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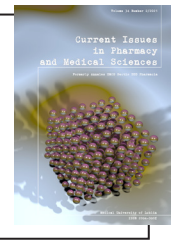

Thyroglossal duct cyst papillary thyroid cancer – the state of the art

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ABSTRACT

Thyroglossal duct cyst is one of the most common congenital malformations in the neck area. The majority of cysts turn out to be benign tumors, however, 0.7-1.5 % of the remnants develop into carcinoma, with papillary thyroid cancer being the most frequent malignant neoplasm. The origin of the cancer has not been clearly established so far. Typically, thyroglossal duct cyst cancer is an enlarging flexible midline or slightly lateral neck mass, most often without other worrisome symptoms. The proper diagnosis can be difficult due to the rare prevalence of thyroglossal duct cyst papillary thyroid carcinoma, as well as a lack of strongly typical features distinguishing benign and malignant lesions before surgery. Thus, diagnosis is usually made postoperatively just after histopathological examination of a resected cyst. However, there are diagnostic procedures that should be considered before the surgery that may be helpful in making a proper diagnosis. These include fine-needle aspiration biopsy, computed tomography or magnetic resonance imaging. Moreover, there are some characteristics revealed through clinical and ultrasound examination that may suggest the presence of such cancer. While the Sistrunk procedure is often considered adequate, currently, there is no clear consensus about concurrent thyroidectomy or radioiodine therapy. In the article, we sum up the preoperative suggestive factors of cancer, as well as the proposed indications that can be helpful in deciding on the extent of surgery and further management.

INTRODUCTION

Papillary thyroid carcinoma is a differentiated, epithelial malignancy. It is one of the most frequent thyroid neoplasm, accounting for 80-85% of all thyroid cancer cases and carrying the best overall prognosis. Based upon the Surveillance, Epidemiology, and End Results (SEER) database in 2012, the prevalence is estimated to be 14.9 per 100.000. It occurs predominantly in middle-aged adults, with a 3:1 female-to-male ratio. The median age at presentation is 50 years [1].

The thyroglossal duct (TD) arises at the time of thyroid gland formation [2]. During embryological development, the thyroid gland descends from a midline endodermal invagination of the foregut, at the level of the foramen cecum, along the TD (a structure originating from the foramen cecum of the tongue, passing through the base of the tongue towards the lower front part of the neck), inferior to the thyroid cartilage, where the thyroid is usually found in adults [3,4].

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TD usually involutes at 7-10 weeks gestation. The most common disorder of the thyroid dysgenesis is its failure to descend from the foramen cecum and the persistence of the thyroglossal duct. This persistence can lead to the formation of cysts (thyroglossal duct cyst; TDC), as well as the development of neoplasms within the mass, including thyroglossal duct cyst cancer (TDCC) [5].

The prevalence of TDC and TDCC

Thyroglossal duct cyst is one of the most common congenital malformations in the neck area. It is present in 7% of all adult patients. In children, TDCs account for 70-75% of all midline neck tumors. Ectopic thyroid tissue may be localized in the thyroglossal duct remnants (in over 50-65% of all cysts), and in 1% of all patients, this is the only functioning thyroid tissue in the body [2,3,6-9]. Most TDCs are benign tumors, however, 0.7-1.5% develop into carcinoma [10,11]. Since the first described case of TDCC in 1911, by Brentano, approximately 300 cases of such cancers have been reported so far. Due to the rarity of the thyroid cancer development

within the TDC, it is difficult to calculate the frequency of TDCC in the general population [10-12]. Despite TDCs being very common in children and adolescents, carcinomas of the TDCs are rare in this group, and just over 30 cases have been diagnosed [7,13].

However, while TDCs have been reported more often in men, TDCCs occur predominantly in middle-aged women (with a 2:1 female-to-male ratio) [5,6]. In children, the mean age of presentation is 6 years [10].

Well-differentiated thyroid carcinomas account for 95% of all TDCCs, with papillary cancer being the most frequent malignant neoplasm seen (75-90% of all cases). However, other types of cancers may occur, including anaplastic thyroid cancer (0.9%), as well as squamous cell carcinoma (5%), follicular (1.7%) or papillary follicular type of cancers (7%). So far, no case of medullary carcinoma has been diagnosed [3-5,10].

The clinical manifestation of TDCC

Typically, TDCC is a neck mass that is enlarging flexible midline or slightly lateral (95% situated on the left side), most often without other worrisome symptoms. Still, some patients suffer from neck pain, dysphagia or relapsing throat infections [3,6-8]. The mass usually moves on swallowing. 75% of these cysts are located below the hyoid bone and measure 2.0-5.0 cm in size [6]. Regional lymphadenopathy due to the lymph node metastases of thyroglossal duct cyst carcinoma occur in only 7.7-15.0% of all reported cases, and local invasion rarely exists. Distant metastases have been described in less than 2% of all cases [4,8].

The theories of TDCC origin

The origins of TDCC have not been established so far [3,4]. There are two theories regarding the start of thyroglossal duct cyst carcinoma [5,14]. One includes the presence of primary lesion in the thyroid gland and the development of metastases within the thyroglossal duct cyst wall [5,6]. This theory has been supported by the fact that some TDCCs have been presented with a concurrent thyroid cancer. In addition, the fibrous tract that connects the TDCC and the thyroid gland is thought to be a possible path for the thyroid carcinoma to spread into the cyst [14].

Based on the other theory, cancer arises de novo within the remnant of thyroglossal duct due to the thyroid ectopic tissue residue or from the epithelium of the cyst wall [5,6]. The lack of medullary carcinoma cases within the TDCs may support the thesis of de novo origin of TDCC rather than a metastatic theory [10,14].

The diagnosis of TDCC

The rare prevalence of TDCC and a lack of strongly typical features distinguishing benign and malignant lesions before surgery bring about a situation wherein proper diagnosis can be difficult and is usually made postoperatively just after histopathological examination of a resected cyst [4,10,15]. However, there are diagnostic procedures that should be considered before the surgery.

The preoperative assessment that may play an important role in the preoperative diagnosis, as well as in the planning of the primary treatment includes fine-needle aspiration biopsy (FNAB) and computed tomography (CT) or magnetic resonance imaging (MRI), [4,13]. Unfortunately, only 53-66% of all FNAB results can detect carcinoma before surgery [3,7,16]. The false-negative diagnosis by FNAB is mostly because of small neoplasm size, marginal location of the tumor in the cyst or the hypocellularity that results from dilution due to the cystic content [14]. Therefore, it has been found to reserve FNAB only for investigation of suspicious findings favoring a diagnosis of malignancy, such as the presence of calcifications or solid components on ultrasound [3,7,16]. Furthermore, TDCC may exist even with a normal FNAB and US imaging outcome [10].

Radioiodine neck scintigraphy is not recommended due to the small amount of thyroid cells located in the cyst that give indication during this procedure [17].

Certain characteristics may suggest the presence of a cancer. On clinical examination, a rapid increase in size of the cyst, as well as firm fixture to the hyoid bone or surrounding structures and palpable mass may be indicative of carcinoma [2,5,14]. Malignancy should be also suspected if the regional lymph nodes are palpable [10,13,14]. On US examination, solid components within the thyroglossal duct cyst and irregular mass shape or an asymmetric cyst wall thickness may indicate the possibility of malignancy [2,5]. Moreover, the presence of microcalcifications in the cyst and in the regional lymph nodes is strongly suggestive of carcinoma [5,13]. Beyond the aforementioned, a history of radiation to the head and neck area may play a role as a carcinoma risk factor [6].

The characteristics that may be predictive factors for malignancy within the cyst are illustrated in Figure 1.

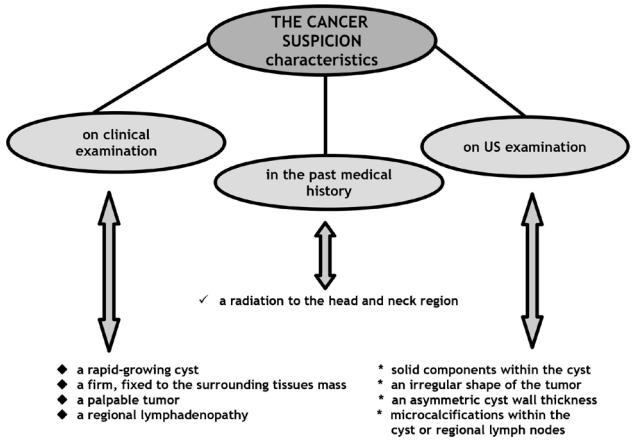

Figure 1. The suggestive factors of TDCC

On histopathological examination, invasion of the cyst wall, the presence of respiratory-type and squamous epithelium, as well as their coexistence with normal thyroid follicular within the walls of the cyst, are crucial in making a diagnosis of TDCC [14,17]. Nowadays, a lack of primary thyroid carcinoma on histopathological examination of the thyroid gland is not needed to diagnose primary TDCC [6,9].

The differential diagnosis of TDC and TDCC includes branchial cleft cyst, lipoma, metastatic thyroid carcinoma, dermoid cyst, sebaceous cyst and an enlarged lymph node. TDCC should also be distinguished from a papillary carcinoma arising from the tip of the pyramidal lobe – which is also found in the midline [4,8].

The management of patients with TDCC

Because of the rarity of thyroglossal duct cyst cancer, the treatment algorithms have not been clearly defined [5]. A rational approach must consider both the intrinsic tumor characteristics and the extension of the disease [2].

The Sistrunk surgery, introduced for the first time in 1920, is recommended as a first-line treatment, it being the gold standard management [4,11,13]. In this procedure, the cyst with the middle part of the hyoid bone, as well as the surrounding tissue around the thyroglossal duct (a portion of duct between the hyoid bone and the foramen cecum) are en bloc resected [2,3,6]. It has been well established that patients after the Sistrunk procedure have better survival compared to those with only simple cyst excision, and the TDCC recurrence rate has been reported to be about 5% *vs* 55%, respectively [2,5].

The effectiveness of total thyroidectomy and radioactive iodine (RAI) treatment are still subject to debate. The change in outcome has not been proved to be advantageous when more aggressive strategies were employed in patients with TDCC so far, especially in low risk patients [10]. In addition, the coexistence of malignant tumor in the thyroid gland varies in many studies from 20% to 60% of all patients with TDCC [2,7].

Although some researchers have posted that total thyroidectomy should be performed in all patients, other practitioners have suggested that total thyroidectomy is associated with a risk of complications (injury to the recurrent laryngeal nerve or parathyroid glands) and should be implicated in a particular group of cases alone [3,5,11]. This alternative approach is performing thyroidectomy only among older subjects (≥ 45 years of age), in those with more aggressive disease or who are subjects with a history of radiation exposure to the head and neck area [11,14,15]. There are some high risk factors that must be considered when applying aggressive treatment. These include: regional lymph nodes involvement, distant metastases, extracapsular or soft tissue invasion and tumor size more than 1.5-4.0 cm [5,6,10,14]. Particular positive margins on histopathological examination are an indicative factor for the application of a more aggressive strategy [14], and thyroid gland removal should be considered in patients with synchronous neoplasm in the thyroid, as well as in patients with high clinical and radiological suspicion of synchronous tumors [5,17].

Some researchers have found that the rationale for adding thyroid resection to every patient with TDCC should be based on three main considerations, the presence of concomitant thyroid malignancy in the main thyroid gland, the utilization of radioactive iodine as an adjuvant treatment, and the role of serum thyroglobulin as a follow-up marker for thyroid cancer [4]. In some cases, FNAB might reveal the malignant nature of the cyst and indicate more aggressive surgical approach [11].

To sum up, there are four approaches regarding surgical management for thyroglossal duct cyst malignancy. These are: Sistrunk procedure alone, Sistrunk procedure with thyroid lobectomy or pyramidal lobe resection, Sistrunk procedure with total or near total thyroidectomy in all patients, and Sistrunk procedure with selective thyroidectomy for high-risk patients [3].

The role of RAI ablation is also controversial. RAI treatment implementation should be considered, similar to total thyroidectomy, in high risk patients, as well as in cases of the coexistence of malignancy in the thyroid gland and the thyroglossal duct cyst [4,5,10]. The benefit of radioactive iodine treatment for low-risk patients remains unclear [4].

Although elective neck dissection has not been generally recommended because of a small risk of metastatic spread for TDCC, it should be performed in subjects with lymph node involvement [5,13].

The indications for more aggressive strategies in TDCC management are summarized in Figure 2.

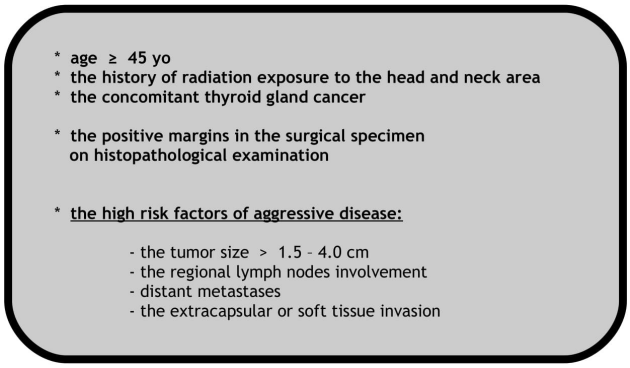

Figure 2. The proposed indications for more aggressive strategies in TDCC.

Levothyroxine therapy should be started after thyroidectomy and RAI ablation, with doses adjusted to achieve thyrotropin suppression (TSH levels of 0.05 to 0.1 mU/L). The disease activity is usually determined based on follow-up studies similarly to those in patients with a primary cancer of the thyroid gland [7,17].

Follow-up check-ups are recommended in all patients with TDCC. All patients must have a neck scan (e.g. US imaging) and be re-assessed every six months during the first year and annually after that. Park proposed that follow-up procedures consist of physical examination, ultrasound of the surgical region and thyroid, and total body scintigraphy [4]. Control of TSH concentration in cases after thyroidectomy are also needed [17].

TDCC survival

The prognosis for TDCC is very good because this type of carcinoma harbors an exceedingly low rate of mortality. It has been reported that the 5-year survival rate is 100%, while the 10-year survival rate is approximately 95% [5,10].

CONCLUSIONS

The rare prevalence of TDCC, a lack of strongly typical features distinguishing benign and malignant lesions before surgery generate a situation wherein proper diagnosis can be difficult. Hence, it is usually made postoperatively. However, there are certain characteristics that may be predictive for malignancy within the cyst that should be considered before making a diagnosis. Although the Sistrunk procedure is often considered adequate, currently, there is no clear consensus

about concurrent thyroidectomy or radioiodine therapy. There are only proposed indications such as that based, i.a. on risk group stratification, which can be helpful in deciding on the extent of surgery and treatment. Therefore, a multidisciplinary approach should be applied to safely identify high-risk patients that will require a more aggressive treatment, and more case reports and case series are needed to determine optimal management.

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