SAS Journal of Surgery
Abbreviated Key Title: SAS J Surg
ISSN 2454-5104
Journal homepage: https://www.saspublishers.com

OPEN ACCESS

Urology

Metastatic Neuroendocrine Carcinoma of the Prostate: A Case Report

Radouane Es-saady[1*], Mohamed Tebaa[1], Alaa Abuqadoum[1], Mohamed Amine Lakmichi[1], Zakaria Dahami[1], Said Mohammed Moudouni[1], Ismail Sarf[1]

[1]Arrazi Urology Service, UHC Mohammed VI, Faculty of Medicine and Pharmacy, Cadi Ayad University, Marrakech, Morocco

DOI: 10.36347/sasjs.2022.v08i05.007 | **Received:** 05.04.2022 | **Accepted:** 09.05.2022 | **Published:** 12.05.2022

***Corresponding author:** Radouane Es-saady
Arrazi Urology Service, UHC Mohammed VI, Faculty of Medicine and Pharmacy, Cadi Ayad University, Marrakech, Morocco

Abstract **Case Report**

Neuroendocrine prostate cancer is a rare entity. It can be presented in a pure form (small or large cell neuroendocrine carcinoma) or in a mixed form, i.e. associated with an adenocarcinomatous contingent. Neuroendocrine carcinoma of the prostate poses both diagnostic and therapeutic problems. Nevertheless, it is a heterogeneous entity encompassing a multitude of histopathological forms with distinct clinical features. Prostate neuroendocrine tumors are often associated with an adenocarcinoma, and are most often a histological discovery. They appear clinically more severe, more advanced with a shorter survival than pure adenocarcinomas. The usually hormoneresistant character of tumors with neuroendocrine differentiation has led to the development of alternative treatments based on chemotherapy and on drugs based on neuroendocrine hormones and/or their antagonists. There is no consensus on the management and prognosis of these various tumor subtypes.

Keywords: Neuroendocrine; prostate; metastatic; treatment.

I INTRODUCTION

Prostate cancer is the second most common cancer and the sixth leading cause of death among men [1]. It appears that prostatic neuroendocrine cells secrete neuropeptides such as bombesin, calcitonin, serotonin, but also growth factors, such as vascular endothelial growth factor (VEGF), to maintain the homeostasis of the surrounding epithelial cell populations. Adenocarcinoma, which is the most common histological type of prostate cancer, may contain neuroendocrine tumor contingents [2-5]. Five treatments are then available and allow, depending on the sequence, a median survival of more than 30 months from this stage: chemotherapy with taxanes (docetaxel and cabazitaxel), new generation hormone therapies (enzalutamide and abiraterone) and alphaRadium-223 transmitter [6-8]. The natural evolution of the disease leads in most cases to a new resistance.

OBSERVATION

L.A, 48 years old, without any particular pathological history, presented bilateral lombalgia, dysuria, and pollakiuria developing in a context of conservation of the general state. The digital rectal examination revealed a large, hard and irregular prostate. The Prostatic Specific Antigen (PSA) assay showed a high-level of 1500 ng/mL. Histology of an ultrasound-guided prostate biopsy showed a morphological and immunohistochemical profile of a high-grade large cell neuroendocrine carcinoma.

The uro scan shows a Magmas of deep and pelvic adenopathies, measuring 27*40mm for the most voluminous, compressive with a moderate bilateral ureterohydronephrosis Figure 1 & 2, the Pet-scan with 18-FDG shows a diffuse pathological hypermetabolic infiltration of the lymph nodes of the supra- and sub-diaphragmatic areas with multiple pathological bone lesions and a hypermetabolic pathological prostatic area (SUV: 8.9).

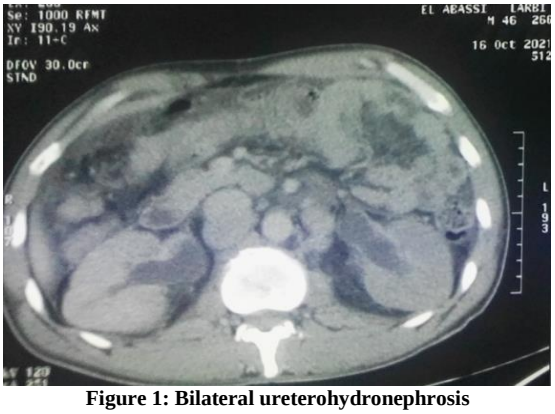

Figure 1: Bilateral ureterohydronephrosis

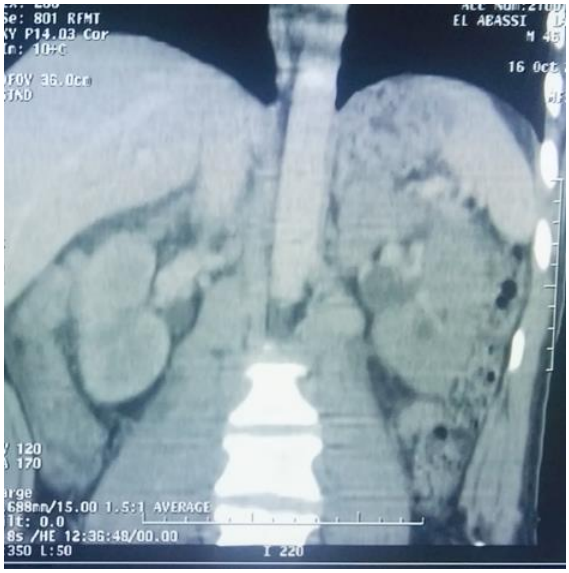

Figure 2: Bone and lymph node damage with dilatation

Because of the aggressive state of the disease, the patient was treated with a combination of complete androgen blockade and docetaxel chemotherapy administered every 3 weeks. After 3 months of treatment, the PSA level remained stable 1500, but the patient presented clinical signs of local progression, in the form of acute obstructive renal failure and a deterioration of the general state. He was then referred to our department. He was treated with JJ tubes and bisphosphonates. At the post-drainage evaluation, an improvement of the renal function was noted.

DISCUSSION

Neuroendocrine carcinomas are de novo extremely rare with an incidence of less than 1%, the classical presentation usually occurring late in the natural history of the disease after resistance to castration, explaining this clinicohistological analogy.

Clinical study

Primary neuroendocrine prostate cancer (which includes small cell cancer) is a rare form of the disease (0.3 to 1% of prostate carcinomas) with an aggressive course and a poor prognosis [9].

Patients often develop visceral (lung and liver) rather than bony metastases, but also in unusual locations: omentum, vocal cords, temporal bone, soft tissue. Local obstructive signs may be prominent at diagnosis.

Anatomopathological examination typically reveals a hyperbasophilic appearance with cells with a high nucleocytoplasmic ratio, rounded or oval nucleus with dense chromatin, poorly visible cytoplasm, numerous mitoses and necrosis areas frequently present.

On the immunophenotypic side, prostate markers (PSA, PSAP, PSMA, P501S) are rarely expressed, unlike neuroendocrine markers (chromogranin, synaptophysin, CD56) [10]. Furthermore, the presence of TMPRSS2-ERG fusion genes seems to be frequently found in FISH, which would indicate an oncogenesis partly common with prostate adenocarcinoma [11].

Imaging

Currently, recommendations do not differ regarding the imaging strategy for different histological subtypes of prostate cancer. Thoracic-abdominal-pelvic CT is used for the evaluation of locoregional extension of lumbo-aortic and pelvic adenopathies as well as for secondary bone locations, which are the two main sites of metastasis [12].

Positron emission tomography (PET) with 18F-choline or sodium fluoride provides important information for the diagnosis of bone metastases, with sensitivity and specificity of 85.2 and 96.5% for 11C/18F-Choline and 86.9 and 79.9% for 18F-FNa. Other radiotracers are being evaluated in prostate cancer, such as 68Ga-labeled Prostate Specific Membrane Antigen (68Ga-PSMA), which has shown superior performance to 18F-Choline PET in several studies [13].

Treatment of metastatic neuroendocrine carcinoma of the prostate

There is a specific management of metastatic neuroendocrine carcinoma of the prostate. The latest recommendations in onco-urology 2016-2018 of the Cancer Committee of the French Association of Urology (CCAFU), advise, in case of undifferentiated, neuroendocrine tumor, very symptomatic visceral or bone metastases or rapid escape after initial hormone therapy (less than one year), the realization of chemotherapy, if the age and general condition allow it [14].

The combination of three chemotherapy molecules proposed by Papandreaou C. N *et al*., i.e. doxorubicin-etoposide-cisplatin, resulted in a median OS of 10.5 months (95% CI, 7.5-14.3 months) with a partial response (PR) on imaging of 61% (95% CI, 43-77%) [15].

The combination of carbolatin and docetaxel studied by Aparicio *et al*., resulted in an imaging response rate of 33%, a median PFS of 5.1 months (95% CI, 4.2-6.0 months), and a median OS of 16 months (95% CI, 13.6-19.0) [16].

Therapeutically, the disease does not respond to hormone therapy, except in cases of associated adenocarcinoma, as the cancer cells of neuroendocrine phenotype do not express the androgen receptor. By analogy with small cell lung cancer, treatment is primarily based on platinum-based chemotherapy, The response rate is classically high (about 60%), but the response is short-lived. Pelvic radiotherapy may also be

considered in non-metastatic forms or to palliate local symptoms [18].

More trials are available for prostate adenocarcinomas with neuroendocrine or anaplastic progression (confirmed by elevated neuroendocrine markers or visceral metastases), which represent 10-20% of castration-resistant prostate cancers.

The combination of docetaxel and carboplatin may be more promising, but without direct comparison to the reference treatment. In any case, it may be reasonable to combine docetaxel and platinum salts in mixed forms [19].

CONCLUSION

Neuroendocrine cancers of the prostate are uncommon clinicopathological entities. Neuroendocrine carcinomas of the prostate are forms with a poor prognosis. They include a multitude of entities with distinct tumor behavior and prognosis. The usually hormoneresistant character of tumors with neuroendocrine differentiation has led to the development of alternative treatments based on chemotherapy and drugs based on neuroendocrine hormones and/or their antagonists. Sequential biopsies during the course of the disease associated with molecular biology techniques will allow a better comprehension of the development mechanisms of neuroendocrine carcinomas of the prostate.

Conflicts of Interest: The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

All authors contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

REFERENCES

1. Jemal, A., Bray, F., Center, M. M., Ferlay, J., Ward, E., & Forman, D. (2011). Global cancer statistics. *CA: a cancer journal for clinicians*, *61*(2), 69-90.
2. Vashchenko, N., & Abrahamsson, P. A. (2005). Neuroendocrine differentiation in prostate cancer: implications for new treatment modalities. *European urology*, *47*(2), 147-155.
3. Mosca, A., Berruti, A., Russo, L., Torta, M., & Dogliotti, L. (2005). The neuroendocrine phenotype in prostate cancer: basic and clinical aspects. *J Endocrinol Invest*, *28*(11), 141-145.
4. di Sant'Agnese, P. A. (2001). Neuroendocrine differentiation in prostatic carcinoma: an update on recent developments. *Annals of Oncology*, *12*, S135-S140.
5. Bonkhoff, H. (2001). Neuroendocrine differentiation in human prostate cancer. Morphogenesis, proliferation and androgen receptor status. *Annals of Oncology*, *12*, S141-S144.
6. Scher, H. I., Fizazi, K., Saad, F., Taplin, M. E., Sternberg, C. N., Miller, K., ... & de Bono, J. S. (2012). Increased survival with enzalutamide in prostate cancer after chemotherapy. *New England Journal of Medicine*, *367*(13), 1187-1197.
7. Fizazi, K., Scher, H. I., Molina, A., Logothetis, C. J., Chi, K. N., Jones, R. J., ... & COU-AA-301 Investigators. (2012). Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study. *The lancet oncology*, *13*(10), 983-992.
8. Parker, C., Nilsson, S., Heinrich, D., Helle, S. I., O'sullivan, J. M., Fosså, S. D., ... & Sartor, O. (2013). Alpha emitter radium-223 and survival in metastatic prostate cancer. *New England Journal of Medicine*, *369*(3), 213-223.
9. Humphrey, P. A. (2012). Histological variants of prostatic carcinoma and their significance. *Histopathology*, *60*(1), 59-74.
10. Wang, W., & Epstein, J. I. (2008). Small cell carcinoma of the prostate: a morphologic and immunohistochemical study of 95 cases. *The American journal of surgical pathology*, *32*(1), 65-71.
11. Guo, C. C., Dancer, J. Y., Wang, Y., Aparicio, A., Navone, N. M., Troncoso, P., & Czerniak, B. A. (2011). TMPRSS2-ERG gene fusion in small cell carcinoma of the prostate. *Human pathology*, *42*(1), 11-17.
12. Rozet, F., Hennequin, C., Beauval, J. B., Beuzeboc, P., Cormier, L., Fromont, G., ... & Méjean, A. (2016). Recommandations en onco-urologie 2016-2018 du CCAFU: Cancer de la prostate. *Progrès en urologie*, *27*, S95-S143.
13. Jadvar, H. (2015). Positron Emission Tomography in Prostate Cancer: Summary of Systematic Reviews and Meta-Analyses. *Tomography*, *1*(1), 18-22.
14. Mosquera, J. M., Beltran, H., Park, K., MacDonald, T. Y., Robinson, B. D., Tagawa, S. T., ... & Rubin, M. A. (2013). Concurrent AURKA and MYCN gene amplifications are harbingers of lethal treatmentrelated neuroendocrine prostate cancer. *Neoplasia*, *15*(1), 1-4.
15. Papandreou, C. N., Daliani, D. D., Thall, P. F., Tu, S. M., Wang, X., Reyes, A., ... & Logothetis, C. J. (2002). Results of a phase II study with doxorubicin, etoposide, and cisplatin in patients with fully characterized small-cell carcinoma of the prostate. *Journal of clinical oncology*, *20*(14), 3072-3080.
16. Aparicio, A. M., Harzstark, A. L., Corn, P. G., Wen, S., Araujo, J. C., Tu, S. M., ... & Logothetis, C. J. (2013). Platinum-based chemotherapy for variant castrate-resistant prostate cancer. *Clinical cancer research*, *19*(13), 3621-3630.

17. Amato, R. J., Logothetis, C. J., Hallinan, R., Ro, J. Y., Sella, A., & Dexeus, F. H. (1992). Chemotherapy for small cell carcinoma of prostatic origin. *The Journal of urology*, *147*(3), 935-937.
18. Stein, M. E., Kuten, A., Bernstein, Z., Abacioglu, U., Sengoz, M., Miller, R. C., ... & Ash, R. (2008). Small cell (neuroendocrine) carcinoma of the prostate: etiology, diagnosis, prognosis, and therapeutic implications—a retrospective study of 30 patients from the rare cancer network. *The American journal of the medical sciences*, *336*(6), 478-488.
19. Aparicio, A. M., Harzstark, A. L., Corn, P. G., Wen, S., Araujo, J. C., Tu, S. M., ... & Logothetis, C. J. (2013). Platinum-based chemotherapy for variant castrate-resistant prostate cancer. *Clinical cancer research*, *19*(13), 3621-3630.