

ORIGINAL

Surgical management of primary thyroid carcinoma arising in thyroglossal duct cyst: An experience of a single institution in Serbia

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Abstract. Thyroglossal duct cyst (TDC) carcinoma is a comparable rare entity and treatment strategies have not been standardized. Here, we report a favorable outcome of TDC carcinoma patients based on our therapeutic strategy. Twelve patients with TDC carcinoma treated in our department from 1986 to 2012 were enrolled. Ten patients underwent Sistrunk's procedure in other institutions and referred to our institution for re-operation after the diagnosis of TDC carcinoma and the remaining two underwent initial surgery in our institution. Eleven patients were diagnosed as papillary and one as follicular carcinoma originating from TDC. We performed total thyroidectomy for 11, and limited thyroidectomy for one patient. Three patients (25%) had carcinoma lesions in the thyroid. We routinely dissected level I bilaterally and 6 of 11 patients (55%) with papillary carcinoma-type TDC carcinoma had metastasis. Level II/III nodes were biopsied and if positive, we performed level II-IV dissection. Of the 5 patients positive for level II/III, 2 were also positive for level IV. For the 3 patients with synchronous carcinoma in the thyroid, we performed level VI dissection and two had metastasis in this level. To date, 1 patient showed a recurrence to the lung, but none of the patients in our series died of carcinoma. For surgery of TDC carcinoma, Sistrunk's procedure, total thyroidectomy with level I dissection is mandatory. Whether level II-IV dissection is performed depends on pathology of biopsied level II/III nodes. Level VI dissection is also recommended especially when carcinoma lesions are pre/intra operatively detected in the thyroid.

Key words: Thyroglossal duct cyst carcinoma, Surgical strategy, Lymph node dissection, Synchronous thyroid carcinoma

THYROGLOSSAL DUCT REMNANT (TDR) fails to involute in approximately 7% of population. The first report of TDR was by Brentano, in 1911 [1]. Most of the authors agree that Sistrunk's procedure (SP), originally described in 1928 – en bloc resection of TDC with hyoid bone body and surrounding soft tissue towards the foramen cecum, is the surgery of first choice considering embryonal development of thyroid

gland [2].

Thyroid cancer in the thyroglossal duct remnant is rare and can be found in only 1-1.6% of cases [3,4]. The most common histological type is the papillary thyroid carcinoma (PTC) [5]. To date, only about 250 cases of thyroglossal duct cyst (TDC) carcinoma have been reported, mostly as case reports [6, 7]. Since TDC carcinoma is so rare, the surgical approach is based on individual experience, although Patel *et al.* have shown that patients with SP have significantly better 10-years survival compared to the patients who had simple TDC excision (100% vs. 75% respectively) [8]. However, it remains unclear whether additional surgery such as thyroidectomy and lymph node dissection is necessary.

Submitted Feb.17, 2012; Accepted Mar. 7, 2012 as EJ12-0070

Released online in J-STAGE as advance publication Apr. 16, 2012

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We encountered 12 patients of TDC carcinoma and here, we show our experience of treatment for TDC carcinoma in order to elucidate appropriate treatment strategies for this carcinoma while demonstrating the incidence and exact location of lymph node metastases as well as the incidence of thyroid carcinoma.

Materials and Methods

We enrolled 12 patients who underwent surgery of TDC carcinoma at the Institute of Oncology and Radiology of Serbia from 1986 to 2012. They consisted of 9 females and 3 males and their age at diagnosis was 40.6 years on average (27-63 years). Ten patients underwent SP as an initial surgery in other hospitals and were referred to our institution for re-operation after the diagnosis of TDC carcinoma on postoperative pathological examination. The remaining 2 underwent surgery in our institution due to midline neck mass and intracystic tumor within TDC visualized on ultrasonography. Diagnosis of TDC carcinoma for those two patients was established by intraoperative rapid pathological examination using a frozen section. All surgeries in our institution were performed by presenting author (R.D.) except one (No. 6) who was operated by a coauthor (I.M.). All patients were diagnosed as TDC carcinoma also on postoperative pathological examination. Molecular analysis of *BRAF* gene was also performed for these tumors by the standard technical procedure [9].

All patients underwent whole body scan (WBS) postoperatively with 3mCi of radioactive iodine (RAI). Five patients also underwent RAI ablation with 60mCi postoperatively, because of the presence of thyroid carcinoma in the thyroid gland, lymph node metastasis, and/or iodine uptake more than 2% after WBS. None of these patients had abnormal uptakes in the scintigraphy thereafter. All patients are on L-thyroxine TSH suppression. Average follow-up period was 11.6 years (4-26 years).

Results

We summarize our series of 12 TDC carcinoma patients in Tables 1 and 2.

Diagnosis of TDC carcinoma

Ten patients (Nos. 1, 3-9, 11, and 12) were diagnosed as TDC based on the findings on ultrasonogra-

phy and underwent SP as an initial surgery in other institutions. They were diagnosed as TDC carcinoma based on postoperative pathological examination. The remaining two patients (Nos. 2 and 10) were initially treated in our institution. They were preoperatively suspected of TDC carcinoma because intracystic mass was detected within TDC on ultrasonography. The definite diagnosis of TDC carcinoma has been confirmed on intraoperative rapid pathological diagnosis using a frozen section. Fine needle aspiration biopsy (FNAB) for TDC lesion was performed only for one patient (No.2), but the lesion could not be cytologically diagnosed as carcinoma. On preoperative imaging studies, nodules in the thyroid were detected in all patients except for one (No. 1). Although none of these patients underwent FNAB for thyroid nodules, nodules of four patients (Nos. 2, 5, 9, and 10) were suspected of malignancy on ultrasonographic findings.

Surgical procedure

As indicated above, 10 patients had undergone SP in other hospitals and 2 underwent SP at the beginning of surgery in our institution. Regardless of whether or not lesions in the thyroid suspected of malignancy could be detected on imaging studies, we performed thyroidectomy for all 12 patients. As shown in Table 1, all patients except for one (No. 6) underwent total thyroidectomy.

None of the 12 patients showed clinical lymph node metastasis detectable on imaging studies. Eleven of these patients, however, underwent prophylactic lymph node dissection. Patient No. 1 underwent total thyroidectomy only, but showed recurrence to regional lymph nodes (level I, II/III) 3.5 years after second surgery. Then, this patient underwent therapeutic lymph node dissection as the third surgery. At the beginning, bilateral level I dissection was performed for all patients. Then, nodes in bilateral level II/III located around common carotid artery bifurcation were biopsied for intraoperative rapid pathological diagnosis. The biopsied nodes were positive in 5 patients (Nos. 1, 3, 5, 9, and 10) and these 5 patients underwent modified radical neck dissection (MRND) on ipsilateral side of the node-positive level II/III. In fact, of these five patients two (Nos. 5 and 10) underwent bilateral MRND, because bilateral biopsied nodes were positive and three patients (Nos. 1, 3, and 9) had unilateral MRND. The remaining 7 did not undergo MRND, because biopsied nodes were negative for carcinoma. For 4 patients with nodules

Table 1 Surgical treatment

Patient	First operation	Second operation	Third operation
1	SP	TT	MRND I-II-III-IV
2	SP, TT, CND VI, LND I, LNB II/III		
3	SP	TT, MRND I-II-III-IV	
4	SP	TT, LND I, LNB II	
5	SP	TT, CND VI, MRND bil I-II-III-IV	
6	SP	Isthmectomy + PR of right lobe, LND I, LNB II/III	
7	SP	TT, LND I, LNB II/III	
8	SP	TT, LND I, LNB II/III	
9	SP	TT, CND VI, MRND bil I-II-III-IV	
10	SP, TT, CND VI, MRND I-II-III-IV		
11	SP	TT, LND I, LNB II/III	
12	SP	TT, LND I, LNB II/III	

SP, Sistrunk procedure; TT, total thyroidectomy; MRND, modified radical neck dissection; Selective neck regions: I (submental/prehyoid), II (a. carotis communis), III (supra-omohyoid), IV (infra-omohyoid), V (central compartment); CND, central neck dissection; LND, lymph node dissection; LNB, lymph node biopsy; bil, bilateral; PR, partial resection

Table 2 Demographics, pathology, genetics, treatment and follow-up for 12 patients with TDC thyroid carcinoma

Patient	Sex	Age	SP	TT	Level I metastatic nodes	Level II/III metastatic nodes	Level IV metastatic node	MRND	Level VI metastatic nodes	CND	Thyroid carcinoma	<i>BRAF</i> mutation	RAI	Recurrence	Follow up (years)
1	F	27	Yes	Yes	2 of 3	1 of 13	No	Yes	N.D.	No			Yes	LN	26
2	F	51	Yes	Yes	No	No	N.D.	No	0 of 7	Yes	FTC				17
3	F	29	Yes	Yes	1 of 4	1 of 20	No	Yes	N.D.	No			Yes		16
4	F	51	Yes	Yes	1 of 3	No	N.D.	No	N.D.	No		V600E			16
5	M	63	Yes	Yes	1 of 2	6 of 12	1 of 15	Yes, bil	3 of 7	Yes		V600E	Yes	Mets (pul)	11
6	F	31	Yes	No*	No	No	N.D.	No	N.D.	No					10
7	F	39	Yes	Yes	No	No	N.D.	No	N.D.	No					9
8	F	51	Yes	Yes	No	No	N.D.	No	N.D.	No					9
9	M	52	Yes	Yes	1 of 2	1 of 9	2 of 20	Yes, bil	1 of 6	Yes	micro PTC		Yes		9
10	F	38	Yes	Yes	1 of 3	1 of 14	No	Yes	2 of 8	Yes	PTC		Yes		7
11	F	20	Yes	Yes	No	No	N.D.	No	N.D.	No					6
12	M	35	Yes	Yes	No	No	N.D.	No	N.D.	No					4

* Isthmectomy with partial resection of right lobe; SP, Sistrunk procedure; TT, total thyroidectomy; MRND, modified radical neck dissection; CND, central node dissection; RAI, radioiodine therapy; LN, lymph nodes; FTC, follicular thyroid carcinoma; bil, bilateral; Mets (pul), pulmonary metastases; PTC, papillary thyroid carcinoma; N.D., not dissected

suspected of carcinoma in the thyroid (Nos. 2, 5, 9, and 10), we performed also level VI dissection.

No patient had permanent postoperative hoarseness or hypocalcaemia. This was verified 3 weeks after surgery by the normal calcium and PTH blood levels and indirect laryngoscope.

Pathological examination

Results of pathological examination of 12 patients are summarized in Table 2. Of the 12 TDC carcinoma, 11 were diagnosed as papillary carcinoma. The

remaining one was diagnosed as follicular carcinoma based on capsular invasion and by finding clusters of malignant cells in the fibrous tissue that surrounds TDC. All patients underwent level I dissection and 6 (50%) were diagnosed as node-positive. Five patients (42%) were positive for carcinoma in biopsied level II/III nodes and underwent unilateral or bilateral MRND. Of these five, 2 (40%) were node-positive in level IV.

Eleven patients had nodules in the thyroid and 4 were suspected of having thyroid carcinoma. Three of these 4 patients were diagnosed as thyroid carcinoma (2

papillary and 1 follicular carcinomas). Nodules of the remaining 8 patients were diagnosed as benign lesions.

Prophylactic level VI dissection was also performed for 4 patients whose thyroid nodules were suspected of carcinoma. Two patients with papillary carcinoma (Nos. 9 and 10) were node-positive and one with follicular carcinoma (No. 2) was node-negative in level VI. One patient (No. 5) whose nodule in the thyroid was benign was also node-positive in level VI.

We performed molecular analysis and two patients (Nos. 4 and 5) had *BRAF*^{V600E} mutation in exon 15.

Prognosis of patients

As indicated above, one patient (No. 1) who did not undergo lymph node dissection showed a recurrence to level I and II/III 3.5 years after second surgery, and underwent therapeutic MRND (I, II, III, IV). One patient (No. 5) showed pulmonary metastasis 3 years after second surgery in our institution (Table 2), which was successfully treated by RAI therapy using 150 mCi. After lymph node dissection, none of these patients showed a recurrence in the neck. None of the patients died of thyroid carcinoma up to date.

Discussion

In this study, we demonstrated our experience of 12 cases of TDC carcinoma in order to elucidate its appropriate therapeutic procedure. Our series consisted of 9 females and 3 males and the mean age of our patients was 40.6 years, which was not discrepant with previous findings [6, 10-15]. Ten patients were diagnosed as TDC carcinoma on postoperative histopathology while the diagnosis for the 2 patients who were initially operated in our institution were made intraoperatively by frozen section analysis. We performed FNAB for TDC lesion of one patient, but could not diagnose it as TDC carcinoma. These findings suggest that TDC carcinoma is difficult to preoperatively diagnose [16] and most patients were diagnosed as TDC carcinoma on pathological examination. In our series, all except one (No.2) were diagnosed as papillary carcinoma, which was not discrepant with previous finding [5], although cases of squamous cell carcinoma and anaplastic carcinoma were reported [17, 18].

It remains debatable regarding the appropriate surgical procedure of TDC carcinoma. Patel *et al.* have shown that patients with SP have significantly better 10-years survival compared to those with simple

TDC excision (100% vs. 75% respectively) [8]. Some authors advocate SP alone in patients younger than 45 years old with clinically or radiologically normal thyroid gland, small tumor with an absence of histologically positive margins, absence of palpable regional lymph node metastases and no history of neck irradiation in childhood [2, 19, 20]. In our series, however, 3 patients (25%) had carcinoma lesions in the thyroid gland. Hartl *et al.* have reported synchronous thyroid gland carcinomas in 9 of the 16 patients (56%) who underwent SP and thyroidectomy, and carcinoma lesions were detected in both lobes in 3 patients [21]. Other studies also reported high incidence of carcinoma lesions detected in the thyroid gland [6, 22, 23]. Although it remains unclear whether latent carcinoma lesions came to be clinical, total thyroidectomy could be a good alternative for TDC patients to decrease the recurrence rate and to make postoperative follow-up easier by monitoring thyroglobulin level [3, 22, 24].

Surgical strategy regarding lymph nodes is also controversial. Most TDC carcinoma is PTC, which frequently metastasizes to the regional lymph node. Ultrasonography is the most useful tool to preoperatively detect and diagnose lymph node metastasis. In our series, none of the patients were diagnosed as node-positive on preoperative ultrasonography. However, Ito *et al.* demonstrated that lymph node metastasis both in levels II-IV and level VI were frequently overlooked on preoperative ultrasound [25-27]. Such a latent metastasis might not be immediately life-threatening, but it has been shown that, in papillary carcinoma larger than 1 cm, metastasis to level VI, which is the nearest from the thyroid, independently predicted a worse disease-free survival [27]. Level I is the nearest compartment from TDC and we routinely dissected this level bilaterally and as many as 5 of 11 patients (45%), who underwent prophylactic level I dissection, was node-positive in this level. Indeed, one patient who underwent total thyroidectomy only showed a recurrence to this level and all level I-negative patients were also negative for level II-IV. Therefore, level I dissection is very important for TDC carcinoma surgery. Whether and how levels II-IV are dissected remains controversial. In our surgical strategy decision whether entire level II-IV dissection is performed depends on the results of rapid pathological diagnosis of biopsied nodes in level II/III, which is based on the concept similar to the concept of sentinel lymph node in PTC [28, 29]. We performed MRND for patients positive for biopsied level II/III

level but not routinely, because patients' complaints significantly increased after MRND and some complications such as chyle leakage and injury of adjacent organs such as the jugular vein and vagus might occur. Indeed, of 4 patients who underwent prophylactic node dissection and were positive for PTC in biopsied level II/III nodes, two were also node-positive in level IV, indicating that the presence of level II/III positive nodes can significantly predict level IV metastasis.

Re-operation for the recurrence to the lateral neck region is not very difficult, but re-operation for the level VI recurrence is problematic, because it may induce severe complications such as recurrent laryngeal nerve injury and persistent hypoparathyroidism. Therefore, we performed prophylactic level VI dissection in patients with nodules suspected of carcinoma in the thyroid. Two patients having PTC lesions in the thyroid gland had also metastases in the central neck compartment. Therefore we can conclude that level VI dissection is mandatory for patients having nodules suspected of PTC in the thyroid. We have to note that one patient who underwent level VI dissection but did not have PTC in the thyroid was also node-positive in level VI. Therefore, routine level VI dissection might be better for TDC carcinoma surgery, but to date, none

of the patients in our series showed lymph node recurrence. We can thus conclude that our surgical strategies are generally appropriate for TDC carcinoma patients.

In our series, 2 of 11 patients with papillary carcinoma-type TDC carcinoma (18%) showed *BRAF* gene mutation. This incidence is lower than previous findings in papillary carcinoma [30, 31]. One of the 2 patients with *BRAF* mutation showed a lung recurrence. Although the number of patients is too small to draw any confirmative conclusions, *BRAF* mutation analysis may be supportive for predicting prognosis of TDC carcinoma patients [31].

In summary, we demonstrated that TDC carcinoma generally shows a favorable prognosis. However, in addition to the Sistrunk's procedure, total thyroidectomy must be performed because of the high incidence of carcinoma lesions in the thyroid gland. Bilateral level I dissection is mandatory because metastasis to this level can predict metastasis to other levels. MRND should be performed at least for node-positive patients in biopsied specimens in level II/III. Level VI dissection is a standard for TDC carcinoma with synchronous carcinoma lesions in the thyroid. It may be better to perform it routinely regardless of absence of thyroid carcinoma.

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