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Original Article

# PAPILLARY THYROID CARCINOMA IN THYROGLOSSAL DUCT CYSTS: CASE SERIES WITH LONG-TERM FOLLOW-UP AND REVIEW OF THE LITERATURE

# CARCINOMA PAPILAR DE TIROIDES EN QUISTES DEL CONDUCTO TIROGLOSO: SERIE DE CASOS CON SEGUIMIENTO A LARGO PLAZO Y REVISIÓN DE LA LITERATURA

Gabriel Sánchez[1], Aníbal Ariza[2], Sebastián Sánchez[2], Tania Yartiza Carrero Barragán[3], Cristian Camilo Ochoa Murillo[4], Luis Felipe Cabrera-Vargas[5,6], Ivan David Lozada-Martínez[6,7]

[1]Head and Neck Surgery Department, Hospital Universitario San Ignacio, Bogotá, Colombia
[2]Department of General Surgery, Hospital Universitario San Ignacio, Bogotá, Colombia
[3]Department of Medicine, Universidad Industrial de Santander, Bucaramanga, Colombia
[4]Department of Medicine, Universidad de Santander, Bucaramanga, Colombia
[5]Department of Surgery, Universidad El Bosque, Bogotá, Colombia
[6]Medical and Surgical Research Center, Future Surgeons Chapter, Colombian Surgery Association, Bogotá, Colombia
[7]International Coalition on Surgical Research, Universidad Nacional Autónoma de Nicaragua, Managua, Nicaragua

[*]**Correspondence Author:**
Ivan David Lozada-Martinez.
Medical and Surgical Research Center, Future Surgeons Chapter, Colombian Surgery Association, Bogotá, Colombia.
Email: ilozadam@unicartagena.edu.co

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**Abstract**

Abnormal embryological development of the thyroid can lead to the presence of remnants of the gland along the thyroglossal duct; of these lesions less than 1% are malignant. A case series study is presented, which evaluated 3 patients who underwent resection of thyroglossal duct cysts. in which histopathological findings compatible with differentiated thyroid cancer were documented with satisfactory results and a critical review of the literature available online. Thyroglossal duct cyst carcinoma is a very rare entity that requires a high degree of suspicion on the part of the surgeon to make a timely diagnosis. Thyroid ultrasound and fine needle aspiration biopsy play a key role in diagnosis; and the treatment of choice is the modified Sistrunk procedure and oncological thyroidectomy according to the specific characteristics of our population.

**Resumen**

El desarrollo embriológico anómalo de la tiroides puede llevar a la presencia de remanentes de la glándula a lo largo del conducto tirogloso; de estas lesiones menos del 1 % son malignas. Se presenta un estudio de serie de casos, que evaluó 3 pacientes llevados a resección de quistes del conducto tirogloso en los cuales se documentaron hallazgos histopatológicos compatibles con cáncer diferenciado de tiroides con resultados clínicos satisfactorios y una revisión crítica de la literatura. El carcinoma en el quiste del conducto tirogloso es una entidad muy poco frecuente que requiere un alto grado de sospecha por parte del cirujano para hacer el diagnóstico oportuno. La ecografía de tiroides y la biopsia por aspiración con aguja fina juegan un papel fundamental para el diagnóstico; y el tratamiento de elección es el procedimiento de *Sistrunk* modificado y tiroidectomía oncológica.

**Keywords**: Papillary Thyroid Cancer, Thyroglossal Tract Cyst, Head and Neck Neoplasms, Case Reports, Colombia.

## Introducción

Abnormal embryological development of the thyroid can lead to the presence of remnants of the gland along the thyroglossal duct [1-3]; in fact, the most frequent congenital anomaly in the neck is the neck duct cyst. Of these lesions, less than 1% are malignant. [4-8]. The first report of thyroglossal duct carcinoma was published more than 100 years ago [9]. It is an entity with a low incidence that requires a high degree of suspicion on the part of the surgeon for its diagnosis and timely treatment. In addition, there are great controversies regarding certain recommendations on its approach [9].

Surgically managed oncologic diseases remain a challenge today, due to barriers to access to specialized surgical services and early initiation of adjuvant therapy [10,11]. In addition, they continue to generate a high burden of disease and costs in health systems globally [12]. Among the objectives of global surgery is the progress in the management and description of situations that help to improve health indicators [10].

Considering that this condition presents a varied behavior, the objective of this study was to share the experience and outcome obtained in the management of 3 cases of papillary thyroid carcinoma in thyroglossal duct cyst in Colombia. This case report followed the CARE guidelines for its realization [13].

## Methods

Case series study evaluating 3 patients who underwent resection of thyroglossal duct cysts in a high complexity hospital in Bogotá, Colombia; histo-

pathological findings compatible with differentiated thyroid cancer were documented with favorable results. Additionally, a literature search was performed using search terms such as "Thyroglossal Duct Cyst", and "Cancer", as well as synonyms, which were combined with the Boolean operators "AND" and "OR", in the search engines and databases PubMed databases. As inclusion criteria, we defined any article related to thyroglossal duct cysts and thyroid cancer, giving priority to original studies and systematic reviews and meta-analyses. In addition, they had to be available in full text. As non-inclusion criteria, it was established that articles published in a language other than Spanish and English would not be included. Considering the breadth of the topic and the great variety of publications, articles published between 1994 and 2022 were included. A total of 15 articles were obtained from the search, of which 10 were identified as meeting the inclusion criteria and the review was completed with classic articles on the topic in question.

## Case series

### Case 1

53 year old male, who was attended by the department of head and neck surgery, for resection of thyroid cyst and thyroglossal duct with preservation of the hyoid (2002). Total thyroidectomy and central emptying was performed. The anatomopathological report reported multicentric papillary carcinoma smaller than 1 cm with involvement in the thyroglossal duct cyst and on the right side associated with chronic thyroiditis. No positive nodes for malignancy were found. He received ablative therapy with I-131 150 mCi. Post-therapy scan showed central remnant on ablation. When evaluating tumor markers at 4,8seriesCase,12 and 16 years of follow-up, thyroglobulin values (<1.5 ng/ml) and negative antithyroglobulin antibodies were founds (< 50 UI/ml). The last control was performed in 2020, with no evidence of loco-regional recurrence (total follow-up: 18 years and 2 months).

### Case 2

39 year old woman who was referred to the department of head and neck surgery for resection of thyroglossal cyst in March 2006, with final diagnosis of papillary carcinoma of 3 mm in the right lobe of the thyroid. Total thyroidectomy was performed. Due to tumor persistence in the left hemicollar, modified radical emptying was performed 2 months later. Histopathological examination showed 2 positive lymph nodes for papillary carcinoma metastasis. The patient received therapy with I-131; 173 mCi and the scan showed central remnant in ablation. The last control was in October 2011, without evidence of loco-regional recurrence, with negative thyroglobulin values (1.2 ng/ml) and antithyroglobulin antibodies (0.3 IU/ml) (total follow-up: 5 years and 7 months).

### Case 3

40 year old man referred to the department of head and neck surgery for thyroglossal duct and cyst resection in September 2010 with preservation of the hyoid bone. At the time of surgery, the definitive diagnosis was classic papillary carcinoma of 2 cm. Oncologic thyroidectomy (total thyroidectomy plus central emptying) was performed, where papillary carcinoma of 1 mm was observed in the left lobe and 1 positive node for metastatic papillary carcinoma. The last control was in 2012, with no evidence of loco-regional recurrence. Until this last time, thyroglobulin values (0.2 ng/ml) and antithyroglobulin antibodies (25 IU/ml) were negative (total follow-up: 20 months)

## Discussion and literature review

### Embryological concepts of thyroglossal duct cyst formation

During the fourth week of life in utero, the thyroid sketch develops from the endoderm of the floor of the primitive pharynx. This tissue migrates in cephalocaudal direction through the so-called thyroglossal duct until it reaches its definitive anatomical position around the seventh week of pregnancy [3,4,8,14,15].

Subsequently, from the IV branchial arch onwards, neuroendodermal cells ventralize and differentiate to become C or parafollicular cells. Once the gland has developed, the remaining duct tissue regresses and atrophies during the eighth to tenth weeks; however, in some scenarios, remnants of the gland may condition the presence of cysts along the thyroglossal duct. Some growth factors related to abnormal migration of the thyroid gland have been identified as follows TITF1/NKX2-1, FOXE1, PAX8 y HHEX [5,7,14,16,17,18).

## Epidemiologic aspects of thyroglossal duct cyst and associated cancer

Cysts of the thyroglossal duct are the most frequent congenital lesion of the neck with an incidence of 0.7 to 7% [4,5,9,14,19]. The incidence of these benign lesions is equal for men and women. This does not occur with carcinoma in thyroglossal duct cysts, which are more frequent in women than in men with a ratio of 2:1 [4]. Thyroglossal duct carcinoma represents less than 1% of all cysts, as described in 1994 by Van Vuuren et al [4], in a study where out of a total of 413 patients with thyroglossal duct cysts, 2 patients (0.48%) had anatomopathological findings compatible with carcinoma [4].

It is an entity that is most frequently diagnosed in the second and third decades of life [19]. However, only 57 cases in patients younger than 21 years of age and about 250 cases in patients between 8 to 86 years of age had been described in the world medical literature as of 2017 [4]. Thompson et al [19] in 2017 in an observational study describes cases in 2 patients aged 12 and 16 years with finding of papillary thyroid carcinoma documented in thyroglossal duct cysts. [19].

Now, regarding the behavior of thyroid cancer in our population, a study published in 2014, describes the experience of a reference center in management of this gland, in Bogota, Colombia, with a total of 501 patients of which 93.6% corresponded to differentiated carcinoma which in 24.5% of cases presents aggressive histological variants, with multiple foci in 53.7% and bilaterality in 31.7% of cases [20,21]

## Clinical manifestations

Patients may present totally asymptomatic and during routine physical examination a cervical midline mass is identified, which is often non-painful, soft, infra hyoid, and may or may not rise with tongue prolapse or swallowing [4,9,20]. In some cases it may present as a painful mass (1.85% of cases) and dysphagia (3.1% of cases) [6].

Thyroglossal duct cysts are usually located in one of the following locations: intralingual, suprahyoid, thyrohyoid, and suprasternal [7,22]. 70 to 90% of cysts are located in the midline between the base of the tongue and the body of the hyoid bone; 30% of cysts are in close relation to, and posterior to, the hyoid bone [5,22].

## Diagnostic

A high degree of suspicion on the part of the surgeon is required to reach the diagnosis [4]. In addition to physical examination findings, imaging studies are imperative; the role of thyroid ultrasound is fundamental [22-24]. Unfortunately to our knowledge, to date, there are no clinical studies with statistical relevance comparing the different paraclinical studies for the diagnosis of thyroglossal duct cancer. However, data from studies useful in differentiated thyroid carcinoma such as scintigraphy, ultrasonography, computed tomography, magnetic resonance imaging and fine needle aspiration (with a described positive predictive value of 69%) are often extrapolated [4,6,7,18,23].

Some authors give greater prominence to fine needle aspiration, an example of this is the study by Choi et al [24], where they report a series of 10 patients diagnosed with thyroglossal duct carcinoma; 9 of which were diagnosed with cytology [24]. Despite advances in diagnostic imaging and immunohistochemistry, most thyroglossal duct cancers are diagnosed as histopathological findings in the postoperative period following resection of thyroglossal duct cysts [6,14,16,22].

## Histological and histopathological findings

Histologically, the cysts are lined with a flat squamous or columnar pseudostratified epithelium with inclusions of thyroid glandular tissue with follicular cells. Their contents may be mucoid, gelatinous or purulent [22]. 79.9% to 92.1% of thyroglossal duct carcinomas are of the papillary carcinoma type, 9.5% poorly differentiated carcinomas, 5.1% squamous cell carcinomas, 2.5% epidermoid carcinomas, 0.6% anaplastic carcinomas and 0.6% Hurtle cell carcinomas [4,5,6,14,16,18,23]. 8.1% of these lesions have capsule invasion involvement, 14.6% adjacent

soft tissue invasion, 1.3 to 2% distant metastasis and 7 to 15% lymph node involvement [4].

Patients with cancer in thyroglossal duct cysts, according to the literature consulted, have thyroid microcarcinomas in 4.4 to 62% of cases. A fairly wide range for such a relevant aspect when defining surgical management [4,5].

## Therapeutic considerations

Cysts have traditionally been considered as a benign entity whose treatment is based on surgical resection in order to reduce the risk of superinfection and malignancy [19]. Resection often involves osteotomy of the central portion of the hyoid bone since non-resection is associated with recurrence in up to 50% of cases, while performing a regular Sistrunk procedure is associated with a recurrence of only 4% [9,17,22]. In Contrast to this, Sanchez et al [21] in 2014 publish the results of a cohort of patients taken to a modification of the Sistrunk technique with preservation of the hyoid taking into account patients operated between the years 2003 and 2012 (N=42), with a median follow-up at 11 months with a recurrence in 1 patient (2.4%) and without the functional and aesthetic sequelae of hyoid osteotomy [21].

The Sistrunk technique was described more than 100 years ago, and involves a median transverse cervicotomy, release of the supra- and infra-hyoid prethyroid muscles, resection of the medial portion of the hyoid bone and resection of the remnants of the thyroglossal duct [4,6,19,22] (Figure 1-2). The Sistrunk procedure modified by Sanchez et al [21] involves a two to three cm transverse cervicotomy, equidistant between the body of the hyoid and the thyroid notch, carving myocutaneous flaps down to the suprahyoid area and the thyroid isthmus, division of the prethyroid muscles along the midline, disinserting the infrahyoid muscles until adequate exposure of the body of the hyoid, the thyroid, the cyst and the remnant of the thyroglossal duct which is resected to the thyroid isthmus [21].

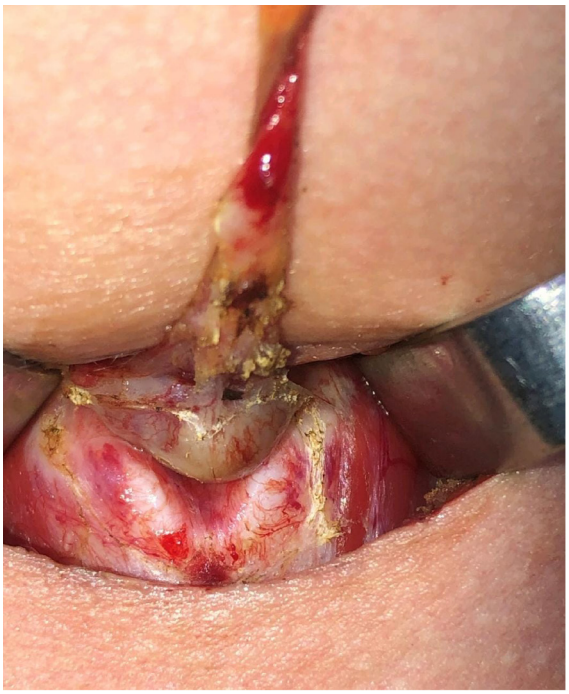

*Figura 1. Intraoperative image of thyroglossal cyst insitu.*

Given that the diagnosis in most cases is made postoperatively, some authors recommend that in the case of thyroglossal duct cyst resection, wide margins should always be given [4]. Authors such as Sturniolo et al [5] recommend cyst resection always accompanied by oncologic thyroidectomy in patients with preoperative diagnosis of cancer in thyroglossal duct cysts and in patients with intraoperative findings suggestive of malignancy [5]. This becomes even more relevant when taking into account the high incidence of multifocality, bilaterality and the presence of aggressive histological variants in our population as described by Sanchez et al [21].

The performance of thyroidectomy during the same surgical moment is of great controversy [14]. Some authors advocate its performance in patients with high surgical risk, older than 45 years, with tumors larger than 4 cm dependent on thyroglossal duct cysts with extension to soft tissues, and evidence of regional or distant metastases [22,23]. Because of the behavior of thyroid cancer in our population, the authors recommend resection of the cyst, thyroglossal duct and oncologic thyroidectomy during the same surgical time [21].

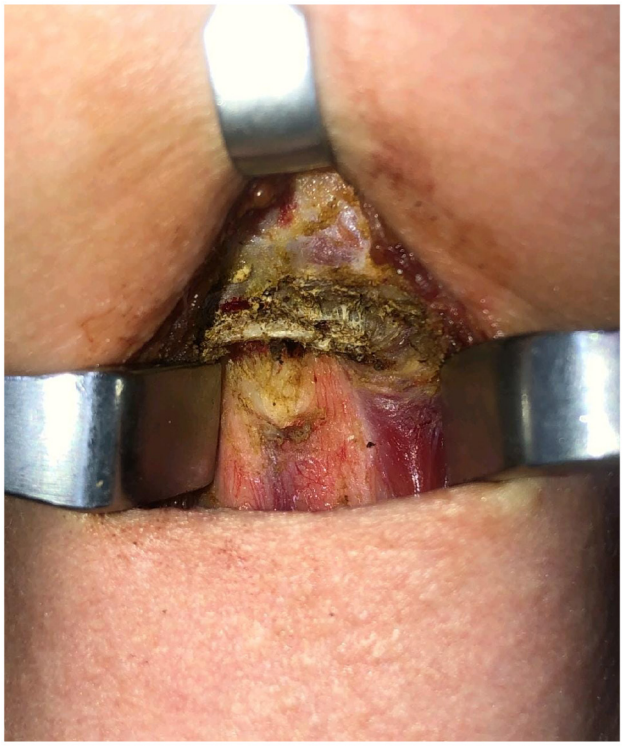

*Figura 2. Complete resection of thyroglossal cyst.*

There are three main reasons for performing thyroidectomy; first, according to the data consulted, the thyroid gland is compromised by tumor in 33 to 45% of cases; second, surgical resection of the thyroid favors an adequate staging, radiometabolic treatment, and allows follow-up with biomarkers such as thyroglobulin and third in the Colombian population the incidence of multifocality, bilaterality and aggressive histological variants, are higher when compared to other populations [5,6,21].

In 2017, Rayess et al [6] presented the most recent systematic review on thyroglossal duct carcinomas; taking into account 98 articles published from 1986 to 2016, including 164 patients with a median age at diagnosis of 39.5 years. 68.3% of the patients were female. 95.1% were totally asymptomatic and the diagnosis was made as a postoperative anatomopathologic finding in 73.3% of the cases, 20.6% by fine needle aspiration and 6.1% by freeze biopsy, being papillary thyroid carcinoma the most usual type (92.1%) [6]. 98.9% of the patients were taken to Sistrunk procedure and 61% of them to total thyroidectomy during the same surgical time. Of the patients who underwent thyroidectomy, 23.4% had cancer in the resected thyroid. There was a recurrence of 4.3% at 3.5 years [6].

In patients with advanced neoplastic disease with nodal involvement, perinodal invasion and other histological risk factors for relapse, as well as positive tumor markers, radioiodine ablation therapy is indicated. Strict oncologic follow-up and hormonal suppression with levothyroxine in these patients is the same as recommended for differentiated thyroid carcinoma [6,8,16,18,19,24].

## Conclusion

Carcinoma in the thyroglossal duct cyst is a very rare entity that requires a high degree of suspicion on the part of the surgeon to make a timely diagnosis. Thyroid ultrasound and fine needle aspiration biopsy play a fundamental role in the diagnosis; however, in most cases the diagnosis is made postoperatively after surgical resection. It is clear that a negative thyroid ultrasound does not rule out the presence of microcarcinoma in the gland.

The procedure recommended by the authors is the modified Sistrunk technique, which has a low incidence of recurrence without the morbidity of hyoid osteotomy; oncologic thyroidectomy should be performed in selected cases, especially in our population where multifocality, bilaterality and incidence of aggressive histological variants is higher than in other populations. Postoperative follow-up should be strict and in accordance with international recommendations for thyroid cancer follow-up.

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