# Clonal Origins of Concurrent Papillary Thyroid Carcinoma in Thyroglossal Duct Cyst and Thyroid: A Case Report

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## Introduction

Thyroglossal duct cysts (TGDC) are the most common congenital neck abnormality with an incidence of approximately 7%. Papillary thyroid carcinoma (PTC) is the most common form of thyroid cancer, accounting for almost 90% of all thyroid cancer cases in the United States. PTC can commonly present multifocally within the gland, leading to much debate within the oncologic community regarding the clonal origin of multifocal PTC and its impact, if any, on prognosis and treatment [1-2]. Tumors of single clonal origin and bilateral gland involvement may have a worse prognosis than their polyclonal counterparts [2]. While PTC has been reported to occur concurrently within the thyroid and TDC, there is a paucity of data on the clonal origins of these concurrent lesions. We describe a case of a patient with concurrent thyroid and TGDC PTC with genetic analysis of each.

## Case Presentation

A 72-year-old male with a familial history of goiter and thyroid cancer of unknown type presented to an outside hospital for an enlarging central neck mass. Initial workup included an unremarkable thyroid panel and thyroid ultrasound (US) showing normal-sized thyroid with three nodules: two hypoechoic nodules on the left measuring 6 and 7 mm and one solid lobulated nodule on the right measuring 1.6 x 1.0 x 1.6 cm, TiRads 5, with fine needle aspiration (FNA) recommended. FNA of the right-sided nodule showed papillary thyroid cancer (PTC). US of the neck revealed a 2.5 x 2.0 x 3.3 cm hypoechoic mass at the level of the hyoid bone, consistent with thyroglossal duct cyst. He underwent total thyroidectomy and excision of the central upper neck mass via Sistrunk procedure. Intraoperatively, suspicious nodes were identified and removed between the thyroid isthmus and the TGDC. Final pathology returned revealing intraglandular multifocal PTC, classic type, with vascular and lymphatic invasion, negative margins, and 3/3 lymph node involvement in neck level VI (Figure 1A). Pathology of the central neck mass confirmed it to be a TGDC, which was also found to have multifocal involvement by PTC (Figure 1B). Both the thyroid gland and thyroglossal duct cyst samples underwent gene sequencing via the OncoSTv2 panel to evaluate the clonal origin and pathogenicity of the samples. The patient underwent radioactive iodine remnant ablation and is currently in surveillance, without evidence of disease.

## References

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## Pathology and Gene Sequencing

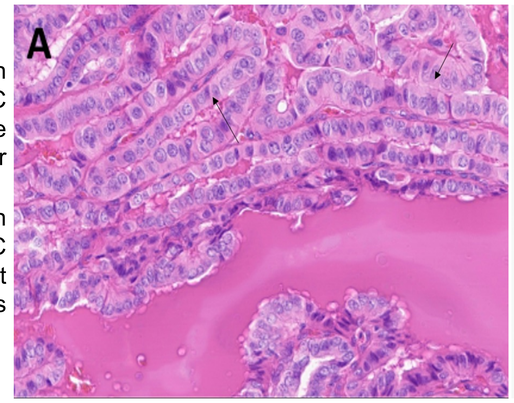


**Figure 1A:** Hematoxylin and Eosin staining revealing classic type PTC at 40x magnification. Arrows indicate nuclear enlargement with nuclear membrane irregularity and grooves.

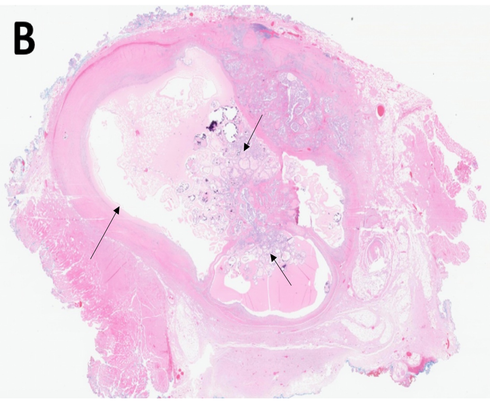


**Figure 1B:** Hematoxylin and Eosin staining revealing multifocal PTC involvement within TGDC with cyst wall at 10x magnification. Arrows denote cyst wall and foci of PTC.

| | Gene | Protein Variant | Transcript Variant | Pathogenicity | Translation Impact | genomAD Frequency |
|---|---|---|---|---|---|---|
| TGDC | BRAF | p.V600E | c.1799T>A | Pathogenic | missense | 0 |
| | FANCD2 | p.D690E | c.2070C>G | Uncertain Significance | missense | 0.001 |
| | ATR | p.S1142G | c.3424A>G | Uncertain Significance | missense | 0.057 |
| Thyroid | BRAF | p.V600E | c.1799T>A | Pathogenic | missense | 0 |
| | FANCD2 | p.D690E | c.2070C>G | Uncertain Significance | missense | 0.001 |
| | ATR | p.S1142G | c.3424A>G | Uncertain Significance | missense | 0.057 |

**Table 1.** OncoSTv2 gene panel of thyroid and TGDC specimens. Identical gene presence and variation, consistent with monoclonal origin. Note: PCTH1, ATM, POLE, PALB2, and NF1 were also tested and showed benign pathogenicity and identical gene presence and variation.

## Discussion

Given the prevalence of multifocal thyroid disease, genetic analysis has become of great interest in the evaluation of the disease and its management, as it has been linked to worse patient outcomes. [3-4]. In our case, genetic analysis found that the patient's TGDC and thyroid gland lesions harbored identical mutations for common oncogenic genes, increasing the likelihood that both thyroid and TGDC PTC were of the same clonal origin. The results suggest either concurrent onset in these disparate sites, or alternately but less likely, lymphatic spread from thyroid to the TGDC. Oftentimes, intrathyroidal, lymph node, and surrounding structure metastases originate from one clone rather than multiple mutations and are thought to lead to worse outcomes. Bilateral gland involvement usually indicates a more aggressive disease and increased likelihood of extra-glandular and nodal metastasis, though there is still much debate regarding this topic [1-2, 5]. A prior study comparing unifocal to multifocal PTC with BRAF+ carcinoma, found that multifocal PTC had different mRNA expression compared to unifocal cancer, specifically from the Wnt pathway, implying more aggressive cancer and increased metastatic potential [6]. Our patient had BRAF+ PTC, but the genetic analysis did not identify pathogenic gene mutations known to be associated with the Wnt, such as NF1 and PALB2, that could contribute to his metastatic potential (Table 1) [8-9]. Additional testing looking more closely at associated Wnt pathway genes such as AXIN1, APC, CTNNB1 could provide better insight into the patient's disease prognosis [7-8]. Aspects of this patient's presentation, including unilateral presentation and lack of Wnt mutation, suggest better disease prognosis, however more prolonged follow up is needed.