CASE SERIES

# Superscan on $^{68}$Ga PSMA PET/CT in patients with metastatic prostate carcinoma: A case series

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**ABSTRACT**

Prostate cancer is the second most common malignancy in men worldwide, with a good prognosis when is detected and treated in early stages, but, when it presents progression to castration-resistant metastatic prostate cancer, most of the cases will have bone metastasis, decreasing the quality of life and life expectancy. For the evaluation of the disease in the routinary clinical practice, $^{68}$Ga-PSMA PET/CT, among others is a valuable tool for the evaluation of the disease extension. $^{68}$Ga-PSMA PET/CT detects the presence of PSMA receptor in the tumoral tissue, but also has physiologic uptake in certain organs, such as liver, spleen, intestine, kidneys, lacrimal and salivary glands. Total or partial absence of uptake in those organs is rare and may be due to a high metastatic tumor burden, a phenomenon originally described in bone scintigraphy as super scan. We describe a case series of seven patients with prostate cancer from the National Institute of Cancerology in Colombia, in which a super scan pattern was found in the evaluation with $^{68}$Ga-PSMA PET/CT, proposing the suppression of uptake in the intestine, liver, spleen, lacrimal and salivary glands as the main criteria for its definition, and showing that renal uptake persists in most cases, considering that, unlike the super scan in conventional bone scintigraphy, this is not a criterion necessary for its definition in the study with $^{68}$Ga-PSMA.

**KEYWORDS:** $^{68}$Ga-PSMA PET/CT; superscan; metastatic prostate carcinoma

## INTRODUCTION

Prostate cancer is the second most common malignancy in men worldwide after lung cancer, and the fifth leading cause of cancer mortality, appearing on average after the age of 50 and increasing its prevalence with age [1]. In Colombia, a prevalence of 4.54 cases per 1000 inhabitants is estimated, based on men over 35 years of age, being significantly higher in the age group over 80 years (33.45 per thousand inhabitants) [2]. The course of the disease, when confined to the prostate, is indolent, with 5-year survival rates greater than 95%; however, most cases will tend to progress to castration-resistant metastatic prostate cancer, of which 90% will present with bone involvement, predominantly at the vertebral level, impacting quality of life and prognosis [3].

For the diagnosis of bone compromise by the disease, the use of conventional bone scintigraphy with $^{99m}$Tc-HMDP [4] is still recommended. One of the causes of potential false negatives in conventional bone scintigraphy is the presence of the superscan phenomenon first described in 1975 in a series of patients with breast, prostate and lung tumors [5], as a diffuse increase in the concentration of the radioisotope at the bone, with a decrease in soft tissue uptake, evidenced a poor or null scintigraphic representation of the renal silhouettes, secondary to diffuse bone metastatic disease, and may also occur in other pathologies, such as Paget's disease or hyperparathyroidism. Under normal conditions, 40% of the injected dose of $^{99m}$Tc-HMDP becomes fixed to the bone and the remaining 60% is excreted in the urine; in extensive metastatic or metabolic processes at the bone and in renal failure, this relationship changes to 85% fixation and 15% excretion, explaining the imaging presentation in conventional scintigraphy [6]. This finding, frequent in bone scintigraphy with $^{99m}$Tc-HMDP, has been reported to a lesser extent in PET/CT images with $^{68}$Ga PSMA [7-10], a study that is currently part of the theragnostic strategy to assess the relevance of treatment with $^{177}$Lu-PSMA.

Prostate-specific membrane antigen (PSMA) is a type II transmembrane glycoprotein, that presents a high expression in prostate cancer however, it is also physiologically present in other tissues, making the $^{68}$Ga-PSMA PET/CT study with have intense physiological uptake at the level of the kidneys and salivary glands, and moderate uptake in the lacrimal glands, liver, spleen, and intestines.

We present a case series of seven patients with metastatic prostate cancer with polyostotic compromise with high expression of the PSMA in metastatic bone regions on $^{68}$Ga-PSMA PET/CT images, displacing the physiological uptake of the radiotracer and becoming markedly decreased or absent, considering these as criteria for characterize them as superscan.

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## CASE SERIES PRESENTATION

The PET/CT studies with $^{68}$Ga-PSMA performed in our nuclear medicine department, from 2019 to march 2023 were retrospectively evaluated, in order to describe those studies in which there was a superscan pattern. All the studies were performed with a Siemens Biograph 64 unit, with a dose of 0.05 mCi/Kg of $^{68}$Ga-PSMA-11, and image acquisition one hour after the injection of the radiotracer and delayed images after 3 hours.

Once the subjects were located in a supine position with their arms raised above their heads, the acquisition parameters consisted of a computed tomography scan from the base of the skull to the middle third of the thighs, a topogram from 1024 to 2048 mm depending on the length of the individual, from 7 beds, with a time for the acquisition of 2 to 3 minutes for each one; kVp setting: 120, mA 100-Caredose, 3mm steps, pitch 1.5. Followed by acquisition of positron emission tomography configured with a field of view (FOV) from the middle third of the thighs to the base of the skull, with an acquisition time of 2 to 4 minutes per bed, 168 x 168 matrix, number of iterations and subsets 7 and 14, respectively; window width at half height (FWHM) of 8.

PET/CT image reconstruction parameters included random coincidence correction, attenuation correction using CT and scatter correction, as well as PET image reconstruction with and without attenuation correction, in order to identify artifacts caused by the algorithm of correction that interfere with the adequate interpretation of the study. Additionally, the following settings were established: 3 mm slices, 2.5 mm reconstruction increment, B31f filter, abdomen window, and 500 mm FOV.

A total of seven patients with acinar adenocarcinoma were found that met the superscan pattern (Figures 1 to 7). The ages of the patients were between 57 and 76 years. The average time between the diagnosis of the disease and the superscan was 6.83 years. All with a Gleason score >7 and Grade Group 3 and 4, classifying them at the beginning of the disease as intermediate or high risk. PSA levels were elevated in all cases at the time of the study, consistent with the metastatic activity of the disease, with a minimum level of 246 ng/ml and a maximum of 2179 ng/ml. All had elevated levels of alkaline phosphatase (ALP) and lactate dehydrogenase (LDH). In most patients there is a decrease and in other cases absence of uptake of the parotid and lacrimal glands and decrease of uptake of the liver, spleen and in the intestine, although in none of the cases there was complete elimination of uptake in the renal parenchyma. The complete relevant data can be found in Table 1.

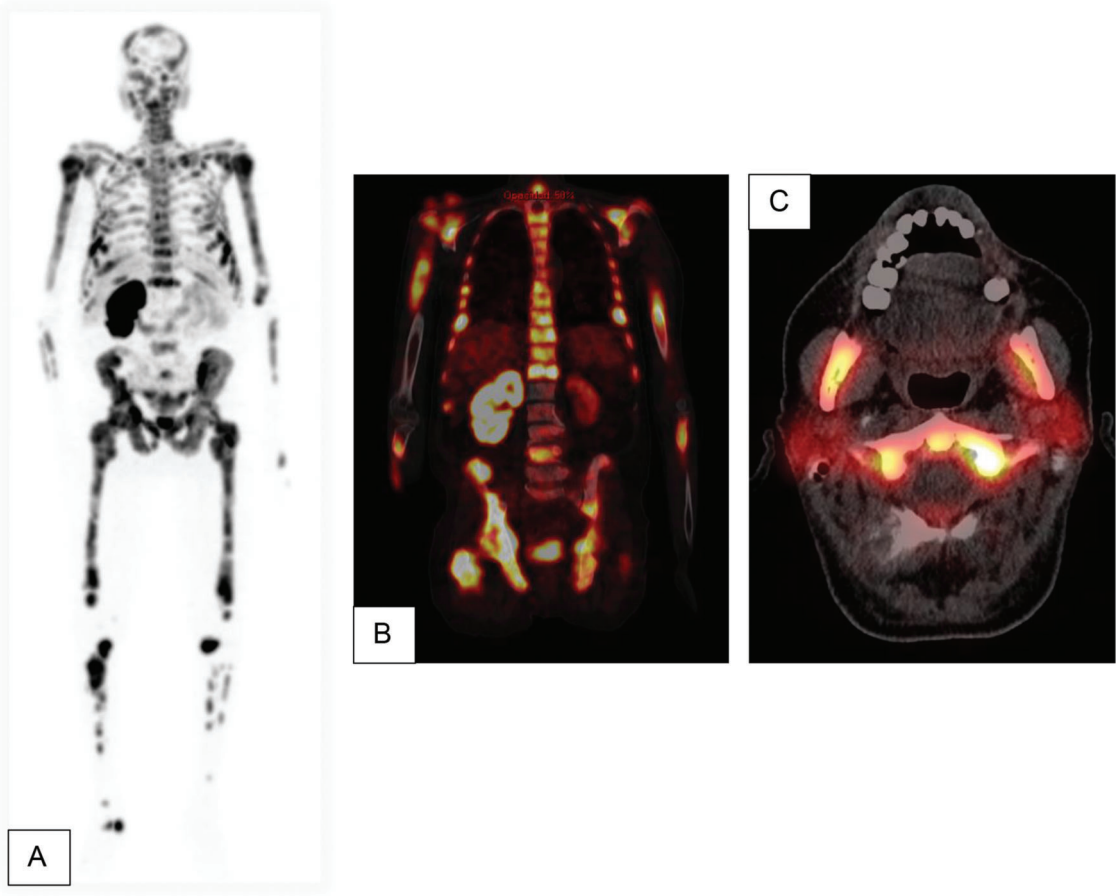


**Fig. 1.** Patient 1. A) Maximum intensity projection (MIP) showing multiple diffuse and intense foci of abnormal PSMA expression (Score 3 according PROMISE score, SUVmax 19.5) in the axial and appendicular skeleton. B) Fused PET/CT left kidney decreased in size, bilateral simple renal cysts, without PSMA expression. C) Fused PET/CT physiologic uptake in lacrimal and salivary glands is decreased in intensity.

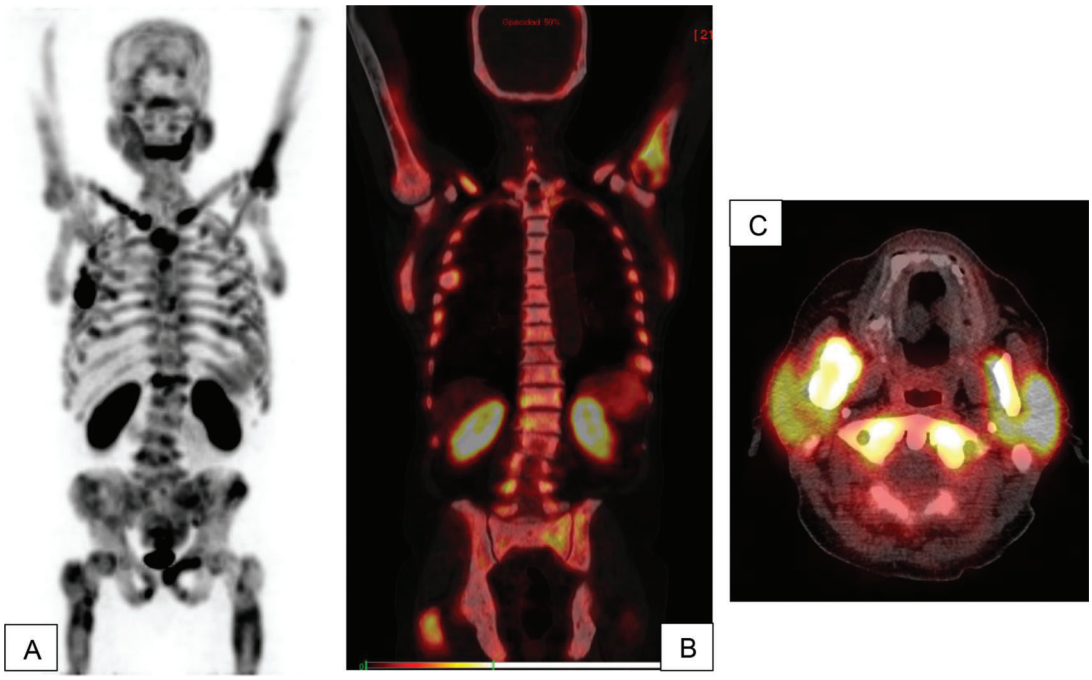


**Fig. 2.** Patient 2. A) Maximum intensity projection (MIP) extensive involvement of the axial and appendicular skeleton was evidenced, with diffuse, irregular, and intense expression of PSMA (SUVmax 11.8, Score 3). B) Fused PET/CT decreased uptake of the radiotracer in the liver parenchyma (SUVmax 1.7). C) Fused PET/CT no uptake of the radiotracer is seen in the lacrimal glands and decreased concentration in salivary glands.

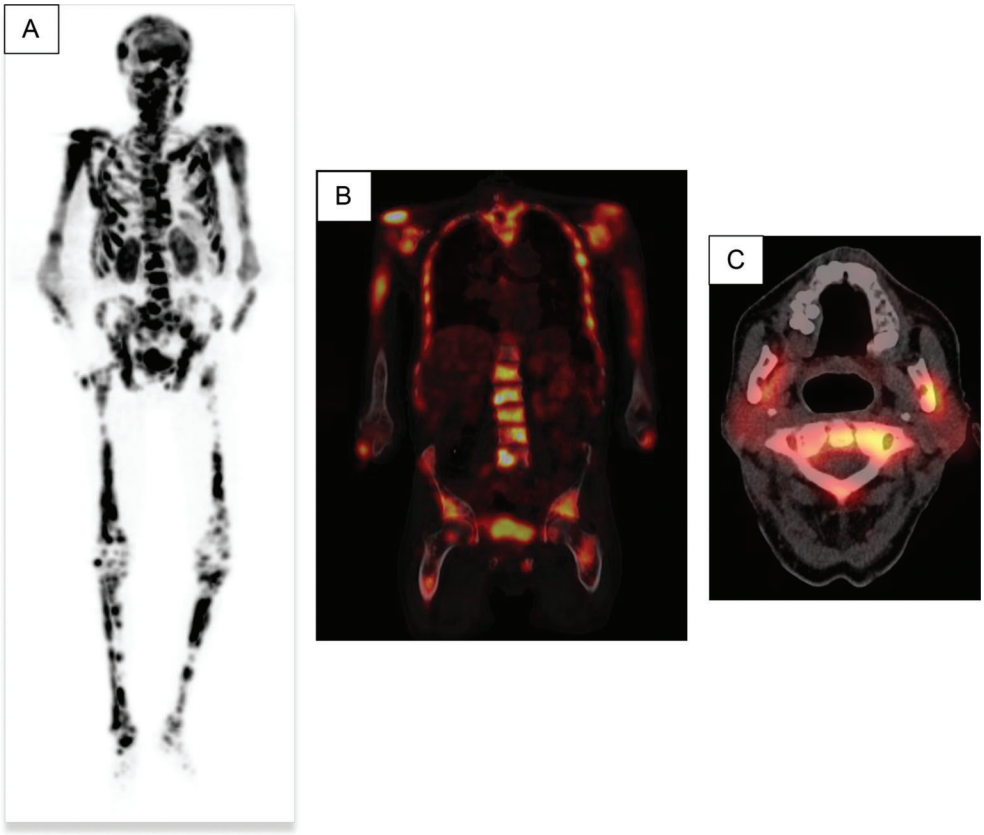


**Fig. 3.** Patient 3. A) Maximum intensity projection (MIP) showing multiple bone lesions with high PSMA expression in the axial and appendicular skeleton (SUVmax 14.3, Score 3). B) and C) Fused PET/CT decreased uptake in the liver, spleen, intestine, and parotid glands.

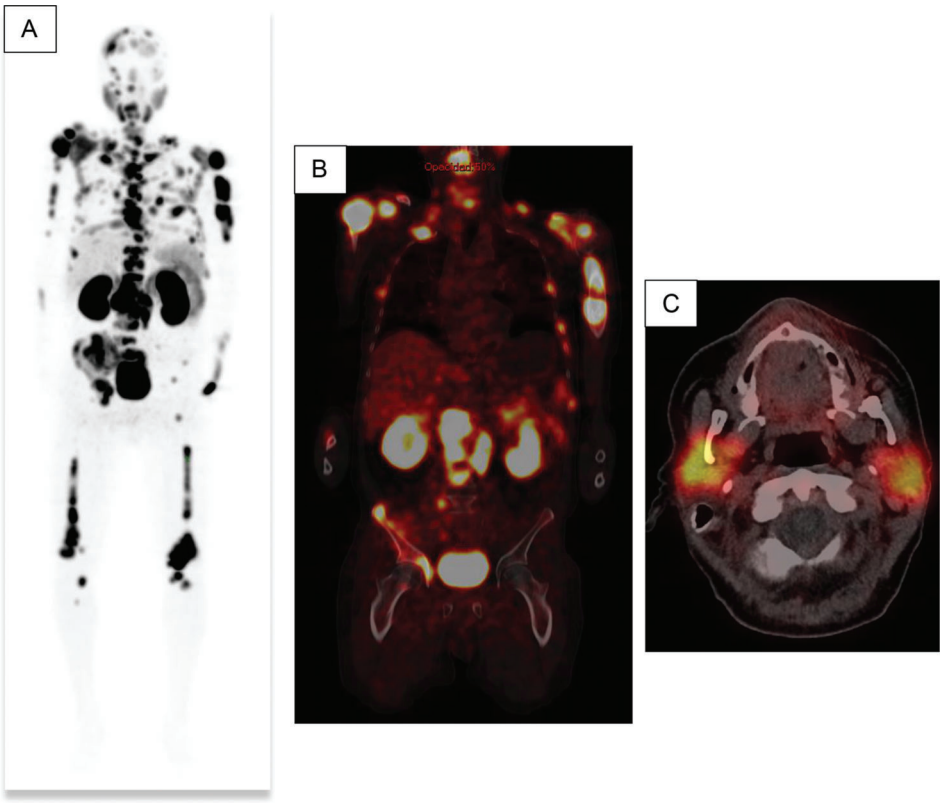


**Fig. 4.** Patient 4. A) Maximum intensity projection (MIP) showing multiple bone lesions with intense expression of generalized PSMA with muscular and spinal extension (SUVmax 34.1, Score 3). B) and C) Fused PET/CT decreased uptake in salivary glands, intestine, and liver.

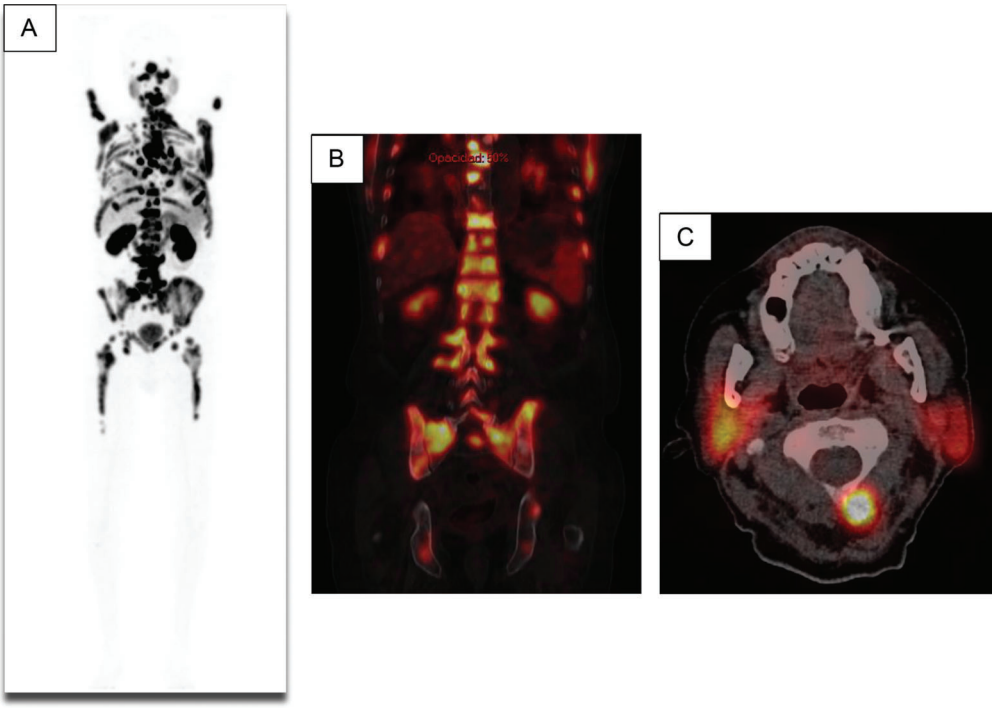


**Fig. 5.** Patient 5. A) Maximum intensity projection (MIP) multiple foci with high expression of PSMA throughout the axial and appendicular skeleton, predominantly proximal. B) and C) Fused PET/CT decreased uptake in the liver parenchyma and parotid glands.

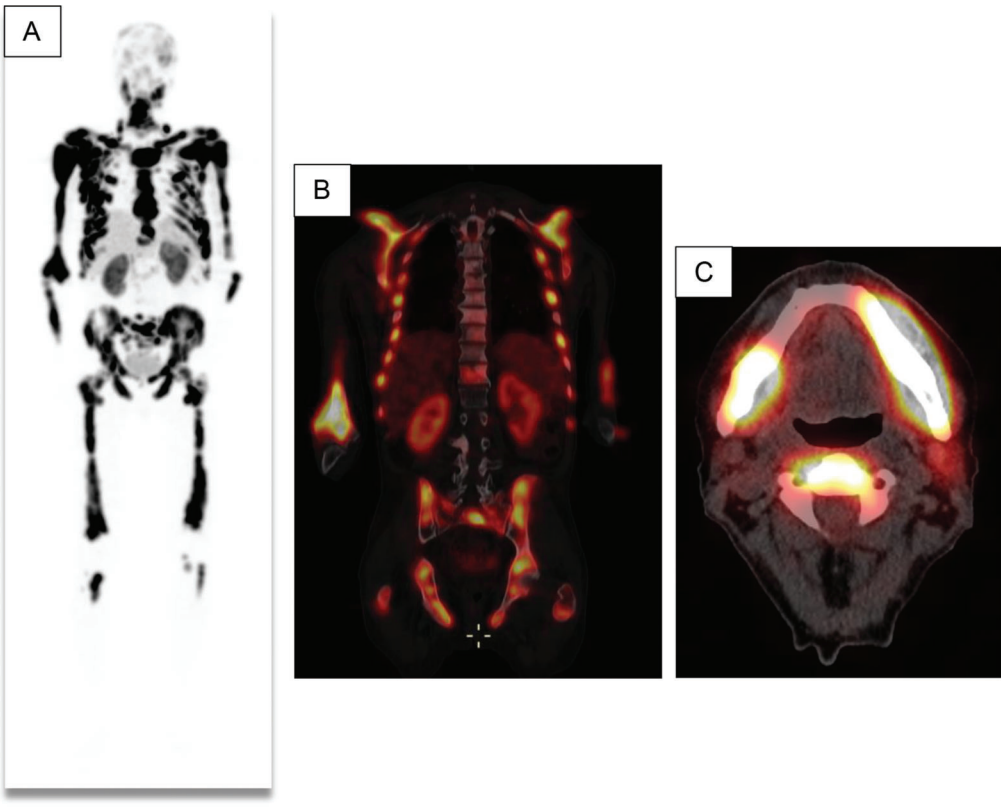


**Fig. 6.** Patient 6. A) Maximum intensity projection (MIP) showing extensive bone involvement with high expression of PSMA. B) Fused PET/CT decreased uptake in the intestine, liver and spleen. C) Fused PET/CT low uptake in parotid glands.

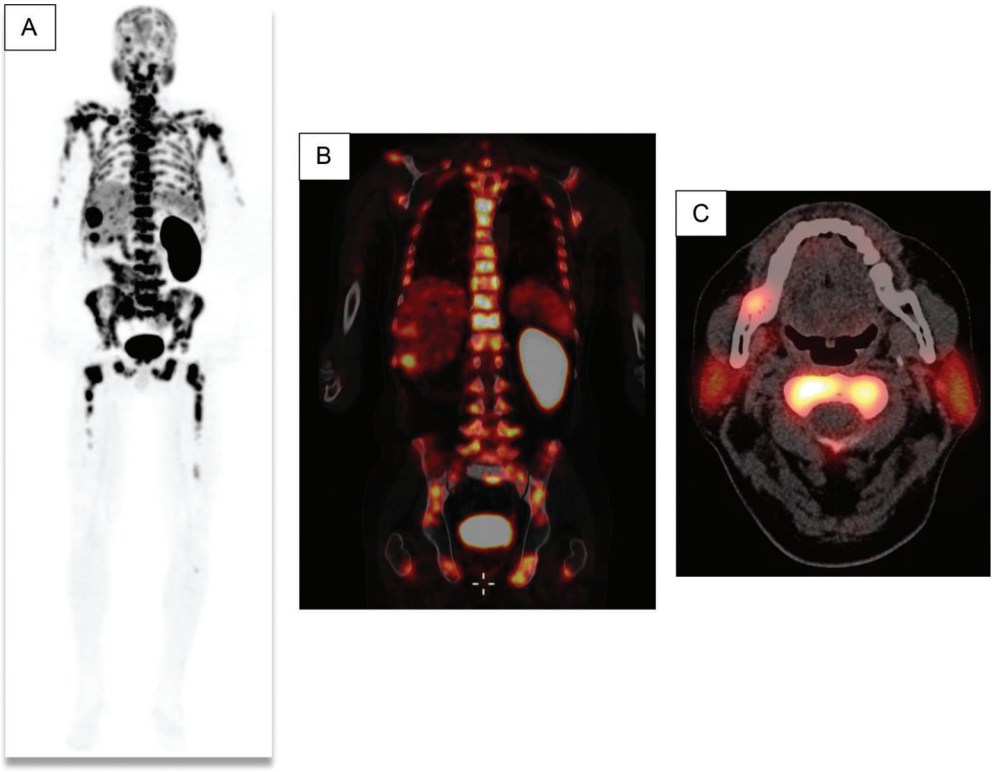


**Fig. 7.** Patient 7. A) Maximum intensity projection (MIP) showing multiple foci with high expression of PSMA in the axial and appendicular skeleton. B) Fused PET/CT right renal atrophy, metastatic liver lesions. C) Fused PET/CT decreased concentration of the radiotracer in the parotid glands.

**Table 1**. Characterization of the patients.

| 6 | Age | Date of Dx | Image date | Gleason | PSA (ng/ml) | LDH | ALP | SUVmax submandibular glands | SUVmax parotid glands | SUVmax lacrimal glands | SUVmax liver | SUVmax spleen | SUVmax bone |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 76 | 2016 | 08.06.2021 | UK | 2179 | 267 | 848 | 6.6 | 3.9 | 3.1 | 2.2 | 2.6 | 19.5 |
| 2 | 69 | 2012 | 25.06.2021 | 4+3 | >1000 | 673 | 537 | 4.9 | 6.5 | WU | 1.7 | 2.8 | 11.8 |
| 3 | 70 | 2013 | 10.01.2023 | 3+5 | 253 | 306 | 801 | 2.9 | 3.2 | WU | 2.2 | 2.0 | 14.3 |
| 4 | 66 | 2019 | 21.01.2022 | 4+3 | 246 | 1811 | 298 | 10.5 | 8.1 | 3.9 | 4.1 | 6.5 | 34.1 |
| 5 | 72 | 2013 | 14.02.2022 | 4+5 | 947 | UK | UK | 10 | 7.1 | 2.0 | 3.2 | 5.6 | 17.6 |
| 6 | 57 | 2017 | 02.02.2022 | 4+4 | 1537 | UK | UK | 5.5 | 2.2 | 2.1 | 3.3 | 4.3 | 24.9 |
| 7 | 66 | UK | 28.02.2023 | UK | UK | UK | UK | 6.1 | 5.6 | 3.0 | 3.1 | 4.3 | 13.2 |

Abbreviations: Dx: diagnosis, UK: unknown, WU: without uptake, AP: alkaline phosphatase, LDH: lactate dehydrogenase.

## DISCUSSION

Prostate cancer is a pathology with an increasing incidence in the last decades, with significant advances in its diagnostic and therapeutic approach, where PET/CT with $^{68}$Ga-PSMA plays a fundamental role in treatment planning in light of the current approach.

In the $^{68}$Ga-PSMA PET/CT images of this series of cases, the distribution of the radiotracer was evidenced with greater avidity due to the extensive polyostotic metastatic involvement with which these patients present, displacing the uptake from the expected physiological distribution and configuring a pattern of superscan, which although they do not present the risk of generating false negatives as has been described for this phenomenon in bone scans, they are an indicator of extensive involvement of the disease.

The description of the superscan for conventional bone scintigraphy is widely documented, but this is not the case for $^{68}$Ga PSMA PET/CT: at the date of writing this series of cases, and according to the literature review carried out, only four cases have been published [5-8], so our study broadens this discussion and we propose for its definition the adaptation of the original description given by Osmond [4], characterizing as superscan, not only diffuse polyostotic involvement, but also displacement of the radiotracer from physiological uptake sites.

Additionally, it is necessary to highlight serum elevation of alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) enzymes observed in four of the seven reported patients (in the remaining three there is no record of their levels).

ALP is an enzyme present in various body tissues, but its increased presence in the bloodstream primarily results from its release by the liver or bones. In bone, it is found in the osteoblast membrane and is a marker of osteoblastic activity as it is active in the production of the organic collagen matrix, so its serum levels increase proportionally to metastatic bone disease. It was one of the first molecules postulated as a tumor marker, and in the specific setting of castration-resistant metastatic prostate cancer it is a prognostic and overall survival marker [11].

For its part, LDH is an enzyme that participates physiologically in the processes of glycolysis and gluconeogenesis, being overexpressed by tumor cells producing lactate through anaerobic glycolysis, a phenomenon explained by the Warburg effect [12]. Its elevation is a reflection of accelerated cell metabolism and growth, and increased levels of this enzyme have been associated with poorer overall survival and progression-free survival rates [13].

In our study, as additional descriptive data and without statistical significance, the patient with the highest bone SUVmax values was in turn the one with the lowest ALP and highest LDH levels, agreeing with what is described by Ertürk et al [14], who found a negative relationship between SUVmax values in the prostate and ALP levels [14], although in their study there was no relationship between SUVmax and LDH levels.

## CONCLUSION

Superscan on $^{68}$Ga PSMA PET/CT could be defined as a high increase in PSMA expression corresponding to sclerotic/lytic lesions on CT involving the entire skeleton. The physiological background in the salivary glands, intestine, and liver and spleen parenchyma may be absent or

diminished. Renal uptake is variable, without showing a clear decrease in the uptake of the radiotracer in our patients, so it should not be chosen as a strict criterion for the diagnosis of superscan.

## Conflicts of interest

The authors declare no conflicts of interest.

## Financial conflicts

This research has not received specific support from public sector agencies, the commercial sector or non-profit entities.

## Informed consent

Our institution is an approved research center, the protocol is that, upon admission, all patients sign a general consent in which they authorize the use of their results for non-experimental retrospective observational research and publishing, clarifying that their personal data will not be exposed.

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