

CASE REPORT

The first report of bilateral retropharyngeal lymph node metastasis from papillary thyroid carcinoma and review of the literature

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Abstract

The sites of lymph node metastasis of papillary thyroid carcinomas are typically the paratracheal and jugular lymph nodes. On the other hand, metastasis to the retropharyngeal or parapharyngeal nodes from papillary thyroid carcinomas is very rare. During the last two decades, limited to cases with a histologically definite diagnosis by surgery, only 39 cases have been reported. All reported cases were unilateral retropharyngeal or parapharyngeal node metastasis except one metachronous bilateral case, and there were no reports of simultaneous bilateral cases within our literature review. We report three cases of retropharyngeal node metastasis from thyroid papillary carcinoma, including a case of bilateral nodal metastasis. Retropharyngeal node metastasis was successfully resected in all three patients by the transcervical approach. As pointed out in past reports, this report also suggests that prior neck dissection and/or metastasis to cervical lymph nodes might alter the direction of lymphatic drainage to the retrograde fashion, resulting in the unusual metastasis to the retropharyngeal lymph nodes, and there is a possibility of a bilateral pattern. Also, it is necessary to consider the possibility of metastasis from a papillary thyroid carcinoma in the differential diagnosis of lymph node swelling in the parapharyngeal space.

Keywords: *Thyroid cancer, papillary carcinoma, parapharyngeal metastasis, neck dissection*

Introduction

Thyroid papillary carcinomas comprise 70–80% of differentiated thyroid carcinomas, and extend to lymph nodes in approximately 40–50% of cases [1–3]. The presence of node metastasis usually occurs in the internal jugular and recurrent laryngeal chain on the side of the lesion [4,5], so metastasis to the retropharyngeal lymph nodes (RPLN) or parapharyngeal lymph nodes (PPLN) is very rare. Only 39 cases (limited to the cases with histologically definite diagnosis by surgery) have been reported during the last two decades within our literature review (Tables I and II) [6–15]. Meanwhile, it was reported that there were two lymphatic pathways that connected with a retropharyngeal metastasis from thyroid carcinomas, one is retrograde from jugular chain lymphatics, and the other is direct

through the superior thyroid pole by way of the posterior lymphatic trunks, which are reported to be present in 20% of the cases [16].

We have experienced surgical treatment of three patients with RPLN metastasis of thyroid papillary carcinoma. One case is the first known case of bilateral RPLN metastasis. So we report here this very rare case (case 1) and also provide a review of the literature. Our study suggests that prior neck dissection and/or metastasis to cervical lymph nodes might alter the direction of lymphatic drainage to the retrograde fashion, resulting in the unusual metastasis to the RPLN, and there is a possibility of a bilateral pattern. It is also necessary to consider the possibility of metastasis from papillary thyroid carcinoma in the differential diagnosis of lymph nodes swelling in the parapharyngeal space.

Table I. Initial cases: retropharyngeal or parapharyngeal metastasis from thyroid carcinoma – a review of the literature.

Patient no.	Ref. no.	Authors	Age (years)	Sex	TNM stage at initial therapy	Treatment of primary	Initial treatment*		Isolated metastasis without cervical metastasis at identification of RPLN or PPLN metastasis	Location and size of RPLN or PPLN metastasis (side/location/mm)	Type of surgical approach to RPLN or PPLN metastasis
							Treatment of neck (side/dissected levels)	131I therapy			
1		Horvath M et al.	55	F	? (N0)	TT	None	?	Yes (O)	L/PPLN/?	?
2		Ferrario F et al.	47	M	T2aN1aM0	TT	R/FND	Yes	No	R/PPLN/45 mm	TCA
3		Sirotmak JJ et al.	53	F	? (N+)	TT	R/MND	No	No	R/PPLN/20 mm	TOA
4		DiLeo MD et al.	65	M	? (N0)	TT	None	Yes	Yes (O)	R/RPLN/?	TCA
5		Saydam L et al.	54	F	? (N0)	TT	Bi/MND	No	Yes (O)	L/PPLN/?	TCA
6		Aygenc E et al.	47	F	? (N0)	TT	L/MRND	No	Yes (O)	L/PPLN/50 mm	TCA
7		Thomas G et al.	46	M	? (N+)	TT	L/ND	Yes	No	L/PPLN/60 mm	TCA
8	7	Erdem T et al.	40	M	? (N0)	TT	Bi/SND	Yes	Yes (O)	R/PPLN/50 mm	TCA
9	8	Lombardi D et al.	40	M	T2aN1aM0	TT	None	Yes	No	L/PPLN/?	TCA
10			52	F	T4bN1aM0	TT	Bi/SND (2–4, 6)	Yes	No	L/PPLN/60 mm	TCA
11	9	Tomoda C et al.	58	F	? (N0)	TT	Bi/ND	Yes	Yes	L/PPLN/40 mm	TCA
12	10	Cetik F et al.	22	F	? (N0)	TT	None	Yes	Yes	R/PPLN/45 mm	TCA
13	11	Le TD et al.	?	?	? (N0)	?	?	No	Yes	Unil/PPLN/?	TOA
14			?	?	? (N0)	?	?	No	Yes	Unil/PPLN/?	TOA
15	15	Kaplan SL et al.	52	F	? (N0)	TT	R/ND	Yes	Yes (O)	R/PPLN/25 mm	?
		Present study	47	M	T1N1bM0	TT	R/MRND (1–6)	No	No	R/PPLN/13 mm	TCA

?, unexplained; Bil, bilateral; FND, functional neck dissection; L, left; MND, modified neck dissection; MRND, modified radical neck dissection; (O), primary is occult; PPLN, parapharyngeal lymph node; R, right; RPLN, retropharyngeal lymph node; SND, selective neck dissection; TCA, transcervical approach; TOA, transoral approach; TT, total thyroidectomy; Unil, unilateral.

*Other than resection of RPLN or PPLN.

Table II. Recurrent cases: retropharyngeal or parapharyngeal metastasis from thyroid carcinoma – a review of the literature.

Patient no.	Ref.	Authors	Age (years)	Sex	TNM stage at initial therapy	Initial treatment*		Treatment at recurrence*			Isolated metastasis without cervical identification of RPLN or PPLN metastasis	Location and size of RPLN or PPLN metastasis (side/location)	Type of surgical approach to RPLN or PPLN metastasis	
						Treatment of neck (side/disectioned levels)	Treatment (side/disectioned levels)	Treatment of primary levels	Treatment of neck (side/disectioned levels)	Treatment of primary levels				131I therapy
1		Imai T et al.	72	M	?	(N+)	TT	Bi/MND	No	None	None	Yes	R/PPLN/40 mm	MSTCA
2		Leger AF et al.	39	M	T4N1M0	TT	Bi/ND	None	None	None	No	Yes	R/RPLN/40 mm	TCA
3			44	F	T4N1M0	TT	Bi/ND	None	None	None	No	Yes	R/RPLN/40 mm	TCA
4		Ducci M et al.	68	M	?	(N0)	ST	None	?	R/FND (2-5)	Yes	No	R/PPLN/35 mm	TCA
5			51	M	T1N0M0	TT	None	None	Yes	R/FND (2-5)	Yes	No	R/PPLN/40 mm	MSTCA
6		Aygenc E et al.	13	F	?	(N+)	TT	Exstirpation of LN	Yes	R/MNRD	No	No	R/PPLN/30 mm	TCA
7	6	Desuter G et al.	?	?	?	(N+)	TT	Bi/ND	No	None	Yes	Yes	Unil/PPLN/?	TCA
8			?	?	?	(N+)	TT	Bi/ND	No	None	Yes	Yes	Unil/PPLN/?	TCA
9			?	?	?	(N+)	TT	Bi/ND	No	None	Yes	Yes	Unil/PPLN/?	TCA
10	11	Le TD et al.	?	?	?	?	?	?	Yes	None	No	?	Unil/PPLN/?	TOA
11			?	?	?	?	?	?	Yes	None	No	?	L (1998) R (2000)/PPLN/?	TOA
12			?	?	?	?	?	?	Yes	None	No	?	Unil/PPLN/?	TOA
13			?	?	?	?	?	?	Yes	None	No	?	Unil/PPLN/?	TOA
14	12	Otsuki N et al.	Average 63, range 40-84	F	?	(N0)	ST or TT	None	?	Unil/MND or Bil/MND	Only 3 patients	Yes	Unil/RPLN/?	TCA
15				F	?	(N0)	?	None	?	Unil/MND or Bil/MND	?	Yes	Unil/RPLN/?	TCA
16				F	?	(N+)	?	Unil/MND	?	None	No	No	Unil/RPLN/?	TCA
17				F	?	(N+)	?	Unil/MND	?	None	Yes	Yes	Unil/RPLN/?	TCA
18				F	?	(N+)	?	Unil/MND	?	None	Yes	Yes	Unil/RPLN/?	TCA
19	13	Shellenberger T et al.	46	F	?	(N+)	TT	R/ND (2-5)	Yes	None	Yes	Yes	R/RPLN/20 mm	TOA
20			56	F	?	(N+)	TT	Bi/ND (6)	Yes	None	Yes	No	L/RPLN/?	TOA
21	14	Ma QD et al.	24	F	?	(N+)	TT	R/ND	Yes	L/SND (2-5)	Yes	Yes	R/RPLN/33 mm	TOA
22	15	Kaplan SL et al.	47	F	?	?	TT	Bi/ND	Yes	?	?	?	L/RPLN/10 mm	?
23			68	F	?	?	TT	R/ND	Yes	?	?	?	R/RPLN/16 mm	?
24			58	F	?	?	TT	L/ND	Yes	?	?	?	L/RPLN/12 mm	?

Table II. (Continued).

Patient no.	Ref. no.	Authors	Age (years)	Sex	TNM stage at initial therapy	Initial treatment*		Treatment at recurrence*		Isolated metastasis without cervical metastasis at identification of RPLN or PPLN metastasis	Location and size of RPLN or PPLN metastasis (side/location)	Type of surgical approach to RPLN or PPLN metastasis		
						Treatment of neck (side/disectioned of primary levels)	Treatment of primary levels	Treatment of neck (side/disectioned of primary levels)	Treatment of primary levels					
		Our case	68	M	T4N1aM0	TT	R/SND (2-6)	Yes	None	L/SND (3, 4), Bil/SND (1, 2)	Yes	No	Bil/RPLN/R 13 mm, L 27 mm	MSTCA
		Our case	62	F	T3N0M0	ST	None	No	TT	R/SND (2-5), L/SND (1-3)	Yes	No	L/RPLN/14 mm	MSTCA

?, unexplained; Bil, bilateral; FND, functional neck dissection; L, left; MND, modified neck dissection; MRND, modified radical neck dissection; MSTCA, mandibular swing transoral approach; (O), primary is occult; PPLN, parapharyngeal lymph node; R, right; RPLN, retropharyngeal lymph node; SND, selective neck dissection; ST, subtotal thyroidectomy; TCA, transcervical approach; TOA, transoral approach; TT, total thyroidectomy; Unil, unilateral.
*Other than resection of RPLN or PPLN.

Case reports

In the past 3 years, three patients underwent surgical treatment for metastasis of thyroid papillary carcinoma to the RPLN at Shinshu University School of Medicine (Tables I and II). One patient was female and the others were male. All three patients had no obvious symptoms associated with RPLN metastasis, and metastasis was found by computed tomography (CT) and magnetic resonance imaging (MRI).

Case 1: recurrence case

A 68-year-old Japanese male presented in January 2009 with bilateral RPLN swelling demonstrated by periodic imaging test (CT and MRI). He had received treatment for thyroid papillary carcinoma (T4N1aM0), total thyroidectomy, and right side selective neck dissection (levels 2-6). He had recurrent cervical lymph node metastases on the left side and received left side neck dissection (levels 3 and 4) in August 2008. He had received ¹³¹I radiation therapy three times. At the time of diagnosis of RPLN metastasis, there were no obvious symptoms. On physical examination by fiberoptic, there was no displacement of the soft palate, and the nasopharyngeal wall was normal. Cranial nerve dysfunction was not observed. CT demonstrated well-enhanced bilateral RPLN swelling; in particular, on the left side the mass extended into the poststyloid component of the parapharyngeal space. MRI showed a slightly enhanced lymph node swelling with gadolinium in the bilateral retropharyngeal region in common with CT findings (Figure 1).

We performed bilateral selective neck dissection (levels 1 and 2), and resection of bilateral RPLN via the transcervical approach with mandibulotomy in October 2009 (Figures 2 and 3). We performed a temporary tracheotomy for prevention of postoperative airway obstruction. There were no complications after the surgical procedure. The pathological diagnosis of the resected RPLN was bilateral metastasis of the papillary thyroid carcinoma (Figure 4). He received ¹³¹I radiation therapy postoperatively. There has been no evidence of tumor recurrence in the 19 months following surgery.

Case 2: recurrence case

A 62-year-old Japanese female presented in January 2010 with left RPLN swelling demonstrated by periodic imaging test (CT and MRI). She had received treatment for thyroid papillary carcinoma, i.e. subtotal thyroidectomy, in April 1983. She had also received treatment for neck recurrence, total thyroidectomy

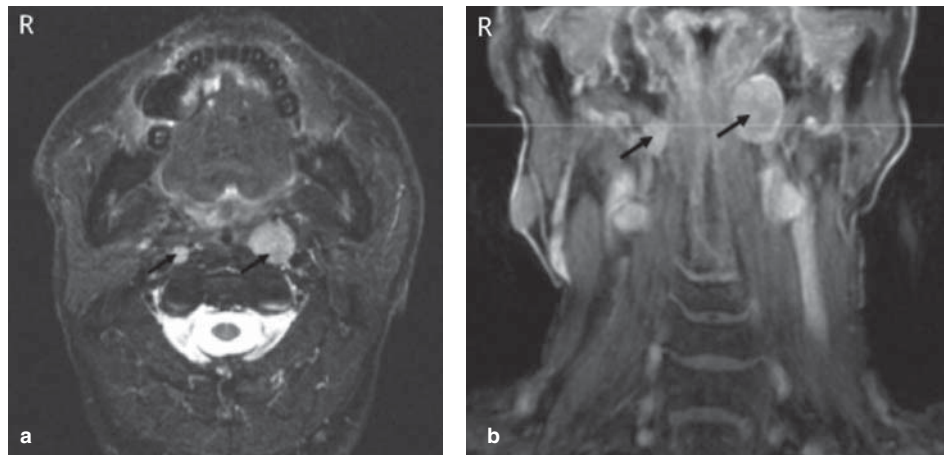


Figure 1. Case 1. MRI (Gd-DTPA) showing enhanced lymph node swelling in the bilateral lateral retropharyngeal space: (a) axial, T1-weighted; (b) coronal, T2-weighted. Arrows indicate retropharyngeal lymph node metastases.

and right selective neck dissection (levels 2, 4, and 5) and left selective neck dissection (levels 2 and 3) in July 1999. She had recurrent cervical lymph node metastases on the right side and lung metastases in March 2008 and received ^{131}I radiation therapy six times. At the time of diagnosis of RPLN metastasis, there were no obvious symptoms. On physical examination by fiberoscopy, there was no displacement of the soft palate, and the nasopharyngeal wall was normal. Cranial nerve dysfunction was not observed. CT demonstrated well-enhanced right cervical lymph node

metastases and left RPLN swelling. Findings on MRI matched findings on CT.

We performed right selective neck dissection (levels 2–5) and left selective neck dissection (level 1), and resection of the left RPLN via the transcervical approach with mandibulotomy in March 2010. There were no complications after the surgical procedure. The pathological diagnosis of resected RPLN was metastasis of papillary thyroid carcinoma. She is alive with disease and under treatment with ^{131}I radiation therapy for metastasis in the lung.

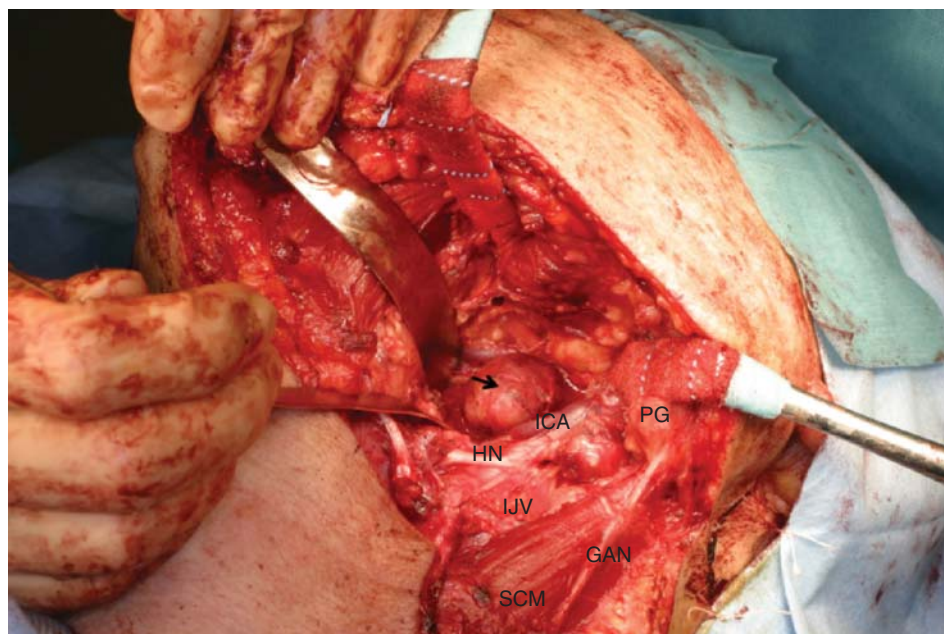


Figure 2. Case 1. The mandible ablation was performed at the midline without resecting the floor of the oral cavity and pushed up in an anterosuperior direction and the retropharyngeal and parapharyngeal space was opened widely. The retropharyngeal dissection was performed safely. GAN, great auricular nerve; HN, hypoglossal nerve; ICA, internal carotid artery; IJV, internal jugular vein; PG, parotid gland; SCM, sternocleidomastoid. Arrow indicates left retropharyngeal lymph node metastasis.

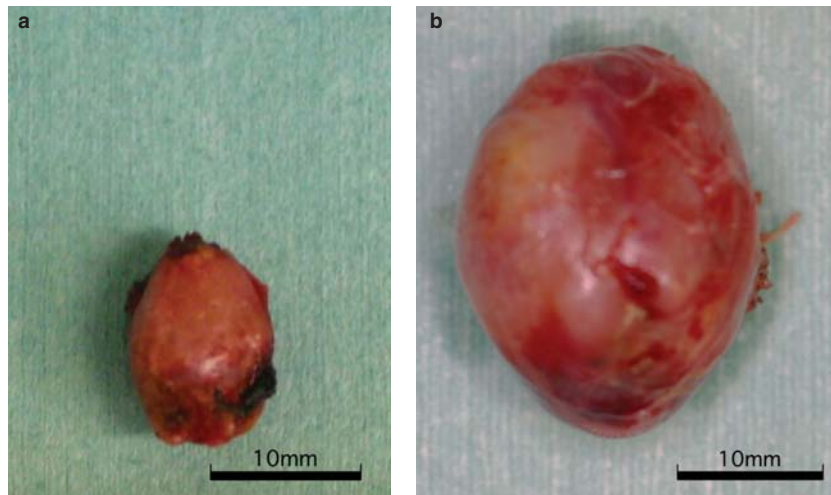


Figure 3. Case 1. Excised retropharyngeal lymph node: (a) right side; (b) left side.

Case 3: Initial case

A 47-year-old Japanese male presented in July 2010 with complaints of right side neck mass from 12 months before. There was no nodule in the thyroid gland on manual palpation, but a small nodule (15 mm in diameter) in the right lobe of the thyroid gland was detected by ultrasonography. On fine needle aspiration cytology (FNAC) the nodule was strongly suspected to be thyroid papillary carcinoma. CT demonstrated well-enhanced right cervical lymph node metastases and left RPLN swelling. Findings on MRI matched findings on CT.

We performed total thyroidectomy and right side modified radical neck dissection (levels 1–6) and resection of right RPLN via the transcervical approach without mandibulotomy in September 2010. We

performed a temporary tracheotomy for prevention of postoperative airway obstruction. There were no complications after the surgical procedure. The pathological diagnosis of resected RPLN was metastasis of a papillary thyroid carcinoma. The disease was therefore staged as pT1N1bM0. There has been no evidence of tumor recurrence in the 8 months following surgery.

Discussion

The lateral retropharyngeal nodes, also known as the nodes of Rouviere, lie deep in the musculature of the pharynx and medial to the internal carotid artery and sympathetic chain and are usually seen at the level of the arch of C1 [12,13]. RPLN or PPLN swelling is found more frequently for lymphoma and metastasis

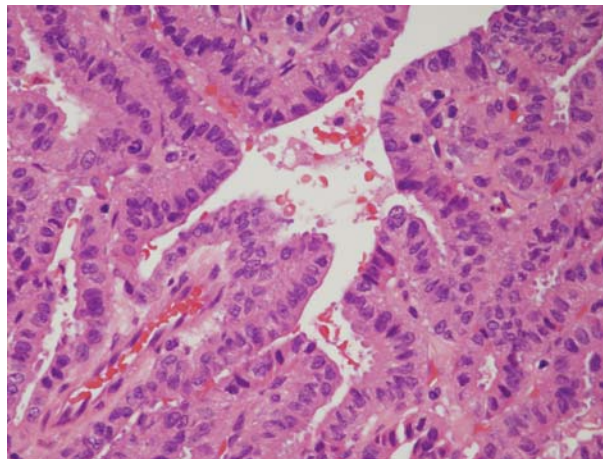


Figure 4. Case 1. The pathological findings for the left side retropharyngeal lymph node reveal well-differentiated papillary carcinoma of the thyroid with typical grooved nuclei (H&E stain, original magnification $\times 140$).

of pharyngeal or sinonasal squamous cell carcinoma (SCC) [8], and is very rare for thyroid papillary carcinoma. Desuter et al. [6] reported that only 0.43% (3/696) of thyroid papillary carcinomas had parapharyngeal node metastasis. During the last two decades, looking at only cases with histologically definite diagnosis by surgery, only 39 reported cases were found in the literature (Tables I and II) [6–15]. Therefore, we reviewed the literature of those 39 cases. The average age was 51.1 years (range 13–84 years). Females were dominant, with 9 males, 21 females, and 9 of unknown gender. This result is consistent with the sex distribution of thyroid papillary carcinomas [1,17]. There were two ways of identification of RPLN or PPLN metastasis: (1) as initial cases of thyroid carcinoma with RPLN or PPLN metastasis, containing occult thyroid carcinoma (Table I), and (2) as a recurrence of previously treated thyroid carcinoma (Table II). The number of initial cases was 15 (of which 10 cases were occult thyroid carcinoma), and there were 24 recurrent cases, showing that recurrence cases were predominant. One of our cases was initial and two were recurrent.

The site of lymph node metastasis was the retropharyngeal space in 14 cases, and the parapharyngeal space in 25. All 39 cases had a unilateral pattern except one metachronous bilateral case (no. 11 in Table II) [11], so there were none with a bilateral pattern like our case 1. As regards the size of lymph node metastasis (maximum diameter), the average for the retropharyngeal space was 24.4 mm and that for the parapharyngeal space was 41.5 mm. There was a tendency for lymph node metastasis of the parapharyngeal space to be larger than that of the retropharyngeal space. On the other hand, the parapharyngeal space and retropharyngeal space are nearby anatomically, and the flow of lymph between these sites is very thick, so it has been reported that retropharyngeal metastasis spreads easily to the parapharyngeal space [18]. If the size of the lymph node is large, it is expected that determination of the origin of the lymph node metastasis (parapharyngeal space or retropharyngeal space) is very difficult, so there is a possibility that the differentiation of the origin of lymph node metastasis was not accurate in some reports.

The thyroid lymphatic drainage is complex, and it can be classified into four main groups: (1) the superomedial route, which terminates in the prelaryngeal node, also called the Delphian lymph node; (2) the superolateral route, which terminates in the upper deep cervical nodes; (3) the inferomedial route draining the trunk and terminating in the pre- and paratracheal lymph nodes (the main route for metastases); and (4) infrolateral draining of the nodes of the supraclavicular and jugulosubclavian nodes [16]. It was

reported that neck dissection and/or metastatic cervical lymph nodes might alter the direction of lymphatic drainage to the retrograde fashion, resulting in the unusual metastasis to the RPLN [12]. All three cases in the present report had regional lymph node metastasis and neck dissection before identification of RPLN metastasis. The other pathway is the direct lymphatic trunk from the upper pole of the thyroid gland to the lateral retropharyngeal nodes, termed the posterosuperior collecting trunk, and this trunk was present in 20% of anatomic dissections [16].

Complete surgical removal is the only curative treatment [6], and there are two main surgical approaches: transcervical and transoral. The traditional approach to RPLN metastases for SCC is a transcervical approach, typically as an extension of a neck dissection and primary tumor resection already being performed [13,19]. Le and Cohen [11] reported that a transcervical approach to the RPLN metastases for papillary thyroid carcinoma was too morbid, because neck dissection may not be part of the initial surgery, and recommended the transoral approach for low morbidity and safety. Shellenberger et al. [13] also recommended the technically feasible and safe transoral approach to the RPLN metastases for papillary thyroid carcinoma. In Tables I and II, there are 27 transcervical approaches, 10 transoral approaches, and 5 are unknown. So the transcervical approach is most common as in cases of metastasis of SCC. There is a subtype pattern of transcervical approach with combined usage of mandibular swing. In our cases, all three were operated by the transcervical approach, and two cases needed combined usage of mandibular swing because of the close adhesion between lymph node metastasis and surrounding tissue. As regards the size of lymph node metastasis (maximum diameter) regionally, the average for the transcervical approach is 44.2 mm, and that for the transoral approach is 24.3 mm. Lymph node metastasis with the transoral approach tends to be smaller than that for the transcervical approach. It has been reported that it is possible to convert from a transoral approach to a transcervical approach during an operation if needed to enhance exposure and safety [14]. So, the transcervical approach is safer and applicable handling.

In cases of recurrence, it may be not so difficult to consider the possibility of PPLN or RPLN metastasis from a papillary thyroid carcinoma from the past medical history. However, in initial cases in which the primary is occult, with isolated lymph node metastasis without cervical lymph node metastases, it may be very difficult. There were six such cases, and all were operated as tumors of the parapharyngeal space. Only one case (16.7%) had undergone total thyroidectomy at the first operation according to the results

of intraoperative frozen-section examination. But another five cases (83.3%) had undergone total thyroidectomy secondarily after first operation of PPLN or RPLN metastasis resection. So it is necessary to consider the possibility of metastasis from a papillary thyroid carcinoma in the differential diagnosis of lymph node swelling in the parapharyngeal and retropharyngeal space, and it is very important to closely examine the thyroid gland preoperatively.

Conclusions

This report supports the reported risk factors (recurrence of neck lymph node metastasis and prior neck dissection) of the RPLN or PPLN metastasis from papillary thyroid carcinoma. In particular, our case 1 is the first report of an operation for bilateral RPLN metastasis and strongly supports this risk factor. Also, regardless of whether they are initial or recurrent cases, those without cervical lymph node metastasis, i.e. isolated RPLN or PPLN metastasis, are most common. So, it is necessary to consider the possibility of metastasis from a papillary thyroid carcinoma in the differential diagnosis of lymph node swelling in the parapharyngeal and retropharyngeal space, and it is very important to carry out close examination of the thyroid gland preoperatively.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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