



# Thyroglobulin in Pleural Effusion in Metastatic Papillary Thyroid Cancer

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## Case Report

Volume 5 Issue 1

Received Date: August 25, 2021

Published Date: August 30, 2021

DOI: 10.23880/oaje-16000156

## Abstract

We report case of massive pleural effusion caused by papillary thyroid cancer, which was accompanied by multiple pulmonary metastasis. A 60-year-old female patient presented with shortness of breath and cough due to massive left pleural fluid. Since cytological and cytochemical studies were not conclusive for the primary tumor, and the measurement of thyroglobulin washout has been recommended as a complementary study in suspicious cervical lymph nodes, we performed it using the cut-off points used in cervical lymph nodes.

**Keywords:** Papillary Thyroid Cancer; Massive Pleural Effusion; Thyroglobulin Washout

## Introduction

Papillary thyroid cancer (PTC) is the most common malignant neoplasm of the thyroid [1], it has an excellent prognosis and a 10-year survival of 95% [1,2]. Most PTCs are indolent and do not recur nor metastasize after resection and treatment with radioiodine, even in the presence of metastases in cervical lymph nodes. At the time of diagnosis, lymphatic metastases can be found in 50-60% of cases and distant metastases in 7-23% [3], being the most frequent sites lung where it manifests as multiple small bilateral nodules [4], and bone. In rare cases, it can metastasize to the pleura and manifest as a malignant pleural effusion (MPE), and it portend a poor prognosis [1]. The physical characteristics of MPEs do not allow distinguishing between PTC and other malignant causes since they usually correspond to exudates. Cytology is important for differential diagnosis as well as immunohistochemistry and immunostaining, which is positive only in differentiated thyroid cancer (DTC) [5,6].

## Objective

Report a case of the use of thyroglobulin measurement

in aspiration needle washout (TgW) in pleural effusion in metastatic PTC.

## Clinical Case

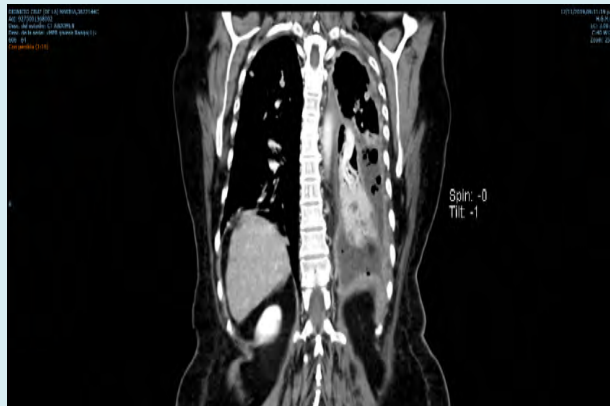
60-year-old female who underwent total thyroidectomy plus lateral neck dissection for PTC in July 2019, reporting classic variant of papillary carcinoma (multifocal tumor, size: 6x4x2 cm, extrathyroid extension: present, lymphovascular invasion: present, 23 lymph nodes were dissected with the presence of neoplastic cells in 14); ATA [7] high risk, AJCC [8] stage IV A; undergoing treatment with levothyroxine sodium 100 mcg/ daily and calcium and calcitriol supplements for postsurgical hypoparathyroidism. Iodine 131 ablation was indicated according to the NCCN guidelines [9], but it was pending at the time of her hospitalization. She was admitted by the pneumology service in October 2019 due to shortness of breath and cough of 2 weeks of evolution. On physical examination with hypoventilation, dullness and decreased vocal vibrations in the left lung field. Chest X-ray: left pleural effusion of approximately 70% (Figure 1), for which an endopleural tube was placed. Chest CT scan revealed a left pleural effusion, with multiple nodules in the right lung and

mediastinum (Figure 2). Blood test: TSH 55.46 mIU/ml, FT3 2.19 pg/ml, FT4 0.43 ng/dl, Tg 4955.36 ng/ml, Tg Ab 0 IU / ml. Hormonal replacement with levothyroxine sodium was adjusted to 175 mcg/ daily. Pleural fluid studies: TgW>

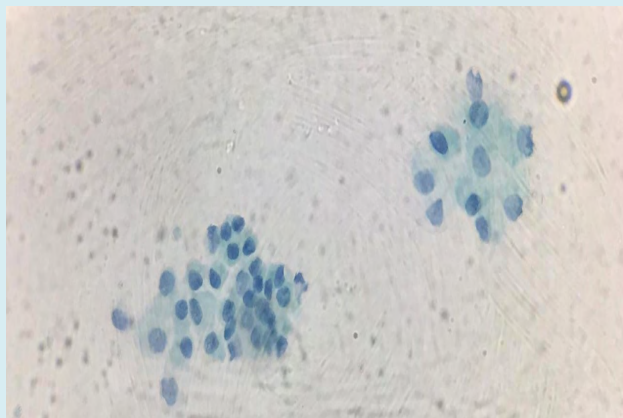
24450 ng/ ml, cytochemistry compatible with exudate and cytological positive for malignant cells, without specifying details of cellularity (Figure 3).



**Figure 1:** Chest X-ray: left pleural effusion of approximately 70%.



**Figure 2:** Chest CT scan revealed a left pleural effusion, with multiple nodules in the right lung and mediastinum.



**Figure 3:** Cytochemistry compatible with exudate and cytological positive for malignant cells, without specifying details of cellularity.

## Discussion

The main causes of MPE are metastatic lung carcinoma, breast cancer, ovarian cancer, cancer of the upper digestive tract, mesothelioma and lymphoma [1,6]. PTC is only responsible in <0.6% (50 cases reported) [5,6], its diagnosis represents advanced systemic disease with low survival rate (<10 months) and poor quality of life. MPE's physical characteristics do not allow distinguishing between malignant causes. The differential diagnosis of PTC and other causes of MPE depends on the presentation of all the typical cytomorphological characteristics of DTC, which are usually not appreciated if the cause of the metastasis to the pleura is a poorly differentiated or anaplastic thyroid cancer [5]; and the use of auxiliary studies (TTF-1, PAX8, napsin- 2 and thyroglobulin) [1,5,6].

TgW in lymph nodes was proposed since the cytopathological diagnoses of these may be inadequate or inconclusive [10]; even the ATA [7], ETA [11] and AACE [12] guidelines have recognized its importance and recommend including it in the complementary evaluation with fine-needle aspiration biopsy of the suspicious cervical lymph nodes [10]. TgW offers the advantage that, even if epithelial cells are not found in the aspirate, Tg may be elevated both inside and outside the lesion. A Tg value greater than 10 ng/ml has been taken as highly indicative of disease [10,13]. To date, the use of TgW has only been described in lymph nodes [10,13]. The cytochemical and cytological studies in our case were not definitive for PTC. Considering that no complementary immunocytochemical studies were made, we performed a TgW of the pleural fluid using the same cut-off values for the interpretation described for the measurements for TgW of lymph node, since there is no cut-off values described for pleural fluid, considering the value obtained in this case with a positive result as compared to those applied for cervical lymph nodes. Leaving no doubt metastatic involvement related to the primary tumor and demonstrating that, given its measurement is readily available, it can be used for the complementary evaluation in patients with history of DTC who have suspected tumor activity, however, it will be necessary to work in the establishment of cut-off values for its best interpretation.

## Conclusion

TgW is a useful tool for the diagnosis of lymph node metastatic disease in PTC, which can also be applied for the evaluation of the presence of metastatic activity in other organs or tissues.

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