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Successful Radiofrequency Ablation of Medullary Thyroid Carcinoma Bone Metastasis

Ugo Albisinni[1], Margherita Bartocci[2]*, Paolo Spinnato[1], Giancarlo Facchini[1], Vincenzo De Biasi[3] and Giorgio Stecconi Ortolani[4]

[1]*Department of Radiological Sciences, Rizzoli Hospital, Bologna, Italy*
[2]*Department of Radiological Sciences, AUSL of Umbria 1, Perugia, Italy*
[3]*Division of Nuclear Medicine, ASMN of Reggio Emilia, Italy*
[4]*Division of Endocrinology, AUSL of Parma, Italy*

Abstract

Purpose: Medullary thyroid carcinoma is a rare cancer that arises from parafollicular or C cells which secrete calcitonin. The prognosis is usually poor because, at the time of diagnosis, either lymph node involvement or distant metastases are frequently present and there is no effective treatment for metastatic disease. We report our experience of the first case of solitary bone metastasis of medullary thyroid carcinoma treated with radiofrequency ablation.

Materials and methods: In September 2014 a patient with bone metastasis of medullary thyroid carcinoma was treated with computer tomography guided radiofrequency ablation. The patient was then followed by periodical physical examinations, serum calcitonin levels and Gallium-68 somatostatin receptor positron emission tomography - computed tomography (^{68}Ga PET-CT) until December 2018.

Results: Neither acute nor long-term complications were observed. Local recurrence at the site of the ablated metastasis was not encountered during follow-up, in particular, the patient obtained a partial response using biochemical parameters and a complete response using metabolic parameters.

Conclusion: Radiofrequency ablation could be a new useful treatment modality in bone metastasis of medullary thyroid carcinoma, but further studies are necessary to determine the precise role that this therapy should play in the management of this pathological condition.

Keywords: Radiofrequency ablation; Medullary thyroid carcinoma; Bone metastasis; Biochemical parameters

Introduction

Thyroid carcinomas represent only 1% of all human malignancies, but more than 90% of endocrine tumors. It can be histologically divided into papillary, follicular, anaplastic oř medullary thyroid carcinomas. Medullary thyroid carcinoma (MTC) is a neuroendocrine tumor originating from the parafollicular C cells of the thyroid, that produce calcitonin which is a sensitive biomarker for the disease. MTC accounts for 3.8% of all malignant thyroid tumors. Around 25% cases of MTC are familiar forms, generally related with Multiple Endocrine Neoplasia, therefore in a family with one or more members affected by this disease it's recommended the screening for MTC for an early treatment of the eventual tumor. However, the vast majority of MTCs, that are sporadic, are diagnosed later when the prognosis is usually poor because of the fact that at the presentation of the disease around a half of these patients have lymph node metastases and a fifth of those patients have extra lymph nodal metastases [1-3]. The 10-year survival rate for MTC for stages I, II, III, and IV is 100% for stage I, 92% for stage II, 70% for stage III, and 22% for stage IV, respectively, referred to TNM staging system. Therefore the stage of disease, besides the age when the patient is diagnosed the tumor, is the strongest predictors of survival for patients with MTC [4]. In fact the patients with multiple lymph node involvement or distant metastasis of MTC represent a clinical challenge because C cells are a responder neither to metabolic radiotherapy with I-131 nor to classic chemotherapy. In recent years, new drugs and treatments have been tried to cure metastatic MTC such as tyrosine kinase inhibitors and somatostatin analogue octreotide labeled to 90-yttrium (90Y- DOTATOC) [5-7]. However, there is no effective treatment for distant metastases and new therapeutic modalities are urgently needed. Radiofrequency (RF) ablation is a relatively new, minimally-invasive technique that has been widely used as an alternative to surgery or other local treatments in patients with bone metastasis from well-differentiated thyroid cancer as papillary and follicular thyroid carcinomas [8]. Therefore, we report our experience of the first case of bone metastasis of MTC treated with RF ablation with the aim to assess its feasibility and efficacy.

Materials and Methods

Patients

A 30-year-old woman with a sporadic MTC was treated in 2005 with total thyroidectomy and lymph node dissection of the neck and of the mediastinum. After surgical treatments, the serum calcitonin level decreased from a pre-operative value of 8314 pg/ml to 642 pg/ml; subsequent medical therapy with somatostatin analog (Octreoctide-Lar) was performed due to high levels of somatostatin receptor expression (SSR3 and SSR5) on mediastinal lymph nodes. At the beginning of 2007, somatostatin receptor scintigraphy with Indium-111 (111-In) pentetreotide and plasma biomarkers showed persistence of disease; therefore peptide receptor radionuclide therapy with Lutetium (177Lu) DOTATATE was administered. This treatment resulted in a short period

***Corresponding author:** Margherita Bartocci, Department of Radiological Sciences, AUSL of Umbria 1, Perugia, Italy; Tel: +393204062543; E-mail: margheritabartocci@libero.it

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of tumor stabilization. During subsequent follow-up, widespread metastatic disease was detected and metastatic lymph nodes of the neck were resected respectively in 2009 and in 2011. These surgical treatments resulted in another period of stabilized tumor progression. Between September 2011 and November 2012, medical therapy with somatostatin analog (Octreoctide-Lar) was suspended due to patient's pregnancy and baby's nursing. The stop of oncological therapy caused an increase of serum level of calcitonin, however without evidence of disease at imaging studies. In December 2013, Gallium-68 somatostatin receptor positron emission tomography - computed tomography (^{68}GaPET-CT) was performed and a focal uptake, attributable to metastasis of MTC, was discovered at the third right wing of the sacrum (Figure 1), for which RF ablation was proposed. An informed consent to treatment was obtained from the young woman before RF procedure, that was performed in September 2014.

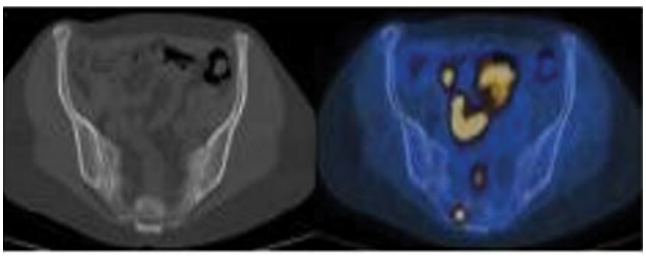

Figure 1: ^{68}Ga-PET-CT pre-RF ablation. Focal uptake at the third right wing of the sacrum, attributable to bone metastasis of MTC.

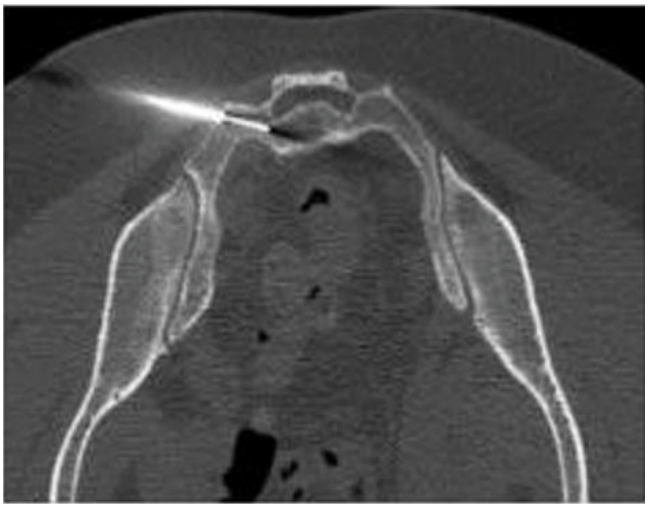

Figure 2: RF ablation CT-guided of bone metastasis of MTC.

Procedure description

After pharmacologic sedation the patient was positioned prone on computed tomography (CT) table (Brilliance CT 16-slice, Philips Medical Systems, Cleveland, USA) before CT-guided biopsy and RF ablation execution. Preliminary CT scan was performed focused on the sacrum and this radiological examination did not show any lesion, so the procedure was planned on the basis of ^{68}Ga PET-CT imaging findings. After preliminary scan, we planned the procedure in order to preserve the nerves while reaching the lesion and obtaining a good bioptic specimen.

Keeping all these aims in mind, we proceeded with a lateral-posterior approach. The sacral region involved was reached using a CT-guide. Two biopsy specimens were obtained from this region by means of a 20 gauge needle inside a 14 gauge external cannula (Bonopty Insertion Set, Radi MS, Uppsala, Sweden). Subsequently, we put in place the electrode (Cosman G4 four-electrode RF generator, Burlington, MA, USA), inside the same 14 gauge cannula used for biopsy. We chose a 15 mm active tip, bigger than the size of the lesion, to be sure to ablate all the pathologic tissue. We acquired a larger CT scan, covering all the lesion, to verify the correct placement of the needle.

Subsequently, RF was discharged initially to reach the first step of temperature (60°) for 2 minutes (in order to reduce, and possibly avoid, tissue carbonization) and then, to reach the treatment temperature (85°) which was maintained for 15 minutes (Figure 2). During RF ablation, we put ice on the lateral-posterior skin surface to prevent heating of the soft tissue. We hospitalized the patient for one night. Follow-up. After discharge, the patient entered a follow-up program that consisted of physical examination with biochemical tests and ^{68}Ga PET-CT. This was done to identify complications, local recurrence of the ablated bone metastasis and new lesions elsewhere. Plasma calcitonin levels (reference values < 15 pg/ml) were measured by chemiluminescence enzyme immunoassay (Sangui Biotech Inc., Santa Ana, CA) every 3 months. Biochemical response measurement was defined as follows: progressive response (an increase of 25% or more in the basal marker values), partial response (a decrease of 50% or more in the basal marker values), complete response (serum marker value below the cut off level) and stable disease (when all of the above were excluded). ^{68}Ga PET-CT (Biograph duo; Siemens Medical Solutions, Erlangen, Germany) was performed every year from December 2014. The response measurement was performed according to criteria defined by the European Organization for Research and Treatment of Cancer (EORTC) [9] as follows: progressive metabolic disease (> 25% increase in SUVmax in the target lesion or new lesions), stable disease (SUV max in the target lesion -15% until 25%), partial metabolic response (15% to 25% decrease in the target lesion) and complete metabolic response (no focal uptake in the target lesion). The follow-up stopped during 2015, when the patient decided to have another baby. After that the follow-up was resumed during 2016 till now days (December 2018).

Results

The treatment was well tolerated by the patient affected by biopsy-proven solitary bone metastasis and no acute or long-term complications were observed. The biochemical response showed partial response of disease, which a decreased of plasma calcitonin level from a pre-RF ablation value of 1900 pg/ml to 828 pg/ml, the latter measured in December 2018, in association with a complete metabolic response at ^{68}Ga PET-TC scan,that showed no focal uptake in the ablated area or elsewhere (Figure 3). Currently, 13 years after her initial diagnosis and 4 years after RF ablation of her bone metastasis, she has a reasonably good life quality which has allowed her to sustain two pregnancies during the desease.

Discussion

MTC is a rare form of thyroid cancer comprising approximately 4% of all thyroid cancers. Patients present a thyroid nodule with or without cervical lymphadenopathy, and frequently with distant metastases to the liver, lungs, and/or bone. Metastatic disease of MTC represent a trouble because C cells are a responder neither to metabolic radiotherapy with I-131 nor to classic chemotherapy.

Local therapies of metastases of MTC include external beam

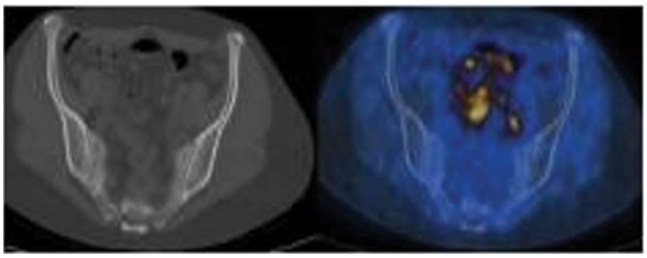

Figure 3: ^{68}Ga-PET-CT post RF ablation. Complete metabolic response of bone metastasis of treated with RF ablation.

radiotherapy and surgical excision, especially in symptomatic patients with bone metastases, but these procedures cannot be managed if the metastatic tumor involve vital structure. In recent years, systematic treatments have been tried to contain metastatic MTC, such as tyrosine kinase inhibitors, that may offer limited efficacy in bone metastatic disease, and receptor radionuclide therapy with 90YDOTATOC, that can enhance the survival but offer low response rate [6,10,11]. Therefore, there is no effective treatment for distant metastases and new therapeutic modalities are needed. RF ablation is an easy-to-perform and low-cost procedure which is less invasive than other options. Moreover, according to our knowledge, it can achieve resolution of primitive thyroid tumors, local recurrences and lymph node/lung/liver mestastases from well-or not well differentiated thyroid cancers [12-15]. However, the data showing its efficacy in treating bone metastases from thyroid cancers are less robust: in fact, according to our knowledge, in few clinical studies RF ablation - in combination with other procedures such as kyphoplasty, cementoplasty and osteoplasty - has been found to reduce pain in a small number of patients affected by skeletal metastases of well-differentiated thyroid cancer as papillary and follicular thyroid carcinomas [16-19], but RF ablation for solitary bone metastasis of MTC has been reported in no case to date.

Conclusion

In this study, we propose and demonstrate that a local bone metastasis of MTC can be treated safely and effectively with RF ablation without acute or long-term complications. Besides, in this first case, RF has killed the metastasis with a partial biochemical response and complete metabolic response and the quality of life of the patient has improved; this could be the first step to organize clinical trial with RF on MTC bone metastasis. We propose RF ablation as a new therapy for bone metastasis of MTC even if further studies are necessary to define its safely and efficacy and to determine the precise role that this therapy should play in the treatment of MTC bone metastasis.

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