



PROSTATE CANCER

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Prostate Cancer

Prostate cancer is the carcinoma of prostate gland that may spread to other parts of the body particularly bones and lymph nodes.

Pathophysiology

In prostate cancer, the cells of these prostate glands mutate into cancer cells. Mutation is majorly in p53 gene, BCL2 and ERK5 or alteration in Akt kinase signaling contribute toward the development of prostate cancer. The prostate glands require hormones, known as androgens that are involved in cell survival and apoptosis. Androgens include testosterone, dehydroepiandrosterone and dihydrotestosterone.

Initially, small clumps of cancer cells remain confined to prostate glands, a condition known as carcinoma in situ or prostatic intraepithelial neoplasia (PIN). Over time, these cancer cells begin to multiply and spread to the surrounding prostate tissue forming a tumor. Eventually, the tumor may grow large enough to invade nearby organs such as the nearby lymph nodes or the rectum, or metastasize to bone, lymphatic system and bladder.

Risk Factors

A complete understanding of the causes of prostate cancer remains elusive.

- Obesity
- Age
- Family History
- Lower levels of Vit. D
- Prostatitis
- Elevated Blood levels of Testosterone

Symptoms

- Weak or interrupted urine flow
- Blood in urine
- Nocturia
- Dysuria
- Pain in Pelvis, spine and ribs
- Lymphedema
- Renal insufficiency

Diagnostic Parameters

1. Prostate-Specific Antigen Blood Test:

Prostate-specific antigen (PSA) is a protein produced by the prostate gland. All men have a small amount of PSA in their blood, and it increases with age. Prostate cancer can increase the production of PSA, and so a PSA test looks for raised levels of PSA in the blood that may be a sign of the condition in its early stages.

PSA level should usually be below 2.5. Mostly PSA levels upto **4.0** ng/mL is considered as normal. Therefore, if a man had a PSA level above **4.0** ng/mL, doctors would often recommend a prostate biopsy to determine whether prostate cancer was present.

If PSA level is very high, cancer has probably spread beyond the prostate.

2. Digital Rectal Examination:

DRE is useful in ruling out prostate enlargement caused by benign prostatic hyperplasia.

3. Biopsy:

This aid in the diagnosis and help to determine the Gleason score.

Gleason score:

The samples of tissue from the biopsy are studied in a laboratory. If cancerous cells are found, they can be studied further to see how quickly the cancer will spread.

This measure is known as the Gleason score.



The lower the score, the less likely the cancer will spread:

- A Gleason score of six or less means the cancer is unlikely to spread.
- A Gleason score of seven means there is a moderate chance of the cancer spreading.
- A Gleason score of eight or above means there is a significant chance the cancer will spread.



4. MRI and CT Scan:

To assess the extension into the bladder and lymph nodes for staging the cancer and to evaluate bone metastasis.

Treatment:

1. Prostatectomy:

Removal of Prostate gland.

2. Radiotherapy:

External Beam Radiotherapy: Radiation directed towards the whole pelvis externally.

Brachytherapy (radioactive seeds): Tiny radioactive seeds are placed in the body close to tumor.

3. Hormone Therapy:

The goal is to reduce levels of hormones, called androgens, in the body, or to prevent them from reaching prostate cancer cells. There are different types of drugs that lower testosterone levels.

Luteinising Hormone (LH) Blockers:

Luteinising hormone blockers stop the pituitary gland making the hormone. So the testicles don't receive the message telling them to make testosterone.

Examples of LH blockers include:

- Leuprorelin
- Goserelin Acetate
- Buserelin
- Triptorelin
- Histrelin

LH blockers are given as injections or as implants under the skin.

Anti Androgens: Anti-androgens stop androgens from working by binding to the receptors and stop testosterone to bind with receptors so that cancer can't be able to grow. Examples of anti androgens include:

- Bicalutamide
- Flutamide
- Enzalutamide

Anti-androgen treatment may be combined with LH blocker as first-line hormone therapy. This is called combined androgen blockade (CAB).

Triple androgen blockade (TAB): Some doctors have suggested taking combined therapy one step further, by adding a drug called a 5-alpha Reductase Inhibitor (drugs that block the conversion of testosterone to the more active dihydrotestosterone (DHT)). – either Finasteride or Dutasteride – to the combined androgen blockade.

Enzalutamide: This drug is a newer type of anti-androgen. When androgens bind to the androgen receptor, the receptor sends a signal for the cells to grow and divide. Enzalutamide blocks this signal from the androgen receptor to the cell.

Abiraterone (Zytiga): Recent advances have demonstrated that androgen-based pathways continue to have a clinically significant role in the progression of castrate-resistant prostate cancer (Relapse cases of cancer that are insensitive to androgens). In addition to androgen production by the adrenal gland and testis, several of the enzymes involved in the synthesis of testosterone and dihydrotestosterone, including CYP17, are highly expressed in tumor tissue especially in relapse cases.

ZYTIGA is an oral androgen biosynthesis inhibitor that works by inhibiting the CYP17 enzyme complex, which is required for the production of androgens at these three sources (Adrenal gland, Testis, Prostate Tumor). Zytiga and prednisone combination is given in such cases.

Another new drug being studied, known as **Orteronel**, works in a similar way to abiraterone. This drug may target CYP17 more precisely, which may do away with the need for taking a steroid drug such as prednisone along with treatment. Orteronel is only available in clinical trials at this time.

4. Chemotherapy:

Chemotherapy is sometimes used if prostate cancer has spread outside the prostate gland and hormone therapy isn't working. For prostate cancer, chemo drugs are typically used one at a time. Some of the chemo drugs used to treat prostate cancer include:

- Docetaxel
- Cabazitaxel

- Doxorubicin
- Etoposide
- Vinblastine
- Paclitaxel
- Carboplatin

In most cases, the first chemo drug given is docetaxel, combined with the steroid drug prednisone.

If this drug does not work (or stops working), a newer drug called cabazitaxel is given specially in cases when cancer has stopped responding to hormone therapy and chemotherapy.

Radium 223 Dichloride (Xofigo): FDA has approved Xofigo (radium-223 dichloride) to treat certain men with advanced prostate cancer. It is intended for men whose cancer has spread (metastasized) only to their bones.

Xofigo is given as injection into a vein, once a month. It binds with minerals in the bone to deliver radiation directly to bone tumors, limiting the damage to the surrounding normal tissues.

5. Vaccination:

Sipuleucel-T (Provenge®) is a cancer vaccine used to treat advanced prostate cancer. Most vaccines are designed to prevent diseases, but this vaccine is aimed at treating prostate cancer, not preventing it.

This vaccine is not mass produced. It has to be made special for each patient from his own blood cells. To make it, white blood cells are removed from the patient's blood and sent to a lab, where they are exposed to a certain protein from prostate cancer cells. These cells are given back to the patient into a vein (IV). This process is done 2 more times, 2 weeks apart, so that the patient gets 3 doses of cells. In the body, the cells cause other immune system cells to attack the patient's prostate cancer cells. Studies are now being done to see if this vaccine can help men with less advanced prostate cancer.



Thankyou

