Peptide receptor radionuclide therapy (PRRT) in radioiodine-refractory thyroid cancer: A case report of significant response to lu177 DOTA-TATE treatment

Saeideh Ataei-Nakhaei[1]
https://orcid.org/0000-0002-7647-2632

Kamran Aryana[1]
https://orcid.org/0000-0003-2403-8903

Sayyed Mostafa Mostafavi[2]
https://orcid.org/0000-0003-1676-8615

Hadis Mohammadzadeh Kosari[1]
https://orcid.org/0000-0002-4693-2183

Mohammad Esmatinia[1]
https://orcid.org/0000-0001-8582-5658

Atena Aghaee[1]
https://orcid.org/0000-0002-1351-3142

[1] Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
[2] Department of Medical Informatics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

SUMMARY

A 59-year-old woman with follicular thyroid carcinoma underwent total thyroidectomy followed by radioiodine treatment. Following treatment, the whole-body scan did not show any abnormal radioiodine uptake. However, during the follow-up, the serum thyroglobulin (Tg) value increased without detectable thyroglobulin-antibodies. We performed a Ga-68 DOTA-TATE PET/CT showing a sternal lesion and several lung nodules with high somatostatin receptor density. Also, on the next day, FDG PET/CT was performed, which confirmed the findings. Considering the high levels of somatostatin receptor expression in such metastases, we planned lu177 DOTA-TATE therapy. After two cycles of lu177 DOTA-TATE injection, serum thyroglobulin significantly dropped, and she claimed that her sternal pain and dyspnea were much better. This was the case of a patient suffering from iodine-refractory follicular thyroid carcinoma, with somatostatin-receptor expression, treated with 177Lu-DOTA-TATE, showing a significant response. Arch Endocrinol Metab. 2022;66(2):269-71

Correspondence to:
Atena Aghaee
Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
Aghaeeat@mums.ac.ir

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INTRODUCTION

The term differentiated thyroid carcinoma (DTC) encompasses papillary, follicular, and hurtle cell carcinomas of the thyroid (1). Medullary thyroid carcinoma is not included in this term. DTCs generally show favorable outcomes when treated promptly. Surgery ± radioactive iodine ablation (RIA) is the gold standard of curative treatment (1). However, some patients may lack the ability to take up radioactive iodine or even lose this ability (previous RIA-responsive cells were destroyed, but some less differentiated cells remained and progressed) as the disease progresses (2). This diminished uptake of radioactive iodine also restricts RIA-refractory patients' survival (1). The family of somatostatin receptors was shown to regulate thyroid cells proliferation (both normal and neoplastic tissue) (1). Additionally, multiple studies detected these receptors on thyroid tumor cells. Such features suggest potential therapeutic effects for agents like 111-In-octreotide, 90Y-DOTA-TOC, and lu177 DOTA-TATE (1). Herein, we report our experience of managing an RIA-refractory FTC with lu177 DOTA-TATE therapy, which alleviated the patient's symptoms and decreased Tg level.

CASE REPORT

A 59-year-old woman was referred to our tertiary clinic with increased thyroglobulin (Tg) levels detected during follow-up of follicular thyroid carcinoma (FTC). She was diagnosed with FTC nine years ago (pT2N0) and treated with total thyroidectomy plus 30 millicuries (mCi) of I-131 at that point. Post-ablation whole-body iodine scan did not reveal any pathologic finding and just post surgical thyroid remnant was evident. His first serum Tg level was 0.01 ng/mL in the TSH stimulated state (serum TSH = 33); the anti-Tg antibody was absent. The neck ultrasonography was unremarkable back then. The patient had poorly adhered to her follow-up visits during that time. an empirical dose (200 mCi) of I-131 was administered, and the post-treatment scan was negative (a) (Figure 1A). On the follow-up(After 14 months), Tg level was more than 500 ng/mL with suppressed TSH. Neck ultrasonography and diagnostic I-131 scan were negative. According to the guidelines of that time and because we had just a diagnostic scan showing no iodine avidity. Rising (After 6 months) serum Tg levels (>30,000 ng/mL) were documented in the absence of anti-Tg antibody, indicating a metastatic disease. Also, the patient reported severe sternal region pain. Thus, FDG PET/CT was performed, which showed pulmonary nodules and a lytic lesion of sternal manubrium with FDG uptake (Figures 1A-D).

By performing Ga-68 DOTA-TATE PET/CT to evaluate somatostatin receptor avidity, we tried to give our patient a chance to be treated with somatostatin-receptor radiopharmaceuticals. It confirmed the findings of FDG PET/CT (Figures 2A-C). Therefore, the patient received 200 mci of lu177 DOTA-TATE, and a post-treatment whole-body scan was performed. The SPECT/CT images showed increased uptake in pulmonary nodules and tracer uptake in the margin of lytic lesion of the sternum (Figures 2D-F). Three months after the first cycle of lu177 DOTA-TATE therapy, blood analysis showed declined Tg level to 1,760 ng/mL and subsequently to 982 ng/mL two months after completing the second cycle. Additionally, the patient declared significant improvement of clinical symptoms.

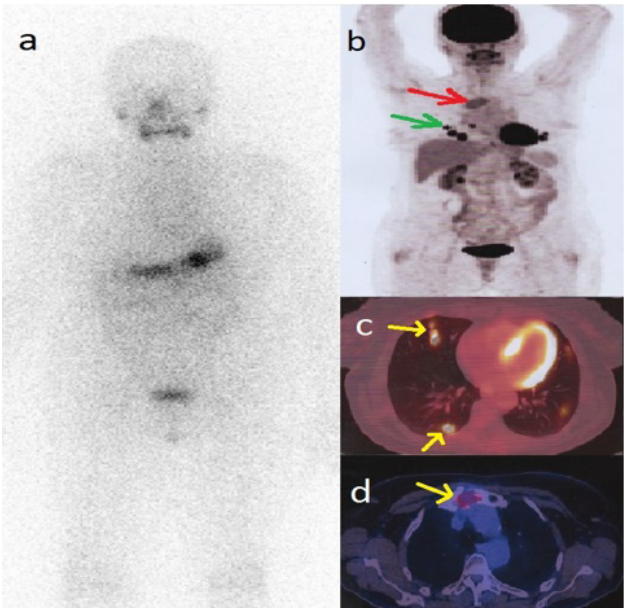

Figure 1. whole-body iodine scan (**a**) after administration of 200 mCi I-131 was negative. FDG PET/CT maximum intensity projection (MIP) (**b**) shows sternal and pulmonary metastases, which are more precisely localized on transaxial slices (**c, d)**.

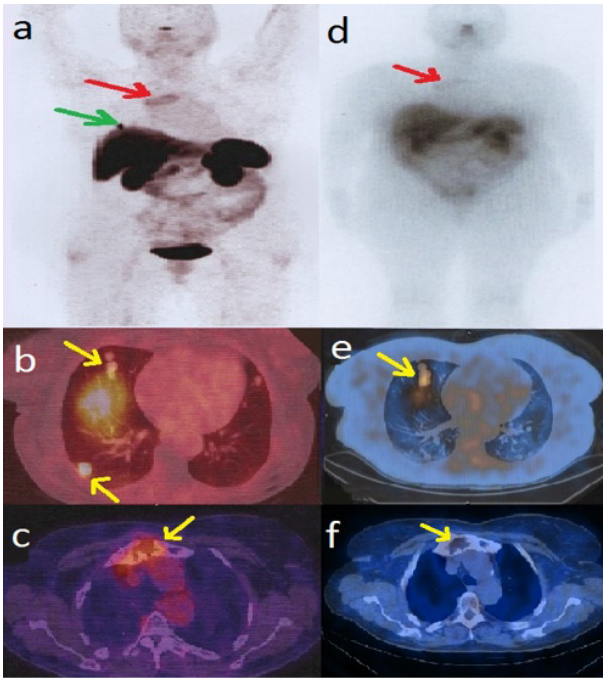

Figure 2. Ga-68-DOTATE MIP (**a**) and PET/CT (**b, c**) confirmed the lesions detected by FDG PET/CT. Therefore, the patient received 200 mci of lu177 DOTA-TATE and performed post-treatment WBS (**d**). lu177 DOTA-TATE SPECT/CT showed increased uptake in pulmonary nodules (**e**) and uptake in the margin of lytic lesion of the sternum **(f)**.

DISCUSSION

We reported a case of RIA-refractory FTC that was successfully managed via lu177 DOTA-TATE. About 25%-50% of patients with locally advanced or metastatic differentiated non-medullary thyroid carcinoma (DTC) become non-responsive to RAI (2,3). Treatment options are limited, one of which is recently proposed as PRRT, and there are few cases in the literature performing this treatment option (1,4-6). It has been reported that this treatment produces stabilization and even partial disease remission in these patients (7). Çinkir and Elboğa conducted a clinical study on ten thyroid cancer patients to assess the efficacy of lu177 DOTA-TATE treatment after detecting the presence of somatostatin receptors via Ga-68 labeled DOTATATE PET scan. Although she included MTC patients in her study, the overall results were promising (8). They had only one FTC stage-IV patient with no metastasis or lymph node involvement who remained stable during the follow-up. Versari and cols. performed a similar study on 11 patients, but they used 90Y-DOTATOC for PRRT; they treated three patients of FTC, two of whom remained stable, and one of them experienced disease progression (9).

In contrast to these promising outcomes, Budiawan and cols. reported 16 RIA-refractory thyroid carcinoma cases, four of which were FTC. They were treated with PRRT using 90-Yttrium, or 177-Lutetium, which showed poor long-term outcomes (1). These findings are explained mainly by these studies' variable inclusion criteria. Çinkir and Elboğa did not include metastatic patients; however, metastasis was an inclusion feature for the Budiawan study. Although lu177 DOTA-TATE significantly reduced Tg levels and improved our patient's sternal region pain and dyspnea, further long-term studies are needed before PRRT can be established as an option in treating RAI-refractory metastatic FTC (8).

In conclusion, lu177 DOTA-TATE therapy could be an effective alternative treatment modality in patients with elevated thyroglobulin and negative iodine scan. A sufficient somatostatin receptor expression must be confirmed in diagnostic imaging modalities like Ga-68 DOTA-TATE PET/CT scan. According to our knowledge, our case is the first RIA-resistant metastatic FTC with such a dramatic response to lu177 DOTA-TATE therapy.

Informed consent: written informed consent was obtained from the patient to publish the mentioned results and images anonymously.

Disclosure: all authors declare no relationships with any company or financial interests related to the pharmaceuticals used in this case report.

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