Clinical impact of $^{18}$F-fluorodeoxyglucose positron emission tomography/computed tomography in the evaluation of small cell carcinoma of the prostate

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**Abstract**

Small cell carcinoma of prostate (PSCC) is an uncommon and aggressive type of prostate malignancy with limited data on the use of $^{18}$F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) in the clinical management of this rare entity. In this report, clinical and imaging findings of a patient with PSCC are presented. We aimed to discuss the role of PET/CT in the evaluation of PSCC in combination with histopathological characteristics of tumor and emphasize the importance of PET/CT in the clinical management of PSCC.

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**Impacto clínico de la tomografía por emisión de positrones/tomografía computarizada con $^{18}$F-fluorodeoxiglucosa en la evaluación del carcinoma de células pequeñas de próstata**

**Resumen**

El carcinoma de células pequeñas de la próstata (CCPP) es una neoplasia prostática agresiva y poco frecuente. Existen datos limitados en la literatura sobre el uso de la tomografía por emisión de positrones/tomografía computarizada (PET/TC) con $^{18}$F-fluorodeoxiglucosa en el manejo clínico de esta rara entidad. Presentamos los datos clínicos y las imágenes en un paciente con CCPP. Nuestro objetivo ha sido discutir el papel de la PET/TC en la evaluación del CCPP en combinación con las características histopatológicas del tumor, así como hacer énfasis en la importancia de la PET/TC en el manejo clínico del CCPP.

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**Introduction**

Small cell carcinoma of prostate (PSCC) is a rare and aggressive type of prostate malignancy. Most of the cases are symptomatic at the time of diagnosis due to advanced disease. The disease tends to spread to local lymph nodes, visceral organs, bones and brain early in its course usually without a rise in prostate-specific antigen (PSA) serum levels. Histopathological diagnosis relies mostly on immunohistochemical stains including neuron specific enolase, synaptophysine and chromogranin A.

Positron emission tomography/computed tomography (PET/CT) with $^{18}$F-fluorodeoxyglucose (FDG) is a validated method used in the clinical oncology practice. However, the clinical use of PET/CT in prostate cancer is still being explored. Although FDG-PET provides important prognostic information, it is generally accepted to have limited value in staging of prostate cancer due to relatively low FDG uptake in the tumor and adjacent intense urinary activity.

In addition, false positive results in case of infection/inflammation were also reported.

The current literature lacks of sufficient data on the use of FDG-PET/CT in PSCC where evidence is based only on few case reports.

In this report, we present a case with PSCC and widespread metastatic disease detected by PET/CT in the initial workup. We aimed to highlight the role of FDG-PET/CT in the staging of this rare and aggressive type of prostate malignancy.

**Clinical case**

A 77-year-old male patient who presented with hematuria was diagnosed to have PSC after transurethral resection of prostate. Neuroendocrine markers (chromogranin A, synaptophysin, CD56) and α-methylacyl-CoA racemase (AMACR) was positive on immunocytochemical analysis. No staining with high-molecular-weight cytokeratin (HMWCK), cytokeratin-7, cytokeratin-20, PSA and P63 was detected and Ki-67 index was reported to be 90%. Serum PSA level was 4.8 ng/ml, which is slightly above the normal range (normal range:0–4 ng/ml). The patient was referred to FDG-PET/CT for initial staging. Imaging was performed by an integrated PET/CT scanner (Siemens Biograph 6 – True Point
PET/CT systems; Siemens, Chicago, Illinois, USA). Patient fasted for 6 hours prior to injection of 5.3 MBq/kg (144 μCi/kg) of 18F-FDG. The blood glucose level was 93 mg/dl at the time of the FDG injection. Unenhanced CT images were acquired for attenuation correction from the vertex to mid thigh using 3 mm slice thickness and calculated effective mAs due to patient weight. Analysis of the PET/CT images revealed multiple liver and bone lesions with intense FDG uptake (maximum standardized uptake values (SUVmax) range: 10.6–12.2), multiple nodules mostly smaller than 1 cm in lung parenchyma with increased FDG uptake (SUVmax: 2.9), and hypermetabolic tumoral lesion in prostate (SUVmax: 8.2) accompanied by locoregional lymph nodes (SUVmax: 8.2) (Fig. 1). Palliative chemotherapy with cisplatin, etoposide and biphosphonates was administered. Disease progression occurred after 3 lines of chemotherapy, new line of chemotherapy could not be started due to poor performance status. The patient is currently under palliative treatment 6 months after initial diagnosis.

Discussion

Increased glucose uptake and metabolism, in association with overexpression of cellular membrane glucose transporters is a hallmark of malignant transformation in tumors. FDG is the most studied tracer in prostate cancer patients. However, there is considerable controversy in the literature on FDG-PET/CT in prostate cancer. Even though prostate cancer shows GLUT-1 overexpression and the glucose metabolism in prostate cancer is GLUT-mediated, the biological heterogeneity of the tumor complicates the use of FDG-PET/CT in prostate cancer. Clinicians generally agree that FDG-PET may not be valuable in diagnosis and primary staging of organ-confined prostate cancer. However, PET/CT takes a step further that allows the characterization of tumor biology. Today, it is well known that aggressive tumors tend to have higher levels of FDG uptake compared to the less aggressive tumors. In addition, recent studies demonstrate that FDG uptake in prostate cancer increases with Gleason score, serum PSA levels and PSA velocity which indicates that FDG-PET may be used as a measure of tumor metabolism and aggressiveness. Moreover, FDG-PET scan may also provide beneficial information in the assessment of patients with rising serum PSA levels after treatment of localized prostate cancer. In addition to the role of FDG in evaluation of patients with prostate cancer, studies of choline analogs labeled either with 11C or 18F show promising results in clinical workup of patients with prostate cancer. Carcinoma of the prostate shows high levels of choline uptake along with elevated levels of choline metabolites, which can be used as potential prognostic biomarkers for the management of prostate cancer patients.

Combining the biological behavior of PSCC with the above-discussed association of FDG avidity and tumor biology, the use of FDG-PET/CT in the clinical management of patients with PSCC may be reasonable. However, mostly depending on the rarity of this tumor, yet, there is not sufficient data on the use of FDG-PET in PSCC. In current literature, only 4 case reports are reported previously. As described in these reports, PSCC shows increased metabolic activity as depicted by increased uptake on FDG-PET. However, no information on the expression of Ki-67, which is a marker of high proliferative activity, was present.

In the present report, similar to previously published cases, we observed intense FDG uptake in the primary tumor as well as in the metastatic deposits. However, to our knowledge, this is the first case report that demonstrates the association of increased Ki-67 index with high FDG uptake in a patient with PSCC and widespread disease. We considered that, intense metabolic activity in PSCC was
in concordance with the aggressive nature of the tumor and poor survival characteristics.

High Ki-67 index correlates with Gleason score and pathological tumor stage in prostate cancers and is associated with aggressive features of prostate cancer. In addition to that it is found to be higher in prostate cancers which are positive for neuroendocrine markers.\(^{11}\) Regarding the association of Ki-67 index with Gleason score, aggressive biological character of the tumor and FDG avidity, we consider that the use of FDG–PET scan in prostate cancers, particularly in adenoacarcinomas, should increase in time with the indications of prognostication, diagnosis and staging of tumors with high Gleason score, detection of locally recurrent or metastatic disease.

High rate of proliferation and high metabolic activity of PSCCs are in line with the known aggressive behavior of PSCC. In the case presented above, Ki-67 index was reported as \(>90\%\) showing high proliferative activity in the tumor, which in turn may contribute to the factors increasing glucose metabolism of the tumor cells as depicted by FDG–PET scan. However, further investigation is warranted to show association of proliferative activity and metabolic activity in prostate cancers as well as in PSCCs.

As a summary, although current literature lacks of large series concerning the use of FDG–PET in PSCC, our report and a few previously published ones highlight that FDG–PET/CT may provide important prognostic information in the initial workup of patients with PSCC as well as offering the advantage of assessing treatment response. Additionally, we consider that FDG–PET may be of great value in detecting metastases when biochemical tumor markers such as PSA are of no use in the follow-up of patients with PSCC.

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**Conflict of interest**

Authors declare that there is no conflict of interest.

**References**