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# An Overview of Rare Prostate Cancers and Their Prognosis!

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## Abstract

**Introduction:** Prostate cancer tends to be slow-growing and slow to spread. For most people who get it is less concerning than other medical conditions they have. It is because of earlier detection that potential prostate cancer has one of the highest survival rates but for two types namely i) Squamous cell carcinoma and ii) small cell neuroendocrine carcinoma the serious variants. After skin cancer, prostate cancer is the most common cancer in men and only 3% of people who have prostate cancer die from it. That's because most prostate cancers are diagnosed in older people in whom the disease is slow-growing and non-aggressive and most of such die from heart disease, stroke, or other causes -- not their prostate cancer. Ninety two percent of all prostate cancers are diagnosed in the early stage- local or regional and only about 7% have more advanced prostate cancer. The proportion of fatality drops from 22 in 1000 cases of those diagnosed under 50 years, to 2% in 50-59 yrs, 5% in 60-69 yrs cohorts and 1.1% among those aged 70 years or more. However, Prostatic squamous cell carcinoma is the ultimate cause of death in two thirds of cases with a median overall survival of 13 months, and Neuroendocrine prostate cancer (NEPC) represents a particularly aggressive subtype of prostate cancer with dismal prognosis, with median survival of 10 - 18 months.

**Materials and Methods:** This article is based on two different cases, one each of rarer varieties of Squamous cell carcinoma and ii) small neuroendocrine carcinoma, the serious variants.

**Outcomes:** While the first case of NEPC dies in 7th month after diagnosis and second case of squamous cell Ca died after 14 months.

**Keywords:** Neuroendocrine prostate cancer; Prostate cancer; Small Cell Neuroendocrine Carcinoma; Computed Tomography; Prostate

**Abbreviations:** BHP: Benign Hypertrophy of Prostate; SCNC: Small Cell Neuroendocrine Carcinoma; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; DRE: Digital Rectal Examination; PSMA: Prostate-Specific Antigen Membrane; PSA: Prostate-Specific Antigen; PET Scan: Positron Emission Tomography (PET) CT scan: Computed Tomography; FDG PET CT Scan: It's A Powerful Method That Mixes Positron Emission Tomography (PET) & Computed Tomography (CT) Uses a Special Tracer Called Fluorodeoxyglucose.

## Introduction

The prostate gland is a part of male reproductive system in males only. The prostate gland is divided into i) the left and ii) the right lobes of a central groove. It lies below the urinary bladder and in front of the rectum and surrounds the first part of the 'urethra' that carries urine from the bladder to the penis. Seminal vesicles, the glands that make the semen fluid, are located just behind the prostate. Prostate gland grows rapidly during puberty, fueled by the rise in male hormones" androgens". In adult men, a typical prostate is about 3 cm thick and 4 cm wide and weighs about 20 grams, but it can be much larger in older men. Prostate gland produces a thick, clear fluid that makes the semen fluid to protect and nourishes sperm cells in the semen. It also plays a part in controlling the flow of urine [1,2].

Prostate cancer forms in the cells of the prostate, despite several types of cells in prostate, almost all prostate cancers develop from glandular cells (adenocarcinomas), rarely other types. If prostate cancer begins to grow quickly or spreads outside the prostate, it is life threatening. Only 3% of people with prostate cancer die from it, as most prostate cancers are diagnosed in older people, who have associated multimorbidity's and in them the disease is slow-growing, non-aggressive & these patients more likely die from comorbidities like heart disease, stroke etc. & rarely due to prostate cancer [3]. Primary Squamous cell carcinoma of the prostate is a rare tumor, making up 0.5% to 1% of all prostate carcinomas & Small neuroendocrine carcinoma of the prostate are rare entities that may be pure or mixed with

conventional acinar adenocarcinoma transition occurring after initial treatments.

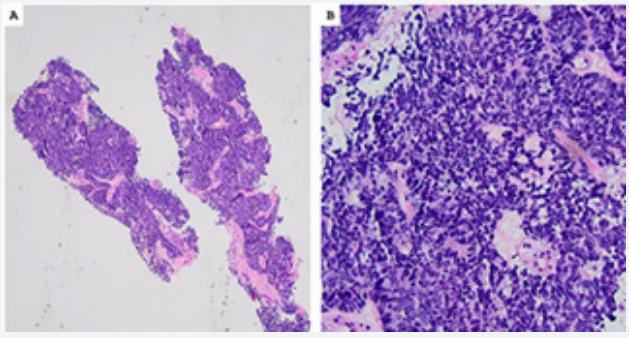
Differentiating small cell neuroendocrine (NE) carcinoma (SCNC) of the prostate from adenocarcinoma with NE differentiation is based on morphological features alone, and therefore, sometimes challenging. Given that treatment strategies vary depending on histological type, an accurate diagnosis is critical [4]. As 92% of all prostate cancers are diagnosed in the early stage- local or regional and only about 7% have more advanced prostate cancer. A 5-year relative survival rate is almost 100%, the 10-year relative survival rate is 98% and the relative 15-year survival rate is 95%. When patient's age crosses 70 years, chances of developing prostate cancer increase.

The proportion of fatality drops from 22 in 1000 cases of those diagnosed under 50 years, to 2% in 50-59 yrs, 5% in 60-69 yrs cohorts and 11.1% among those aged 70 years or more. The stage of prostate cancer at diagnosis determines the fatality -i) If it is localized or regionally spread, has 5-year relative survival rate of 99%, ii) but for those with Stage IV prostate cancer it drops to 34%. Presented here are a case each of primary squamous cell carcinoma & a small cell neuroendocrine carcinoma of the prostate, among two close friends of the author with a complicated presentation of metastatic disease. Unfortunately, both died in 6-8 months of the second diagnosis after metastasis.

## Case Report 1

Dr. AK a Plastic Surgeon in his 75th year started noticing Back Pain in June 2022. For first few weeks he attributed it to his profession of plastic surgery, which demanded long hours of erect standing and tried to manage with NSAID. As the pain became severe and even while sleeping supine, he took second opinion of a local Orthopedic surgeon. After a thorough clinical examination, he sought the opinion of a general surgeon who did a Digital rectal examination (DRE) which revealed a markedly enlarged prostate with extensive induration and multiple hard nodules throughout both lobes. The gland felt irregular and asymmetric with obliteration of the median sulcus, findings highly suggestive of malignancy.

Then they ordered for i) (PSMA) ii) CBC and comprehensive metabolic panel iii) CT of the abdomen and pelvis with nuclear medicine bone scan and iv) Serum alkaline phosphatase and calcium testing. The patient's serum PSA level was markedly elevated at 151 ng/mL. The elevated PSA, a prostate-specific antigen membrane (PSMA) and PET scans were performed. PET scan demonstrated extensive, intensely active bone lesions consistent with widespread osseous metastases, along with enlarged lymph nodes in the abdomen and pelvis. The CBC was normal, and the metabolic panel showed a creatinine level of 1.60 mg/dL and an alkaline phosphatase level of 285 U/L (elevated). All other values were within normal limits.



(A) Low power H&E: Lymph node biopsy specimen showing diffuse involvement by an epithelioid neoplasm arranged sheets, trabeculae, and rosettes. (B) High power H&E: Demonstrates small, round-to-oval cell with a high nuclear to cytoplasmic ratio, scant cytoplasm, salt and pepper chromatin, and frequent mitotic figures and apoptotic bodies.

**Figure 1:** Histopathology of prostate.



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A biopsy of the lumbar spine was done which confirmed metastatic prostate adenocarcinoma of the typical gland-forming type. The patient was put on androgen deprivation (leuprolide), docetaxel, and enzalutamide. In 6 weeks, his PSA level decreased to 0.15 ng/mL, signaling an excellent biochemical response. However, 6 months into treatment, in January 2023, he complained of back ache and inability bend forwards. A routine imaging showed no change in the size of the primary prostate mass or osseous lesions despite low PSA on repeat measurements. To investigate the discordance, a transrectal biopsy of the prostate was performed which revealed small-cell neuroendocrine carcinoma involving 11 of 12 sampled cores (Figure 1).

Based on immune-profile the diagnosis of neuroendocrine differentiation, with loss of prostate lineage marker expression and gain of neuroendocrine marker expression was done consistent with treatment-emergent neuroendocrine prostate cancer (therapy consists of androgen deprivation (ADT), chemotherapy, and an androgen receptor pathway inhibitor). However, he succumbed to the disease 6 months after the second diagnosis, though treatment options that may produce a significant response are said to be available. Only palliative care gave him some comfort in his last days.

## Case Report 2

Mr. K Wadhwan, one of our colleagues aged 76 yrs. a cold chain engineer was diagnosed in July 2020, with a history of mainly hypertension, was referred to a private hospital in Jaipur for an episode of acute urinal retention caused by a benign prostatic hypertrophy. The digital rectal examination (DRE) was normal at the time, with an estimated 200 ml soft and even prostate gland. PSA level was 13.00 ng/ml, correlated to the gland volume. The patient was followed up in urology with several urinal catheter ablation failures and urinary tract infections. Another digital prostatic examination in October 2020, disclosed an uneven swollen gland of stone-hard consistency, with multiples suspicious nodules. PSA level was then 15.62 ng/ml.

Prostate MRI revealed an important prostatic hypertrophy (340 ml), with a postero-superior voluminous and irregular mass of the peripheral zone (70 mm) invading the bladder's postero-inferior wall, both seminal vesicles and likely the mid-rectum's anterior wall, with multiples iliac and retro-peritoneal enlarged lymph nodes. A Thorax, Abdominal and Pelvis scanner (CT-TAP scan) confirmed the irregular prostate tumor, infiltrating the bladder wall, peri-prostatic and peri-bladder soft tissues, as well as multiple precaval, lateral Caval and retroperitoneal enlarged lymph nodes, with a dilated left UVJ due to distal obstruction by the advanced prostate tumor. FDG-PET/CT scan confirmed the prostate malignancy and the lymph nodes involvement, with no other evidence of metastatic disease [5-7].

No bone or cerebral metastases were found on bone scintigraphy and cerebral MRI. The tumor was classified. Transrectal prostate biopsies were performed, which revealed a mildly to poorly differentiated non-small cell eosinophil carcinoma with squamous differentiation with no glandular nor neuroendocrine expression on the histology and immunohistochemical analysis. The tumor staining was positive for epidermoid markers (p63, CK5/6) and for urothelial markers (CK7 mainly and CK20 focally, GATA3). Prostatic markers were negative (PSA, EGR, NKX3.1), as well as keratin expression. The tumor was therefore classified as an invasive squamous cell prostate carcinoma, even though the primitive or secondary prostatic origins could not be clearly determined.

However, the blood measurements of NSE, chromogranin A and SCC were within normal range, whereas CYFRA 21-1 was elevated at 63.0 ng/ml. The patient was reviewed at the institution's multidisciplinary tumor board with recommendation of i) Orchidectomy, ii) exclusive chemotherapy, considering the number of lymph node metastasis & the patient's comorbidities and iii) Radiotherapy. While patients refused Orchidectomy, given its limited utility, instead opted to have hormone therapy, chemotherapy and Radiotherapy. Chemotherapy consisted of three cycles of Carboplatin-Paclitaxel every 21 days (Carboplatin AUC 2 and Paclitaxel 80.00 mg/m2 on day 1, 8 and 15). The treatment was well tolerated except for a grade 3 sensitive neuropathy of both hands and feet (CTCAE v5), forcing the termination of the paclitaxel on day 15 of cycle 2.

At the three months follow up in March 2021, the CT scan showed a significant response with reduction of the prostate tumor volume (20 mm vs. 70 mm) and the loss of contact with the rectum's wall and the disappearance of all metastatic lymph nodes. Considering the great treatment outcome at 3 months, chemotherapy continued with 6 cycles of carboplatin every 21 days. No new metastasis appeared for next 2 years. PSA levels were marginally high; therefore, radiotherapy was continued. As of May 2024, his PSA was mildly raised, and he was put on 2 capsules of chemotherapy along with steroids. In June 2024 he complained of Back bone and buttocks pain while sitting on hard surface. A FDG PET scan was advised to visualize any secondary spinal cord or any bones or post-therapeutic squamous cell transformation into metastatic adenocarcinoma or treatment-emergent neuroendocrine prostate cancer. However, his general condition deteriorated & he died in mid-January 2025.

## Discussion

Despite several types of cells in prostate, almost all prostate cancers develop from glandular cells (adenocarcinomas). Only 3% of people who have prostate cancer die from it, because most prostate cancers are diagnosed with older people in whom the


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disease is slow-growing, non-aggressive and such patients die from comorbidities like heart disease, stroke etc. rather than prostate cancer. But once prostate cancer begins to grow quickly or spreads outside the prostate, it is life threatening.

## Prostate cancer is divided into four stages:

Localized Prostate Cancers: Stage I: Cancer cells are limited to within the prostate gland, usually in half or less of one side. Stage II: The cancer is still contained within the prostate but is more likely to spread. It may be in the supportive tissue that surrounds the gland.

**Regional Metastatic Cancers of Prostate: Stage III:** Cancer cells have spread beyond the prostate to nearby areas, like the seminal vesicles.

**Distant or Advanced Metastatic Cancers of Prostate: Stage IV:** The cancer has moved farther out to areas like the bones, lymph nodes, liver, or lungs. In an older male patient in whom imaging shows widespread bone metastases, prostate cancer must be strongly considered in the differential diagnosis. A PSA blood test is the appropriate initial investigation, as it is highly sensitive for prostate adenocarcinoma, in advanced stage. While a CBC and comprehensive metabolic panel may reveal associated findings, like anemia or kidney function impairment, they are not diagnostic. CT scans and nuclear medicine bone scans assist with staging but do not establish the tissue of origin. Alkaline phosphatase & calcium levels are elevated in bone metastases but do not confirm the diagnosis.

## Diagnosis

A Per rectal (PR) or Digital rectal examination (DRE) is mandatory supported by PSA level. DIR will reveal a markedly enlarged prostate, maybe even extensive induration & multiple hard nodules throughout both lobes. The feeling irregular and asymmetric prostate gland with obliteration of the median sulcus, are highly suggestive of malignancy & possible extracapsular extension. A blood sample for PSA, CBC and Serum alkaline phosphatase and calcium and comprehensive metabolic panel and a CT scan of abdomen and pelvis must follow. An elevated PSA level must make the doctor suspect Prostate cancer and seek for a prostate-specific antigen membrane (PSMA) and PET scans were performed (Figure 2).

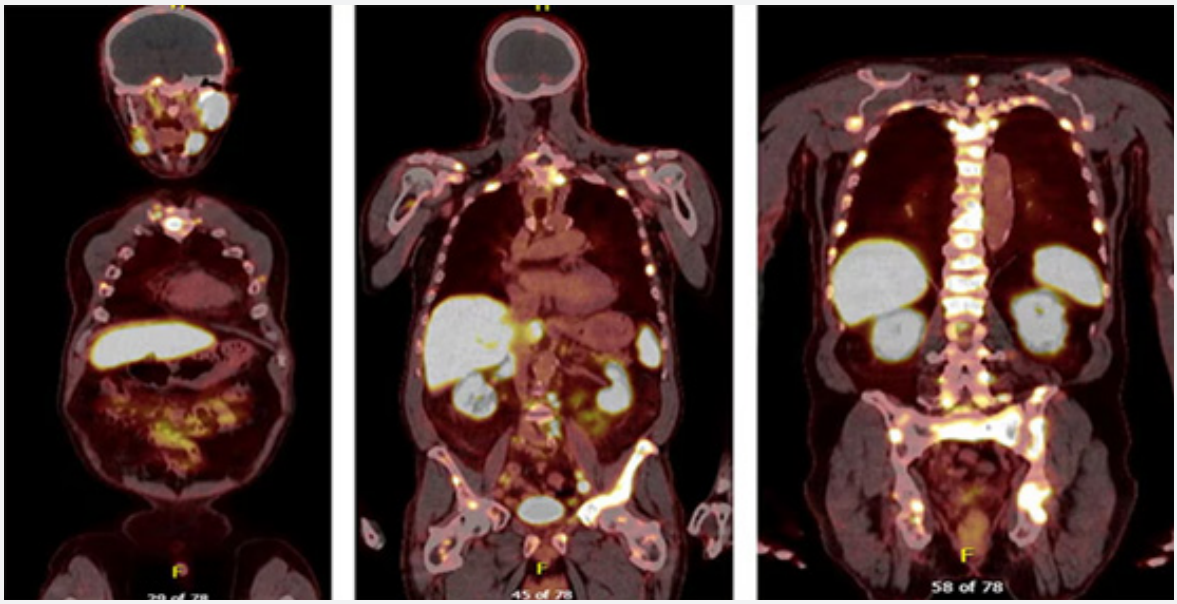


**Figure 2:** Coronal view of fused PSMA PET scan showing Evidence of diffuse bony metastatic Disease.

These patients initially present with classic findings of advanced prostate adenocarcinoma like elevated PSA level, and diffuse bony disease, and PSA levels drop in response to standard-of-care systemic therapy. Despite the reassuringly low PSA, recurrence of back pain and inability to bend and the lack of radiographic response prompt, Prostate biopsy to evaluate for treatment-emergent neuroendocrine transformation. The importance of clinical suspicion and tissue confirmation in patients with discordant imaging and biochemical findings is needed. The emergence of small-cell neuroendocrine carcinoma in the prostate after treatment initiation indicates treatment-emergent transformation, a recognized but rare clinical phenomenon.


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## Epidemiology

Both small cell neuroendocrine carcinoma and Primary adenocarcinoma of the prostate are rare.

➢ **Small Cell Neuroendocrine Carcinoma:** Small cell neuroendocrine carcinoma of the prostate is more common in patients with metastatic disease after androgen receptor axis targeted therapy for conventional acinar adenocarcinoma. Pure neuroendocrine prostate cancer is exceedingly rare and presents without an elevated PSA level (Figure 3).

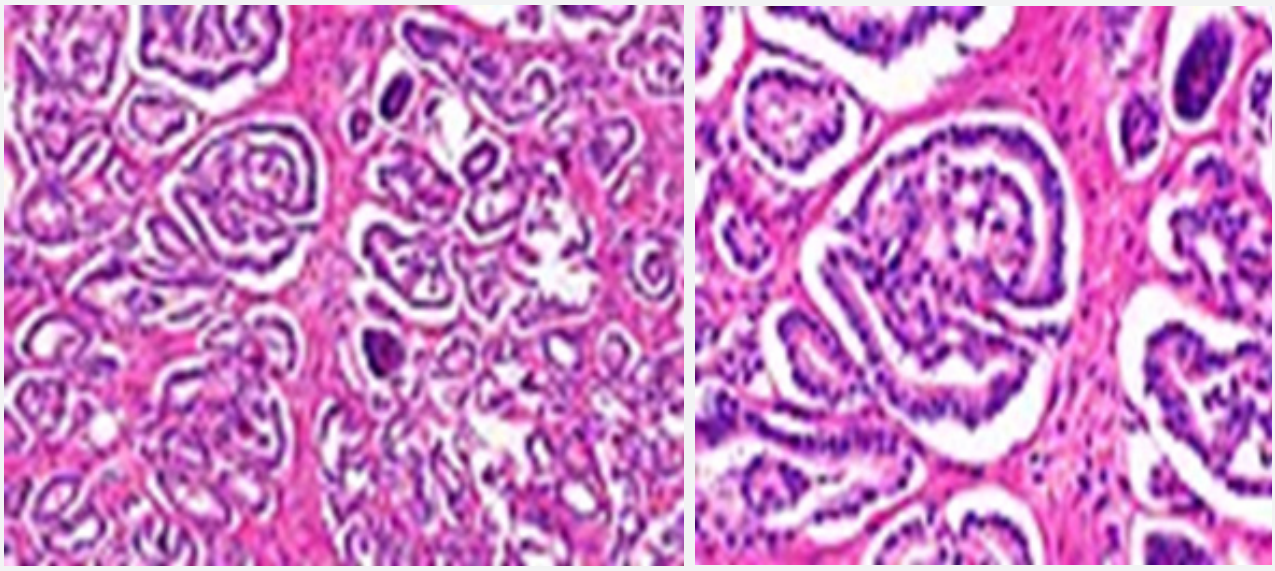

**Figure 2:1.** Small cell neuroendocrine carcinoma.
2.Primary squamous cell carcinoma (PSCC) of the prostate.

➢ **Primary Squamous Cell Carcinoma (PSCC) of the Prostate**: PSCC of the prostate continues to be an infrequent and aggressive malignancy found in less than 1% of men worldwide. The criterion used to define the histologic characteristics of PSCC include:

i. a clear malignant neoplasm as judged by invasion, disordered growth, & cellular anaplasia;

ii. definite squamous features of keratinization, squamous pearls, and/or numerous distinct intercellular bridges;

iii. lack of any glandular or acinar pattern;

iv. no prior estrogen therapy; and

v. the absence of PSCC elsewhere, particularly in the bladder.

In our first case, the initial metastatic site biopsy demonstrated typical adenocarcinoma and the initial PSA response to therapy confirmed conventional prostate adenocarcinoma as the origin, followed by transformation after treatment initiation. This change in histology, despite biochemical control, was consistent with treatment-emergent neuroendocrine prostate cancer, a rare but aggressive form of prostate cancer that can arise under the selective pressure of androgen receptor-targeted therapies. Neuroendocrine differentiation must be suspected in any patient with prostate cancer who develops rapidly progressing clinical or radiographic disease despite suppressed or undetectable PSA levels or in patients who no longer respond to ADT and have residual metastatic disease amenable to biopsy.

Biopsy of the prostate or metastatic sites is essential to establish diagnosis. Clinical presentation may be i) Painless gross or microscopic hematuria-the most common ii) Flank or back pain due to hydronephrosis iii) Weight loss iv) Rarely, dysuria, change in urinary frequency or recurrent urinary tract infections (UTI) v) Rarely, abdominal mass. Diagnosis is based on histopathology of the biopsy material. A high Gleason Pattern score (GPS) at the time of initial prostate cancer diagnosis is the most consistent predictor of earlier development of treatment-emergent neuroendocrine prostate cancer.

In a systematic review involving 123 patients across 54 studies, the median time from diagnosis of prostate adenocarcinoma to development of neuroendocrine prostate carcinoma was 20 months. Among the clinical variables analyzed, only a high Gleason score at baseline was independently associated with earlier transformation to the neuroendocrine phenotype.


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Although uncommon, neuroendocrine prostate cancer is widely believed to arise from histologic transformation of conventional androgen receptor-positive prostate adenocarcinoma into an androgen receptor-independent, poorly differentiated small-cell neuroendocrine phenotype.

Emergent neuroendocrine prostate carcinoma does not respond to hormonal therapies, instead, systemic chemotherapy with a platinum agent (eg, cisplatin or carboplatin) combined with etoposide is the standard approach. Palliative care may become appropriate later in the disease course as the prognosis of treatment-emergent neuroendocrine prostate is poor, and median survival ranges from 7-15 months from neuroendocrine transformation. Pathologists must look for Squamous cell carcinoma of the prostate in histologic evaluation as was in our second case. Treatment regimens are variable but surgical resection with platinum agent based neoadjuvant or adjuvant chemotherapy is most implemented. Glucocorticoids are prescribed along with Chemotherapy in prostate cancer (Table 1).

**Table 1:** PC Gleason pattern 4 <<Medium & High>> Magnification.

| GPS 1&2 | GPS3 | GPS4 |
|---|---|---|
| Gleason pattern 1 - probably represents what today would be called adenosis. | Glands smaller than normal prostate glands + loss of epithelial folding. | Loss of gland lumina. Gland fusion. |
| Gleason pattern 2 - used by few GU pathology experts occasionally. | Can draw a line around each gland. | Benign looking cords ('hyper nephroid pattern'). |
| | May have gland branching. | Cribriform. |
| | Glands have an X, U, V or Y shape. | Glomeruloid pattern - resembles a glomerulus |

They work by binding to proteins called glucocorticoid receptors and make cells to produce anti-inflammatory chemicals. Reducing inflammation can ease the side effects of cancer treatments. Corticosteroids reduce production of androgen, if standard hormone therapy does not work, corticosteroids are an option to relieve symptoms. Prognosis: People with prostate cancer that's localized to the prostate or regional spread just have a high long-term survival rate with 5-year relative survival rate of 99%. However, Stage IV prostate cancer survival rate for those whose prostate cancer has spread to distant areas, like their bones, relative 5-year survival rate is just 34%.

## Conclusion

Prostate cancer tends to be slow-growing and less concerning, because of its potential of earlier detection and it has one of the highest survival rates but for two types namely i) Squamous cell carcinoma and ii) small cell neuroendocrine carcinoma the serious variants. Small cell neuroendocrine carcinoma of the prostate is more common in patients with metastatic disease after androgen receptor axis targeted therapy for conventional acinar adenocarcinoma. Primary squamous cell carcinoma (PSCC) of the prostate is an infrequent and aggressive malignancy found in less than 1% of men worldwide.

Neuroendocrine differentiation must be suspected in any patient with prostate cancer who develops rapidly progressing clinical or radiographic disease of bones despite suppressed or undetectable PSA levels or in patients who no longer respond to ADT and have residual metastatic disease amenable to biopsy. Stage IV prostate cancer (spread to bones, lymph nodes, liver etc.), has a 5-year survival rate of just 34%. Treatment regimens are variable but surgical resection with platinum agent based neoadjuvant or adjuvant chemotherapy is most implemented. Glucocorticoids are prescribed along with Chemotherapy in prostate cancer.

## References


1. Prostate-cancer (2025) ICMR – National Institute of Cancer Prevention & Research.
2. Bhargavi R, Barkha Khilwani, Bhumandeep Kour, Nidhi Shukla, Rajaguru Aradhya, et al. (2023) Prostate cancer in India: Current perspectives and the way forward. J Reprod Healthc Med 4: 8.
3. Prostate Cancer Survival Rates.
4. Primary prostatic squamous cell carcinoma, Kevin Hanna et.al. (2020) Urol Case Rep 2(34): 101478.
5. Squamous Cell Carcinoma of the Prostate.
6. Intractable-back-pain-65-year-old-man-after-starting-new-exercise regimen.
7. Corticosteroids for Prostate Cancer (2024) HU Medical Review Board.




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