

# Is There Any Indication for Prophylactic Brain Irradiation in the Management of Small Cell Prostate Cancer?

Joseph Kattan\*, Hampig Kourie, Pierre Sarkis, Joseph Gharios, Joelle Antoun

Saint Joseph Hospital, Raymond and Aida Najjar Medical Center, Saint Joseph University, Beirut, Lebanon.  
Email: \*jkattan62@hotmail.com

Received February 20<sup>th</sup>, 2013; revised March 21<sup>st</sup>, 2013; accepted March 28<sup>th</sup>, 2013

Copyright © 2013 Joseph Kattan *et al.* This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

Small cell prostate carcinoma (SCPC) is an extremely rare pathology with an aggressive behavior, characterized by early brain metastases. We describe three cases of SCPC where brain metastases occurred despite response to chemotherapy. The benefit of prophylactic brain irradiation (PBI), as part of the management of SCPC, is discussed and compared to its indications in small cell lung cancer.

**Keywords:** Small Cell Carcinoma; Prostate Cancer; Brain Metastases; Prophylactic Brain Irradiation

## 1. Introduction

Small cell carcinoma is a distinct clinicopathologic entity, usually arising in the lung. It can also originate in a wide range of extrapulmonary sites called extrapulmonary small cell carcinoma (EPSCC). The most frequent sites of origin, when known, are the female genital tract, the gastrointestinal tract, the genitourinary tract and head and neck [1]. Approximately 10% of cases occur in the prostate, making it one of the most common extrapulmonary sites [2].

Pure SCPC is an extremely rare disorder compared to classical prostate adenocarcinoma. These tumors appear at a younger age than prostate adenocarcinoma (40 to 60 years) and behave more aggressively by early metastases spread, including the brain [3]. The majority of these have unexpected low PSA levels compared to patients with conventional adenocarcinoma [4].

We reviewed retrospectively 280 prostate cancer records treated during the last six years in our department, and we found only three cases of SCPC. They were all treated with Etoposide and Cisplatin, and suffered early thereafter from brain metastases. We discuss the importance of prophylactic brain irradiation (PBI) as part of the management of these small cell prostate carcinomas.

### 1.1. Case 1

J. B., a 67-year-old man, presented with urinary retention

secondary to an enlarged prostate volume. A transurethral resection showed a small cell carcinoma of the prostate. An abdominal and pelvic MRI showed prostate enlargement with capsular rupture invading the rectum and the seminal vesicles, associated with multiple bilateral pelvic and iliac lymph nodes.

After 4 cycles of Etoposide and Cisplatin, abdominal and pelvic MRI showed a regression of the prostate enlargement and a complete disappearance of pelvic nodes. Complementary radiotherapy to the hall pelvis was delivered thereafter.

Three weeks after the end of radiotherapy, the patient presented a sudden left hemiplegia with dysarthria, and cerebral CT scan showed diffuse multiple cerebral metastases.

### 1.2. Case 2

J. G., a 69-year-old patient, presented with sacral pain, left lower limb deficiency and hematuria. Cystoscopic resection showed a small cell carcinoma of the prostate, and disease work-up revealed left paralumbar and parasacral tumor deposit.

After 4 cycles of Platinum and Etoposide, a partial response was obtained with prostate shrinkage, 50% regression of paravertebral infiltration, and a complete neurologic recovery of his lower limb deficiency. According to an ongoing phase II trial, sequential Vinorelbine 60 mg weekly was initiated. Immediately after the third injection, he presented many episodes of convulsion

\*Corresponding author.

secondary to multiple cerebral lesions.

### 1.3. Case 3

A. R., a 76-year-old man, was treated elsewhere by a complete hormone blockage for a locally advanced adenocarcinoma of the prostate. He was referred two years later, without any documentation, for local prostate cancer progression, bone and liver metastases, and normal PSA. A new biopsy was done and showed poorly differentiated neuroendocrine tumor of the prostate. He received 6 cycles of VP16 and Cisplatin every 3 weeks, resulting in a sustained partial response. Two months after his last course, he returned with confusion. Brain CT scan showed multiple cerebral metastases.

## 2. Discussion

First described in 1977 by Wenk *et al.*, small cell prostate carcinoma is a rare entity of prostate tumors [5]. Although many of the EPSCC have biological and histological characteristics similar to small cell lung cancer (SCLC), many differences exist in the evolution, the prognosis and the treatment regarding the primary subsites [1].

The current treatment recommendations of EPSCC are based on retrospective analyses of small single-institution experiences or mainly extrapolated from studies of SCLC [6]. Therefore, the standard treatment includes 4 to 6 cycles of chemotherapy based on VP16 and cisplatin, delivered every 3 weeks, followed by local radiotherapy in some cases. Prophylactic brain irradiation (PBI) remains controversial in all EPSCC and is not routinely indicated as in responding SCLC [7].

Published studies showed that the incidence of cerebral metastases in SCLC ranges from 20% to 40%, while it was relatively low in the EPSCC (13%). Thus, PBI is routinely delivered in all cases of responding SCLC with a 5.4% survival benefit at 3 years [7], but it lacks any clear indication in EPSCC [8]. In fact, Brennan *et al.* discourage the use of PBI in EPSCC; they considered that brain metastases were less frequent in patients with EPSCC than in patients with SCLC, and therefore the potential benefit of PBI was not worthy despite an improvement in overall survival [1]. Früh *et al.* considered that more studies were necessary before routinely offering PBI to patients with EPSCC [8]. Eckert *et al.* concluded that the poor median survival (2 months) after the diagnosis of secondary brain metastases might be a reason to discuss and evaluate PBI for EPSCC patients responding to initial therapy [9]. Moreover, Muller *et al.* reported that PBI might be unrequired in EPSCC and discussed its utility only in head and neck small cell carcinomas [10]. Finally, no study discussed the incidence of brain metastases in small cell prostate cancer and there is no specific recommendation concerning the utility of PBI in this type of EPSCC.

We reported here our experience with SCPC with only 3 documented cases. Early brain metastases occurrence was uniformly encountered despite good initial response to the standard chemotherapy. We believe that PBI in the management of this special subsite of small cell carcinoma is beneficial, although the confirmation of its utility necessitate more extended studies in the future.

## REFERENCES

- [1] S. M. Brennan, D. L. Gregory, A. Stillie, A. Herschtal, M. Mac Manus and D. L. Ball, "Should Extrapulmonary Small Cell Cancer Be Managed Like Small Cell Lung Cancer?" *Cancer*, Vol. 116, No. 4, 2010, pp. 888-895. [doi:10.1002/cncr.24858](https://doi.org/10.1002/cncr.24858)
- [2] S. Giordano, T. Tolonen, S. Hirsimäki and V. Kataja, "A Pure Primary Low-Grade Neuroendocrine Carcinoma (Carcinoid Tumor) of the Prostate," *International Urology and Nephrology*, Vol. 42, No. 3, 2009, pp. 683-687. [doi:10.1007/s11255-009-9660-8](https://doi.org/10.1007/s11255-009-9660-8)
- [3] J. R. Mackey, H. J. Au, J. Hugh and P. Venner, "Genitourinary Small Cell Carcinoma: Determination of Clinical and Therapeutic Factors Associated with Survival," *Journal of Urology*, Vol. 159, No. 5, 1998, pp. 1624-1629. [doi:10.1097/00005392-199805000-00058](https://doi.org/10.1097/00005392-199805000-00058)
- [4] P. Furtado, M. V. Lima, C. Nogueira, M. Franco and F. Tavora, "Review of Small Cell Carcinomas of the Prostate," *Prostate Cancer*, Vol. 2011, 2011, Article ID: 543272, 5 Pages. [doi:10.1155/2011/543272](https://doi.org/10.1155/2011/543272)
- [5] R. Wenk, B. Bhagavan and R. Levy, "Ectopic ACTH, Prostatic Oat Cell Carcinoma, and Marked Hyponatremia," *Cancer*, Vol. 40, No. 2, 1977, pp. 773-778. [doi:10.1002/1097-0142\(197708\)40:2<773::AID-CNCR2820400226>3.0.CO;2-I](https://doi.org/10.1002/1097-0142(197708)40:2<773::AID-CNCR2820400226>3.0.CO;2-I)
- [6] K. Haider, R. K. Shahid, D. Finch, *et al.*, "Extrapulmonary Small Cell Cancer," *Cancer*, Vol. 107, No. 9, 2006, pp. 2262-2269. [doi:10.1002/cncr.22235](https://doi.org/10.1002/cncr.22235)
- [7] A. Auperin, A. Arriagada, J. Pignon, *et al.*, "Prophylactic Cranial Irradiation for Patients with Small Cell Lung Cancer in Complete Remission," *The New England Journal of Medicine*, Vol. 341, 1999, pp. 476-484. [doi:10.1056/NEJM199908123410703](https://doi.org/10.1056/NEJM199908123410703)
- [8] M. Früh, B. Kacsir, S. Ess, T. Cerny, R. Rodriguez and L. Plasswilm, "Extrapulmonary Small Cell Carcinoma: An Indication for Prophylactic Cranial Irradiation? A Single Center Experience," *Strahlentherapie und Onkologie*, Vol. 187, No. 9, 2011, pp. 561-567. [doi:10.1007/s00066-011-2222-x](https://doi.org/10.1007/s00066-011-2222-x)
- [9] F. Eckert, C. Gani, M. Bamberg and A. C. Müller, "Cerebral Metastases in Extrapulmonary Cell Carcinoma. Implications for the Use of Prophylactic Cranial Irradiation," *Strahlentherapie und Onkologie*, Vol. 188, No. 6, 2012, pp. 478-482. [doi:10.1007/s00066-012-0084-5](https://doi.org/10.1007/s00066-012-0084-5)
- [10] A. C. Müller, C. Gani, M. Weinmann, F. Mayer, B. Sipos, M. Bamberg and F. Eckert, "Limited Disease of Extrapulmonary Small Cell Carcinoma. Impact of Local Treatment and Nodal Status, Role of Cranial Irradiation," *Strahlentherapie und Onkologie*, Vol. 188, No. 3, 2012, pp. 269-273. [doi:10.1007/s00066-011-0045-4](https://doi.org/10.1007/s00066-011-0045-4)