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# RAI- REFRACTORY PAPILLARY THYROID CARCINOMA: ONE OF THE FIRST PATIENTS TO USE LENVATINIB IN THE COUNTRY, CASE REPORT

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Abstract: Introduction: Thyroid represents the most common tumor in women, approximately 10 to 20% of differentiated thyroid carcinomas (DTC) develop metastases, failure in treatment with iodine occurs in 50% of cases. The advent of Tyrosine Kinase Inhibitors (TKIs) has undergone a radical change in the pattern of treatment for DTC. Objectives: To report a case of Rai- refractory metastatic DTC, whose patient is one of the first to use lenvatinib in the country. Conclusions: With treatment, a patient under surveillance for metastatic diseases and multiple treatment line, exhibited response rates consistent with literary data, decreasing biochemical markers and manageable toxicity.

Keywords: Carcinoma, Thyroid, Toxicity.

# INTRODUCTION

The incidence of thyroid cancer is growing, it is estimated that in 2018 there were 9,610 new cases in Brazil, representing the fifth most frequent tumor in women, according to INCA data. Approximately 10 to 20% of patients with differentiated thyroid carcinoma (DTC) develop distant metastases and failure to treat with radioiodine therapy is a reality in at least half of these patients. [1,2,5] The advent of therapy with antityrosine kinases (TKIs) has led to a radical change in the standard of care of the disease with impressive and unprecedented clinical responses in DTC. [2-5]

# **GOALS**

To report a case of refractory metastatic DTC, whose patient is one of the first to use Lenvatinib in the country. Thus, it is intended to present the evolution of the case, management and other measures adopted.

# **CASE REPORT**

Patient, female, 60 years old, diagnosed

with papillary thyroid carcinoma (2009) who underwent total thyroidectomy, anatomopathological evidence showed solid papillary carcinoma, grade 2, (3.2 x 2.9 cm), vascular/capsular invasion, ATA moderate risk, BRAF mutated V600E, pT3bN1M1, treated with Iodotherapy and TSH suppression. Pulmonary and bone progression showed avidity retracted, after progression Iodine, the refractory iodine tumor, anti-algesic radiotherapy was instituted followed by TKIs Sorafenib, suspended for palmoplantar erythrodysesthesia. The exchange of TKIs for Vandetanib is poorly tolerated due to skin rashes and grade 3 colitis. In evolution, chemotherapeutic cytotoxicities manifested, use of bisphosphonates, treatment bone health. Fractionated stereotactic radiosurgery was performed due to brain metastasis (2017). Started using Lenvatinib (04/2019), staggered dose due to a history of tolerance to TKIs. Adaptation to the third adjustment/dose, grade 1 adverse events, consequent improvement in pain and quality of life. Restaging showed a decrease in the marker: Thyroglobulin, response of lung and bone lesions. Among the available treatment options, the patient has shown good adaptation, the need to control toxicities, with a high response rate.

# DISCUSSION

For patients with metastatic DTC that persist despite ARI, TSH-suppressing thyroid hormone therapy, and external radiation therapy, treatment options include observation, TKIs that primarily target angiogenesis, and traditional cytotoxic chemotherapy. [2-5]

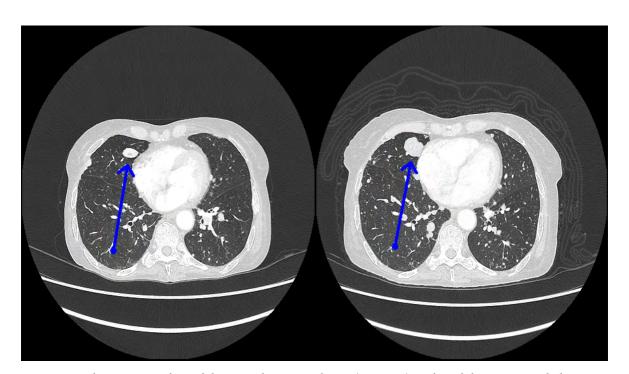


Figure 1: Chest tomography with lung window, in axial view (07/22/19), with nodular opacity with density of soft tissues with lobulated contours and defined limits, the largest of them located in the medial segment of the middle lobe, measuring about  $2.1 \times 1.1 \text{ cm}$  in its major axial axes with partial response compared to the previous examination of  $2.6 \times 2.1 \text{ cm}$  performed on 11/08/18, related to secondary neoplastic implants.

Direct comparisons between TKIs were not performed and the various studies recruited patients with different eligibility criteria. Selection of which agent to use for initial treatment must prioritize a somewhat subjective rating of drug efficacy and adverse events. [1,3,4]

There is a predilection for lenvatinib as a first-line therapy because of its efficacy. Patients who progress or are intolerant to one kinase inhibitor may benefit from treatment with another. Although cross-resistance has not been reported, the probability of response is likely to be slightly lower with each successive regimen. [1-5]

Targeted therapy with lenvatinib has significant toxicities such as diarrhea, fatigue, anorexia, hypertension, and proteinuria, similar to other TKIs.

The typical starting dose is 24 mg orally once daily, although lower doses may be better tolerated. [2-5]

A comprehensive and standardized approach to the assessment of adverse events during therapy, including limited drug interruptions and dose modifications, is highly recommended, carefully observing the balance of continued antitumor efficacy and reduced toxicity. [2-5]

A pivotal phase III clinical trial of the drug use demonstrated a median progression-free survival of 18.3 months and a significantly better 64.8% response rate in the lenvatinib group. A similar response was observed in patients previously treated with other TKIs, indicating benefit despite previous therapy. [2-5]

This treatment was approved by the FDA in 2015 and recently by the Brazilian regulatory body, so there are few cases using this therapy, but, as shown in this patient, lenvatinib is a promising treatment in AKI-refractory metastatic papillary thyroid carcinoma.

# **CONCLUSIONS**

With treatment, a patient with extremely adverse prognostic factors, prolonged survival over 10 years in the presence of metastatic disease and polytreated with four lines of systemic treatment including two TKIs and with low class tolerance, presented a promising perspective with a response rate that is in agreement with literature data, in addition to a significant decrease in biochemical markers, with manageable toxicity.

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