

Papillary carcinoma in thyroglossal duct cyst with uninvolved thyroid. Case report and review of the literature

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The thyroid gland in embryogenesis develops as the first pharyngeal derivative, primarily appearing as an invagination in the floor of the pharynx and then migrating caudally to the trachea. During embryogenic development, it remains attached to the tongue by the thyroglossal duct, which usually undergoes atrophy after birth. If it fails to involute, it can persist as a cyst, a duct, or ectopic tissue, which is localized in the midline between the base of the tongue and the pyramidal lobe of the thyroid gland [1].

A remnant of a thyroglossal duct, usually a cyst (TGDC), is the most common congenital abnormality of thyroid gland development. The ectopic thyroid tissue in TGDCs varied from 1.5% to 45% of cases [2]. Other frequent locations of thyroid ectopy are the tongue, larynx, trachea, esophagus, mediastinum, pericardium, diaphragm and neck branchial cyst [3].

Clinically, most thyroglossal duct cysts are benign and present as slow-growing, asymptomatic neck masses [2, 4]. It is estimated that they occur in 7% of the adult population [5]. However, most patients with TGDC are children and adolescents and only one-third of them are at a minimal age of 20 [6]. In some studies, the age of presentation ranged from 1 to 82 years with an average of 39 years [2, 7, 8].

Criteria for TGDC diagnosis were first published by Roses *et al.* [9]: the cyst must be located in the median region of the neck and be composed of cuboidal epithelial cells; both lymphatic tissue and normal thyroid follicles should be present in the cystic wall. The TGDCs are considered to be caused by mutations in genes such as the thyroid transcription factors TITF1, TITF2 and PAX8 responsible for the development of thyroid follicular cells [10].

It is claimed that ectopic thyroid tissue does not represent an increased risk of malignant transformation in comparison with the thyroid gland [11, 12].

The malignant neoplasm in the TGDC is a very rare tumor, which encouraged us to present the case of a papillary thyroid carcinoma, arising in the ectopic thyroid tissue in the TGDC, with a long follow-up period.

A 64-year-old man presenting a pre-laryngeal tumor that had been gradually increasing in size within a 4-month history was admitted to the Department of Otolaryngology in 1994 in order to be diagnosed and treated. The medical history included hypertension and diabetes

but the general condition of the patient was good. The patient had not been previously exposed to radiation or other known carcinogens. Also the family history was negative for thyroid or neoplastic disease. Neither blood and urine tests nor electrocardiogram and chest X-ray disclosed abnormalities.

Physical examination revealed a soft, painless, well-demarcated midline 4 cm × 5 cm tumor with a smooth surface. The mass was situated in the median region of the neck between hyoid bone and thyroid cartilage with unchanged skin over the lesion (Figure 1). The tumor was moveable superficially, but deeply attached to the larynx, and non-tender.

The thyroid gland was apparently normal in size and consistency and no associated cervical lymphadenopathy was found. An indirect laryngoscopy revealed the larynx to be of normal mobility with no abnormalities. Axial computed tomography (CT) revealed an irregular lesion in front of the hyoid bone, whereas the hyoid bone was not damaged (Figure 2). The neck ultrasonography indicated a cyst-like lesion. The fine-needle aspiration biopsy

revealed cyst-like liquid, and the presence of carcinomatous cells was not confirmed.

The patient was treated surgically; the Sistrunk procedure was performed, and the tumor was excised with margins of the normal tissue (Figure 3).

Histopathological examination revealed an inhomogeneous, poorly circumscribed tumor with an irregular surface, very difficult to detach, not attached to the hyoid bone. Microscopic images showed papillary cancerous focal infiltration of the wall of the thyroglossal duct remnant. The histopathological diagnosis was papillary carcinoma in thyroglossal duct cyst (Figure 4).

Paraffin-embedded tissue sections were stained with monoclonal antibodies raised against thyroglobulin (NCL-THY, clone 1D4, 1 : 50, Novocastra) and cytokeratin 19 (NCL-CK19, clone b170, 1 : 100, Novocastra) using a peroxidase labeled streptavidin-biotin kit in standard immunohistochemistry techniques. Cancer cells demonstrated immunopositivity for thyroglobulin (Figure 5) and for cytokeratin 19 (Figure 6).

There were no complications in the postoperative period. One month after the operation, in the

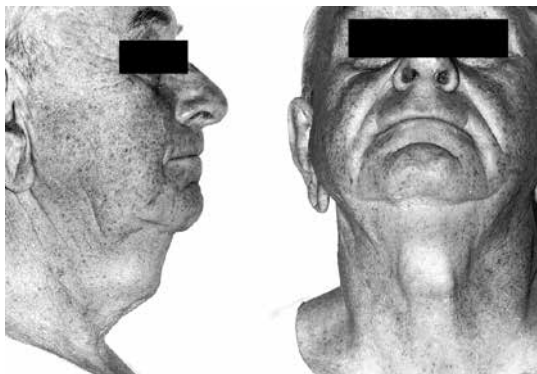


Figure 1. Patient before surgical procedure with the enlarging anterior midline neck mass



Figure 2. The CT scan showing polycyclic neck mass closely adjacent to laryngeal cartilages without infiltration



Figure 3. Tumor resected during Sistrunk's surgical procedure. A mass of 4 cm × 3 cm × 3 cm was removed including the entire duct from the thyroid gland to the level of the foramen cecum and the middle portion of the hyoid bone

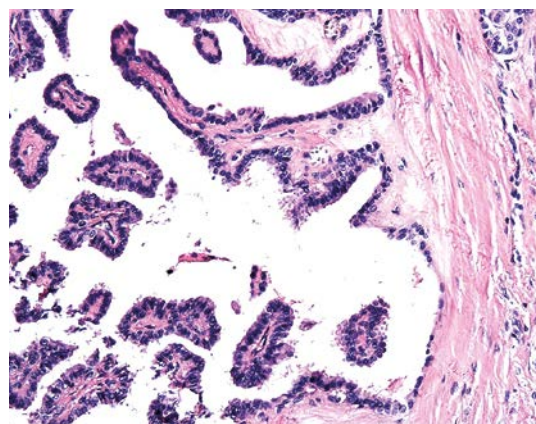


Figure 4. Papillary carcinoma within a thyroglossal duct cyst. Focal infiltration of the thyroglossal duct remnant is noted showing the fibrovascular core with the line of epithelial cells (hematoxylin and eosin staining, magnification 200×)

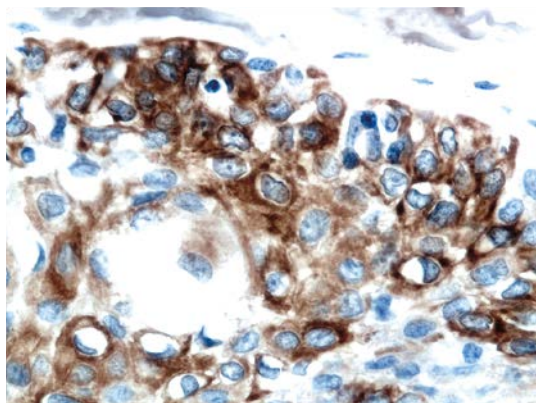


Figure 5. Diffuse cytoplasmic immunostaining for thyroglobulin in papillary carcinoma cells within thyroglossal duct cyst (immunohistochemistry technique, magnification 400×)

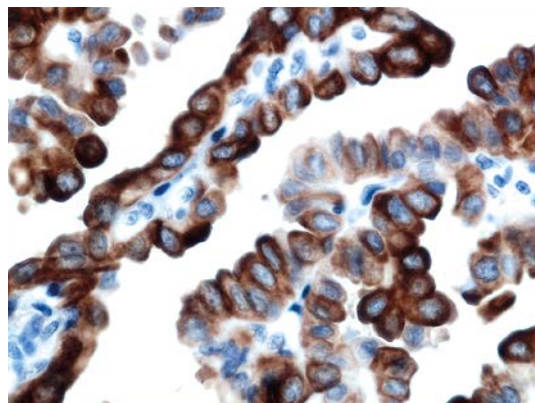


Figure 6. Immunostaining for cytokeratin 19 shows positive cytoplasmic reaction in most cells of papillary carcinoma in thyroglossal duct cyst (immunohistochemistry technique, magnification 400×)

control scintiscanning of the thyroid neither enlargement nor abnormalities were present in the gland. There were no focal lesions. The patient remained free of the disease at 16 years follow-up, which was performed by clinical and ultrasound examination.

Carcinoma arising in a TGDC is a very rare lesion, occurring in fewer than 1% of patients [8, 12]. Approximately 215 cases of malignant tumors in TGDC were reported up to 2002 [7] and only several since then, which indicates that malignancies of TGDC are extremely rare. Female to male predominance is noticeable [2, 4, 7, 13]. The most common histologic type is papillary carcinoma (80-95%), followed by mixed papillary-follicular carcinoma (8%) and squamous cell carcinoma (6%) [6, 12-17]. There are some characteristic histological hallmarks such as: formation of papillary structure; nuclear morphological variations such as ground glass nuclei, pseudo-inclusions, intranuclear grooves and filaments; and concentrically calcified structures named psammoma bodies that are regarded as strong indicators of papillary carcinoma. Moreover, immunopositivity for thyroglobulin, a glycosylated protein synthesized by follicular epithelial cells of the thyroid, which provides iodination sites for the formation of thyroid hormones, is also crucial for diagnosis (Figure 5).

Cytokeratin 19 reacts with the smallest human cytokeratin filaments and shows a heterogeneous staining pattern in non-keratinizing squamous epithelia and hair follicles with strong staining of the basal layer. In all cases of papillary carcinomas immunostaining for cytokeratin 19 was strongly positive in contrast to non-papillary carcinomas where immunohistochemistry revealed negative results. Therefore immunopositivity for cytokeratin 19 was a highly sensitive marker in the diagnosis for papillary thyroid carcinoma [18].

Other types of TGDC carcinoma, such as follicular, anaplastic, squamous cell carcinoma and

Hurtle cell carcinoma, are described rarely in the literature [16, 19-21]. It is very important to emphasize that papillary carcinoma is associated with genetic rearrangements, especially in thyroid transcription factors (TTF1, TTF2 and PAX8) and the gene for the thyroid-stimulating hormone receptor (TSHR). It is frequently a multifocal lesion [10]. The frequency of multifocal malignant papillary tumor ranges from 18 to 75% in the literature [9, 22].

Carcinoma of the TGDC should be suspected when the lesion is hard, fixed and irregular. However, as in the present case, often it imitates a benign lesion. It is worth noting that 80% of TGDC carcinomas are 2-5 cm in size [4].

There are some useful methods of carcinoma in TGDC diagnosis, but none of them is applied in all cases. The importance of CT and ⁹⁹Tc scans in thyroid diagnosis is underlined [11, 12]. However, they are advisable only in patients with either abnormal thyroid function tests or absence of the thyroid gland proper during ultrasonography [6, 23].

Some authors strongly recommend fine-needle aspiration biopsy (FNAB) as a safe, well-tolerated and cost-effective procedure in diagnosing thyroglossal duct lesions. It is believed that the procedure, when carried out correctly by an experienced specialist, is an important tool in the evaluation of thyroglossal duct lesions [5, 13]. Nevertheless, cytology smears are inconclusive in approximately 50% of the described cases. High cellularity, the presence of papillary formations and cells with enlarged nuclei with anisonucleosis and powdery chromatin with definitive nucleoli are supposed to be the major diagnostic criteria for papillary carcinoma, regardless of its location. Some authors claim that FNAB is especially recommended in head and neck lesions because of the possibility of being performed in an outpatient clinic as well as being repeated until an appropriate specimen is obtained [5, 6, 8, 13, 24].

Establishing what is the origin of TGDC carcinoma (primary ectopic or metastatic from thyroid gland proper) has an influence on treatment decision making. It was believed that in the presence of the thyroid gland proper, each malignancy of the ectopic tissue should be considered as a metastasis, whereas absence of orthotopic thyroid tissue indicated an obvious non-metastatic origin [25]. This imposed the necessity of thyroidectomy in cases of thyroid gland presence. However, Renard *et al.* [14] demonstrated that out of 43 patients with TGDC carcinoma, who underwent total thyroidectomy, the carcinoma in the thyroid gland proper was revealed only in 6 patients. Others were in agreement with this [4, 13]. Nevertheless, numerous doubts related to treatment methods have persisted till today. Currently, the performed methods include the Sistrunk procedure, near total thyroidectomy, total thyroidectomy, ¹³¹I ablation and thyroid suppression therapy. Some authors prefer treating thyroglossal duct carcinoma with a near total or total thyroidectomy and ¹³¹I ablation as the recurrence rate is the lowest [8, 17]. Others believe that the malignancy is primary and prefer removal of all thyroglossal duct remnants in cases of absence of the suspicion of thyroid malignancy followed by long-term observation due to the prolonged course of papillary thyroid carcinoma. In such cases total thyroidectomy for exclusion of metastases from the thyroid is unnecessary and the Sistrunk procedure is sufficient for recovery [7, 15, 26]. No recurrence was observed in a group of patients treated by the Sistrunk procedure [4, 27, 28], as in the present case. It has also been reported that total thyroidectomy following the Sistrunk procedure does not have a significant impact on the treatment outcome [29]. The controversy in the treatment encouraged Plaza *et al.* [8] to propose an algorithm for the management of TGDC and neoplasm in it. However, thyroid suppression therapy after the Sistrunk procedure in patients with low risk disease has probably no significant effect [6]. The present patient, who underwent the Sistrunk procedure without total thyroidectomy and for 16 years remained free of the disease, is a very good confirmation that routine thyroidectomy and the necessity of lifelong thyroxin supplementary therapy is unnecessary in low risk patients and can be a slight modification of the proposed algorithm and the significant findings of the presented review.

In conclusion, the prognosis of papillary carcinoma arising in TGDC is very good. The overall survival rate is 95.5% at 10 years. Moreover, carcinomas of the TGDC demonstrate lower frequency of regional lymph node metastasis in comparison with that arising in the thyroid gland proper [5, 6].

References

1. Organ GM, Organ CH Jr. Thyroid gland and surgery of the thyroglossal duct: exercise and applied embryology. *World J Surg* 2000; 24: 886-90.
2. Allard RH. The thyroglossal cyst. *Head Neck Surg* 1982; 5: 134-46.
3. Fumarola A, Trimboli P, Cavaliere R, et al. Thyroid papillary carcinoma arising in ectopic thyroid tissue within a neck branchial cyst. *World J Surg Oncol* 2006; 4: 24.
4. Naghavi SE, Jalali MM. Papillary carcinoma of thyroglossal duct cyst. *Med Sci Monit* 2003; 9: CS67-70.
5. Yang YJ, Haghiri S, Wanamaker JR, Powers CN. Diagnosis of papillary carcinoma in a thyroglossal duct cyst by fine-needle aspiration biopsy. *Arch Pathol Lab Med* 2000; 124: 139-42.
6. Ishay A, Elmalah I, Luboshitzky R. Papillary carcinoma in a thyroglossal duct cyst. *Isr Med Assoc J* 2008; 10: 312-3.
7. Chu YC, Han JY, Han HS, Kim JM, Min SK, Kim YM. Primary papillary carcinoma arising in a thyroglossal duct cyst. *Yonsei Med J* 2002; 43: 381-4.
8. Plaza CP, López ME, Carrasco CE, Meseguer LM, Peruchó Ade L. Management of well-differentiated thyroglossal remnant thyroid carcinoma: time to close the debate? Report of five new cases and proposal of a definitive algorithm for treatment. *Ann Surg Oncol* 2006; 13: 745-52.
9. Roses DF, Snively SL, Phelps RG, Cohen N, Blum M. Carcinoma of the thyroglossal duct. *Am J Surg* 1983; 145: 266-9.
10. Macchia PE. Recent advances in understanding the molecular basis of primary congenital hypothyroidism. *Mol Med Today* 2000; 6: 36-42.
11. Batsakis JG, El-Naggar AK, Luna MA. Thyroid gland ectopias. *Ann Otol Rhinol Laryngol* 1996; 105: 996-1000.
12. Pérez JS, Muñoz M, Naval L, Blasco A, Diaz FJ. Papillary carcinoma arising in lingual thyroid. *J Craniomaxillofac Surg* 2003; 31: 179-82.
13. Falconieri G, Della Libera D, Zanella M. Papillary thyroid carcinoma of the thyroglossal duct cyst: comparative cytohistologic and immunochemical study of 2 new cases and review of the literature. *Int J Surg Pathol* 2001; 9: 65-71.
14. Renard TH, Choucair RJ, Stevenson WD, Brooks WC, Poulos E. Carcinoma of the thyroglossal duct. *Surg Gynecol Obstet* 1990; 171: 305-8.
15. Weiss SD, Orlich CC. Primary papillary carcinoma of a thyroglossal duct cyst: report of a case and literature review. *Br J Surg* 1991; 78: 87-9.
16. Deshpande A, Bobhate SK. Squamous cell carcinoma in thyroglossal duct cyst. *J Laryngol Otol* 1995; 109: 1001-4.
17. Heshmati HM, Fatourehchi V, van Heerden JA, Hay ID, Goellner JR. Thyroglossal duct carcinoma: report of 12 cases. *Mayo Clin Proc* 1997; 72: 315-9.
18. Nga ME, Lim GS, Soh CH, Kumarasinghe MP. HBME-1 and CK19 are highly discriminatory in the cytological diagnosis of papillary thyroid carcinoma. *Diagn Cytopathol* 2008; 36: 550-6.
19. Woods RH, Saunders JR Jr, Pearlman S, Hirata RM, Jaques DA. Anaplastic carcinoma arising in a thyroglossal duct tract. *Otolaryngol Head Neck Surg* 1993; 109: 945-9.
20. Cote DN, Sturgis EM, Peterson T, Miller RH. Thyroglossal duct cyst carcinoma: an unusual case of Hürthle cell carcinoma. *Otolaryngol Head Neck Surg* 1995; 113: 153-6.
21. van Zuiden LJ, Machin GA, Mydland WE. Follicular carcinoma in a thyroglossal duct. *Can J Surg* 1979; 22: 590-2.

22. McConahey WM, Hay ID, Woolner LB, van Heerden JA, Taylor WF. Papillary thyroid cancer treated at the Mayo Clinic, 1946 through 1970: initial manifestations, pathologic findings, therapy, and outcome. *Mayo Clin Proc* 1986; 61: 978-96.
23. Kessler A, Eviatar E, Lapinsky J, Horne T, Shlamkovitch N, Segal S. Thyroglossal duct cyst: is thyroid scanning necessary in the preoperative evaluation? *Isr Med Assoc J* 2001; 3: 409-10.
24. Powers CN, Silverman JF, Geisinger KR, Frable WJ. Fine-needle aspiration biopsy of the mediastinum. A multi-institutional analysis. *Am J Clin Pathol* 1996; 105: 168-73.
25. Zink A, Raue F, Hoffmann R, Ziegler R. Papillary carcinoma in an ectopic thyroid. *Horm Res* 1991; 35: 86-8.
26. Kennedy TL, Whitaker M, Wadiah G. Thyroglossal duct carcinoma: a rational approach to management. *Laryngoscope* 1998; 108: 1154-8.
27. McNicoll MP, Hawkins DB, England K, Penny R, Maceri DR. Papillary carcinoma arising in a thyroglossal duct cyst. *Otolaryngol Head Neck Surg* 1988; 99: 50-4.
28. Soh EY, Clark OH. Surgical considerations and approach to thyroid cancer. *Endocrinol Metab Clin North Am* 1996; 25: 115-39.
29. Patel SG, Escrig M, Shaha AR, Singh B, Shah JP. Management of well-differentiated thyroid carcinoma presenting within a thyroglossal duct cyst. *J Surg Oncol* 2002; 79: 134-9.