testicular Sertoli cell tumours.

- Squamous cell carcinoma antigen: this is a plasma tumour marker of potential use in squamous cell carcinoma of the cervix.
- Chromogranin A is released from neuroendocrine cells such as in phaeochromocytoma and carcinoid tumours.
- Protein S100B is a calcium-binding protein. It is expressed in brain astrocytes and glial cells and also in melanocytes and may be useful in monitoring therapy in malignant melanoma.
- Human epididymis protein (HE4) is being used as a tumour marker for ovarian carcinoma.