**Case Report**

# Small cell neuroendocrine tumor of prostate presenting with sphenoidal metastasis: Case report

**Anshuma Bansal[1], Neeru Bedi[1], Raja Paramjeet Singh Banipal[2], Harjot Bagga[2], Ripanpreet Kaur[3], Gurpreet Singh[3], Vinod Kumar Dangwal[3]**

[1]Assistant Professor, [2]Professor, [3]Medical Physicist, Department of Radiation Oncology
Government Medical College and Rajindra Hospital, Patiala

**Corresponding Author:**
**Dr Anshuma Bansal,** Assistant Professor, Department of Radiation Oncology, Government Medical College and Rajindra Hospital, Patiala, Punjab, India
dranshubansal3@gmail.com

**Abstract**

This case report highlights the management of small cell neuroendocrine tumor of prostate presenting with sphenoidal metastasis.

**Keywords:**

'Prostate cancer', 'Neuroendocrine tumor', 'Sphenoidal metastasis'

## Introduction:

Small cell neuroendocrine tumor of prostate (SCNP) is a rare lethal malignancy that affects <1% of population [1]. It has a median survival rate of 1-2 years from the time of diagnosis [2]. Diagnostic accuracy for SCNP poses challenge. This case report highlights the management of this tumor on the lines of prostate adenocarcinomas, rather than primary small cell neuroendocrine tumors, and also focuses on the decision making factors while choosing the line of treatment.

## Case report

73 years old male patient, presented in May 2021, with double vision and pain in right eye for the last 15 days. CEMRI (Contrast enhanced Magnetic resonance Imaging) done on 03.05.2021 shows 3.4 * 2.6* 2.5 cm soft tissue lesion in right side of sphenoid space and right cavernous sinus encasing right internal carotid artery and causing mass effect on sella. (Figure 1). Biopsy from sphenoid sinus growth was suggestive of small cell neuroendocrine tumor of prostatic origin. Immunohistochemistry was positive for CK, Synaptophysin, CD99, NKX 3.1, focally positive for PSA (Figure 2) and negative for CD45 and HMB45. CECT (Contrast enhanced computed tomography) was suggestive of enlarged prostate with irregular margins and enlarged obturator lymph nodes on left side. S. PSA was raised (103.2 ng/ml). S. Chromogranin A was normal (57.8 ng/ml). Transurthral resection of prostate was done and biopsy was suggestive of poorly differentiated tumor cells with with focal neuroendocrine cells. PSMA PET (Prostate specific membrane antigen Positron emission tomography) done on 19.6.21 was suggestive of intense uptake (SUV 33.16) soft tissue mass arising from prostate 5.9* 6.1* 7.3 cc. FDG avid (SUV 52.4) 3.7* 2.5 cm bilateral internal iliac lymph nodes. FDG avid (SUV 45.12) 3.2* 2.5 cm soft tissue mass was seen in sphenoid and basilar part of occipital bone, bilateral scapule, multiple ribs, multiple cervical- dorso-lumbar vertebrae, sacrum (SUV 42.8), bilateral femora and iliac bones (Figure 3).

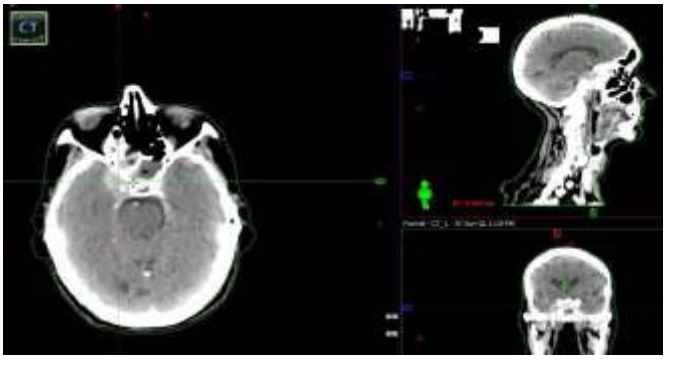

**Figure 1: Pre-treatment CECT Brain showing sphenoid metastasis**

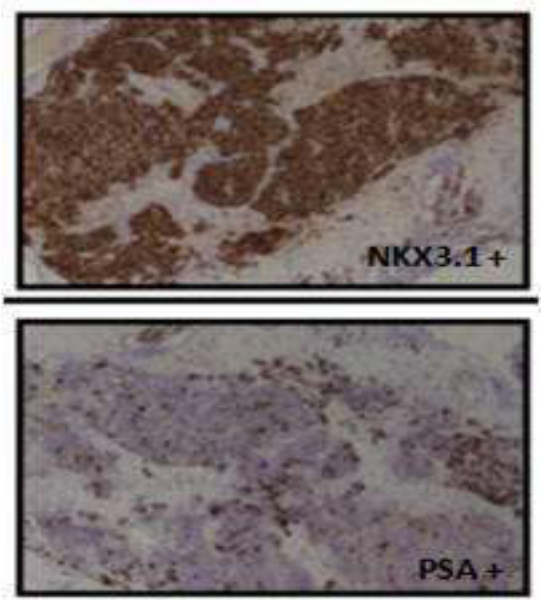


**Figure 2: Immunohistochemistry on sphenoid biopsy showing NK 3.1 and PSA positivity**

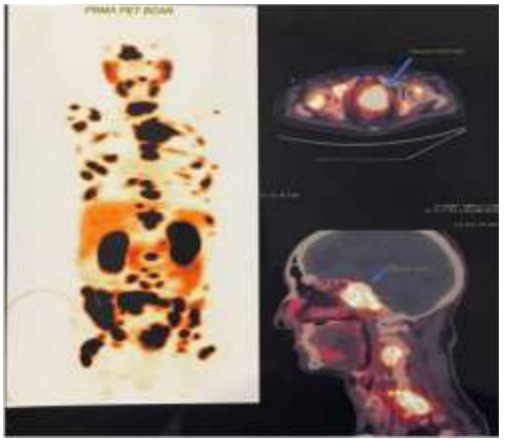

**Figure 3: Pre-treatment PET scan showing widespread metastasis**

Patient was started on Inj Leuprolide 22.5 mg IM 3 monthly. He was planned and treated with radiation to Sphenoidal metastasis by Voulmetric modulated arc radiotherapy to dose of 40 Gy in 15 fractions in 3weeks, with two semi arcs (201º Clockwise 131º and 131º to 201 º) with 6 MV beams on Varian True Beam Linear Accelerator (Figure 4).

Patient was then started on Tab Abiraterone 1 gm daily and Tab Prednisolone 5 mg twice a day for 4 weeks, and monthly Inj Zoledronic acid 4 mg was also planned.

S. PSA done after 6 months of treatment on 18.1.22 was 0.01 ng/ml. PET done on 20.1.22 showed resolution of primary prostatic lesion (SUV 3 vs 33.16) and decrease in size (2.5*3.1 cm vs 5.9*6.1 cm)). Also, non tracer avid sclerosis was seen in sphenoid bone (SUV 1.9 vs 45.12), and in all other vertebrae, ribs and pelvic bones (Figure 5). Patient is now on regular follow up and is continued on same therapy with Tab Abiraterone and Inj Zoledronic acid.

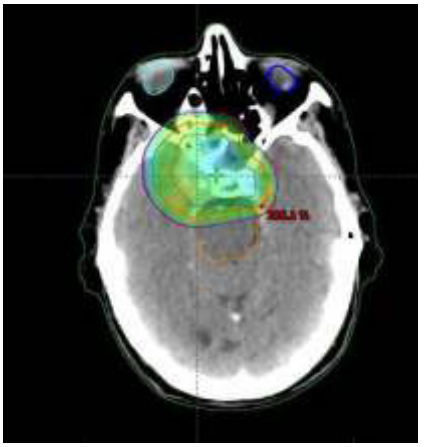

**Figure 4: VMAT Radiation Plan for Sphenoidal metastasis**

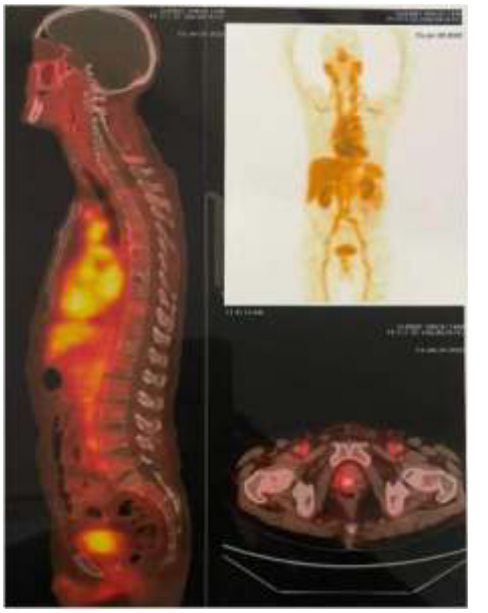

**Figure 5: Post- treatment PET scan showing complete resolution**

## Discussion

Pure neuroendocrine tumors constitute rare prostatic malignancies with poor prognosis. There is a relative scarce information on the clinicopathologic behavior and optimum treatment strategies for this

tumor. In 2016, WHO reclassified neuroendocrine tumors of the prostate into 6 categories as follows: adenocarcinoma with neuroendocrine differentiation with 2 subtypes (focal and diffuse); adenocarcinoma with Paneth cell-like neuroendocrine differentiation; well-differentiated neuroendocrine tumor (carcinoid tumor); small-cell neuroendocrine carcinoma; and large-cell neuroendocrine carcinoma [3].

Out of all these, adenocarcinoma with focal neuroendocrine differentiation has the best prognosis and small-cell neuroendocrine carcinoma is a high-grade epithelial neoplasm with worst prognosis, and therefore, the line of treatment is entirely different for these two variants [4].

SCNP should be considered in patients with a low serum PSA level, inadequate response to hor-monal therapy, poor differentiation of tumor cells on histology, and rapidly metastasizing disease. It is managed similar to small cell carcinoma lung with a regimen consisting of cisplatin and etoposide or carboplatin and docetaxel. Many authors have suggested to continue androgen deprivation therapy during chemotherapy due to the concomitant presence of mixed tumors and the potential of worsening when not addressing the associated adenocarcinoma [5]. Local control of the SCNP is achieved either by external beam radiation therapy or radical prostatectomy. Palmgren et al. [6] reported that chemotherapy with radiation provides the best survival benefit.

SCNP is an aggressive variety of prostate cancer with a median survival time following diagnosis of ~10 months, depending on the disease stage however, 2 yr survival is <5% [7].

The case presented in this report had aggressive metastatic disease on presentation. On histopathology, it came out to be mixed tumor with adenocarcinoma component along with small neuroendocrine cells. On IHC, the tumor cells had high mitotic index Ki > 20%, were positive for both synaptophysin and chromogranin A and there was only focal positivity for PSA. However, S. Chrmogranin A was normal and S. PSA was raised >100 ng/ml. Based on these variable histopathological and biochemical reports, the line of treatment became uncertain. In view of high S PSA levels, the decision was made to plan this patient on the lines of adenocarcinoma prostate, and was started on androgen depletion therapy along with molecular therapy. The response evaluated after 6 months, showed excellent response with complete metabolic response and biochemical response. Beltran et al [8] suggested that treatment-related SCNP arises clonally from prostate adenocarcinoma during the course of disease progression, retaining early genomic events and acquiring new molecular features that lead to tumor proliferation independent of androgen receptor activity, and ultimately demonstrating a lineage switch from a luminal prostate cancer phenotype to a SCNP. In view of presence of small neuroendocrine cells along with carcinoma cells, this patient needs close follow up with 3 monthly Serum PSA levels and metastatic workup, so as to detect early disease relapse.

**Conclusion**

Reaching accurate diagnosis is the key to treatment in neuroendocrine tumors of prostate. Along with histopathological features, biochemical levels of tumor markers determine tumor burden, and can help in deciding the line of treatment.

**References**

1. Ketata S, Ketata H, Fakhfakh H, Sahnoun A, Bahloul A, Boudawara T et al. Pure primary neuroendocrine tumor of the prostate: a rare entity. Clinical genitourinary cancer. 2006 Jun 1;5(1):82-4. 2. Lim KH, Huang MJ, Yang S, Hsieh RK, Lin J. Primary carcinoid tumor of prostate presenting with bone marrow metastases. Urology. 2005 Jan 1;65(1):174.
3. Parimi V, Goyal R, Poropatich K, Yang XJ. Neuroendocrine differentiation of prostate cancer: a review. Am J Clin Exp Urol. 2014;2 (4):273–85. 4. Bhandari R, Thomas TV, Giri S, Kumar PP, Cook-Glenn C. Small Cell Carcinoma of the Prostate:A Case Report and Review of the Literature. Cureus. 2020; 12(2): e7074.
5. Kumar K, Ahmed R, Chukwunonso C, Tariq H, Niazi M, Makker J et al. Poorly differentiated small-cell-type neuroendocrine carcinoma of the

prostate: a case report and literature review. Case reports in oncology. 2018;11(3):676-81.

6. Palmgren JS, Karavadia SS, Wakefield MR. Unusual and underappreciated: small cell carcinoma of the prostate. Semin Oncol. 2007 Feb;34(1):22–9.
7. Alves D, Calmeiro ME, Silva R, Coelho H. Small-cell neuroendocrine cancer of the prostate: an atypical presentation of a common disease. BMJ Case Rep. 2016 Oct;2016:bcr2016216199.
8. Beltran H, Demichelis F. Therapy considerations in neuroendocrine prostate cancer: what next?. Endocrine-related cancer. 2021;28(8):T67-78. LEGEND FOR FIGURES Figure 1: Pre-treatment CEMRI Brain Figure 2: Immunohistochemistry on sphenoid biopsy Figure 3: Pre-treatment PET scan Figure 4: VMAT Plan for Sphenoidal metastasis Figure 5: Post- treatment PET scan