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INTERESTING IMAGE

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68Ga-PSMA: a One-stop Shop in Radioactive Iodine Refractory Thyroid Cancer?

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Abstract
We report a case of a 47-year-old female known with metastatic papillary thyroid cancer. Her treatment history included total thyroidectomy and 3 previous radio ablations with a cumulative dose of 950 mCi of ^{131}I. On follow-up, her thyroglobulin levels had demonstrated a rising trend (from 3789.0 to 4240.0 ug/L) despite a ^{123}I whole-body scan demonstrating a reduction in tracer avid lesions. She was suspected of having radio-resistant disease. The patient underwent both ^{18}F-FDG and ^{68}Ga-PSMA PET/CT imaging with both scans demonstrating congruent lesions however with far greater intensity on the ^{68}Ga-PSMA study.

Keywords ^{68}Ga-PSMA · ^{18}F-FDG · Thyroid cancer · Radioactive iodine refractory thyroid

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Table 1 Comparison of ^{18}F-FDG and ^{68}Ga-PSMA SUVR of reference lesions

Lesion	Thyroid primary	Lung lesions	Lytic T10 lesion	Right femur lesion	Left first rib
^{18}F-FDG SUVR	19.01	21.15	20.17	12.27	5.07
^{68}Ga-PSMA SUVR	75.51	21.34	139.55	137.98	31.24

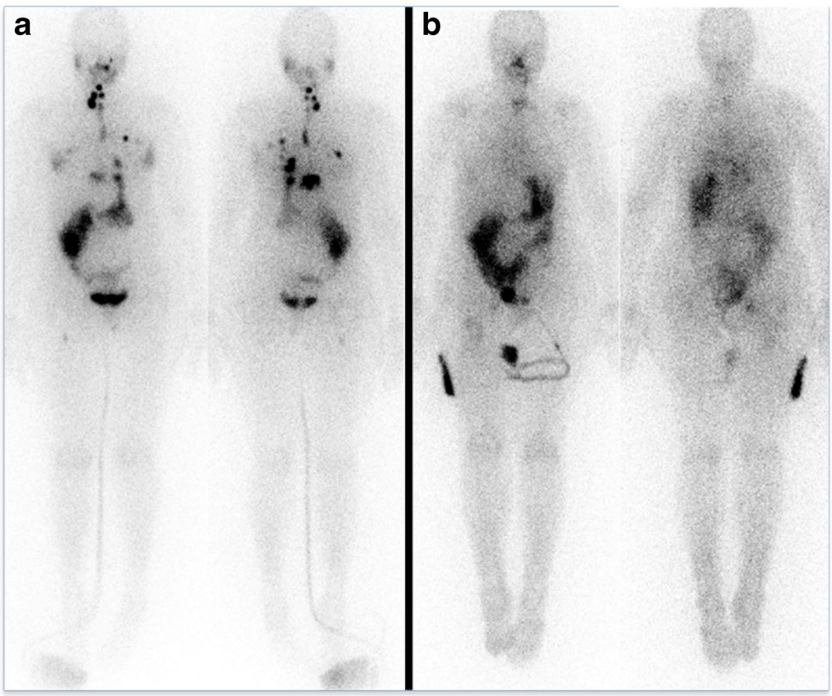

Fig. 1 A 47-year-old female with papillary thyroid cancer with metastases to the lungs, spine, and right proximal femur as demonstrated on her baseline ^{123}I whole-body anterior and posterior images (**a**). Her treatment history included a total thyroidectomy in 2015, decompression and fusion T8–L2 in 2015, and 3 previous radio ablations with a cumulative dose of 950 mCi ^{131}I. On follow-up, she presented with rising thyroglobulin levels, from 3789.0 to 4240.0 ug/L. ^{123}I whole-body anterior and posterior images (**b**) demonstrated minimal ^{123}I avid disease in keeping with radioactive iodine (RAI)–refractory disease [1]. Whilst patients with differentiated thyroid cancer can expect to have a good prognosis, those with RAI-refractory disease have poorer outcomes and succumb to their condition early [2].

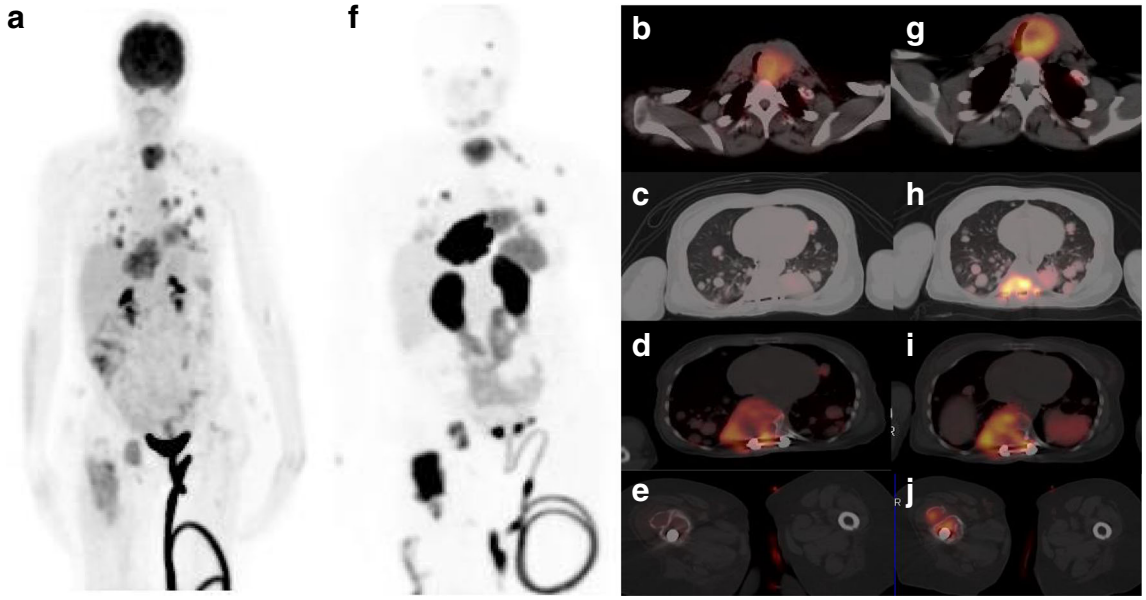

Fig. 2 ^{18}F-FDG PET/CT MIP (**a**) and fused axial soft tissue and lung window images (**b**, **c**) demonstrate residual thyroid tissue and lung metastases. Axial (**d**, **e**) ^{18}F-FDG PET/CT fused bone window images demonstrated thoracic spinal and right femur metastatic lesions. The related standard uptake value ratio (SUVR) readings of lesions demonstrated in this figure are presented in Table 1. ^{18}F-FDG PET/CT remains the recommended imaging modality in RAI-refractory disease, with an increasing sensitivity with rising thyroglobulin levels [3, 4]. Compared with the ^{123}I whole-body scans (Fig. 1) the PET/CT images demonstrated a flip-flop phenomenon [5]. ^{68}Ga-PSMA PET/CT, done 9 days after ^{18}F-FDG PET/CT, MIP (**f**) and fused axial soft tissue and lung window (**g**, **h**) and axial skeletal window (**i, j**) demonstrated ^{68}Ga-PSMA avid thyroid residual tissue, lung, and skeletal metastases. ^{68}Ga-PSMA PET/CT images demonstrated far greater intense tracer uptake in the soft tissue and skeletal lesions compared with the ^{18}F-FDG PET/CT scan; this was also confirmed by respective SUVR reference value comparison as noted in Table 1. Due to the fact that the injected activity for ^{18}F-FDG is weight based whilst that for ^{68}Ga-PSMA is fixed, SUVR rather than SUV max was the preferred semiquantitative method to compare lesion uptake between the two scans. The SUVR was calculated as a lesion to quadriceps muscle ratio using SUV mean. PSMA is a type II membrane antigen that is not only overexpressed in prostate cancer cells but has been demonstrated in other malignancies including thyroid and breast cancer as it overexpressed in tumor-associated neovasculature [6–8]. Tyrosine kinase inhibitors have taken a leading role in the management of patients with RAI-refractory thyroid cancer but suffer from side effects [9, 10]. To date, targeted radioligand therapy with ^{177}Lu-PSMA has demonstrated good outcomes with limited side effects in the management of patients with metastatic castrate–resistant prostate cancer [11]. High uptake of the PSMA ligand on imaging is part of the requirements for consideration for treatment with ^{177}Lu-PSMA radioligand therapy. To date, however, there is still limited evidence on the internalization and retention of therapeutic PSMA-labelled radioligands in de-differentiated thyroid cancer which is essential in the successful application of this radioligand treatment option for these patients. Imaging with ^{68}Ga-PSMA in our case not only demonstrated the lesions visualized on ^{18}F-FDG PET/CT but did so with a greater intensity suggesting possible suitability for theranostics with ^{177}Lu-PSMA. ^{68}Ga-PSMA PET/CT imaging in patients with RAI-refractory disease may prove to be a one-stop shop and should be considered as part of workup in these patients (Figure 2).

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Compliance with Ethical Standards

Conflict of Interest Thabo Lengana, Ismaheel O. Lawal, Kgomotso Mokoala, Mariza Vorster, and Mike M. Sathekge declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016;26:1–133.
2. Pfister DG, Fagin JA. Refractory thyroid cancer: a paradigm shift in treatment is not far off. J Clin Oncol. 2008;26:4701–4.
3. Silberstein EB. The problem of the patient with thyroglobulin elevation but negative iodine scintigraphy: the TENIS syndrome. Semin Nucl Med. 2011;41:113–20.
4. Vural GU, Akkas BE, Ercakmak N, Basu S, Alavi A. Prognostic significance of FDG PET/CT on the follow-up of patients of differentiated thyroid carcinoma with negative 131I whole-body scan and elevated thyroglobulin levels: correlation with clinical and histopathologic characteristics and long-term follow-up data. Clin Nucl Med. 2012;37:953–9.
5. Feine U, Lietzenmayer R, Hanke JP, Held J, Wohrle H, Muller-Schauenburg W. Fluorine-18-FDG and iodine-131-iodide uptake in thyroid cancer. J Nucl Med. 1996;37:1468–72.
6. Chang SS, Reuter VE, Heston WD, Bander NH, Grauer LS, Gaudin PB. Five different anti-prostate-specific membrane antigen (PSMA) antibodies confirm PSMA expression in tumor-associated neovasculature. Cancer Res. 1999;59:3192–8.
7. Sathekge M, Lengana T, Modiselle M, Vorster M, Zeevaart J, Maes A, et al. (68)Ga-PSMA-HBED-CC PET imaging in breast carcinoma patients. Eur J Nucl Med Mol Imaging. 2017;44:689–94.
8. Bychkov A, Vutrapongwatana U, Tepmongkol S, Keelawat S. PSMA expression by microvasculature of thyroid tumors - potential implications for PSMA theranostics. Sci Rep. 2017;7:5202.
9. Brose MS, Nutting CM, Jarzab B, Elisei R, Siena S, Bastholt L, et al. Sorafenib in radioactive iodine-refractory, locally advanced or metastatic differentiated thyroid cancer: a randomised, double-blind, phase 3 trial. Lancet. 2014;384:319–28.
10. Paeng JC, Kang KW, Park DJ, Oh SW, Chung JK. Alternative medical treatment for radioiodine-refractory thyroid cancers. Nucl Med Mol Imaging. 2011;45:241–7.
11. Kim YJ, Kim YI. Therapeutic responses and survival effects of 177Lu-PSMA-617 radioligand therapy in metastatic castrate-resistant prostate cancer: a meta-analysis. Clin Nucl Med. 2018;43:728–34.