



Functional and oncological outcomes after retropharyngeal node dissection for papillary thyroid carcinoma

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Abstract

Background Papillary thyroid carcinoma frequently metastasizes to central and lateral neck lymph nodes, but metastasis to retropharyngeal lymph nodes (RPLN) is rare.

Patients and methods We retrospectively reviewed 16 patients with RPLN metastasis of PTC who underwent therapeutic dissection of RPLN metastases.

Results Among 16 patients, 7 patients underwent RPLN dissection with initial surgery and remaining 9 patients as salvage surgery. RPLN metastasis arose unilaterally in 15 patients and bilaterally in 1 patient. Eleven patients showed temporal dysphagia and four patients showed temporal vocal cord paralysis, but both symptoms eventually recovered in all cases. Two patients with salvage RPLN dissection died of distant metastasis and six patients survived with distant metastasis and/or persistent loco-regional disease. Other eight patients have been alive without disease.

Conclusions Although transcervical approach for RPLN metastases of PTC provided acceptable functional and oncological outcomes, half of the patients with RPLN metastasis have had distant metastasis and/or persistent locoregional disease. Indications of surgery for patients with RPLN metastasis need to be performed carefully in consideration of patients' prognosis and quality of life.

Keywords Retropharyngeal node · Metastasis · Thyroid carcinoma · Functional and oncological outcome · Surgery

Introduction

Papillary thyroid carcinoma (PTC) frequently metastasizes to the central and lateral neck lymph nodes (LNs), but it rarely affects the retropharyngeal LNs (RPLNs) [1–10]. RPLN lies within the retropharyngeal space (RPS), a thin virtual space bordered anteriorly by the pharyngeal constrictor muscles and posteriorly by the prevertebral fascia and RPS has been known as a site of lymph node metastases from thyroid cancer. RPLN metastases is classified as N1b in the 8th Edition of Union for International Cancer Control TNM classification of differentiated thyroid cancer because it can affect survival similar to lateral neck LN [11, 12]. Although surgical extirpation is needed for radical treatment

of RPLN metastases, intraoperative injury of the cranial nerves and vessels during dissection might lead to lethal complications and decrease long-term quality of life [1, 10]. Besides, patients with RPLN metastasis of PTC might have locally advanced primary, multiple cervical LN metastases, distant metastasis, and/or a history of surgical treatment for the disease [7]. Thus, a balance between curability by surgery and expected postoperative quality of life should be considered in the decision-making for the treatment of RPLN metastasis. In this study, we retrospectively reviewed data of patients who underwent therapeutic dissection of RPLN metastasis of PTC and evaluated the functional and oncological outcomes to assess the effect of therapeutic RPLN dissection for patients with PTC.

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Patients and methods

Sixteen consecutive patients who underwent surgical resection of metastatic RPLN of PTC between 2003 and 2017 at Kobe University Hospital were retrospectively reviewed. Characteristics of patients, including age, sex, TNM staging, location and size of RPLN metastasis, surgical procedures, postoperative complications, pathological diagnosis, and functional and oncological outcomes, were obtained from medical records. Swallowing and speech functions were evaluated via video-laryngoscope with speech therapist guidance.

Surgical technique of RPLN dissection

All patients underwent RPLN dissection by transcervical approach. As the lateral neck LN metastasis was affected simultaneously in all patients, RPLN dissection was performed following lateral neck dissection (Tables 1, 2). For RPLN dissection, the patient was transnasally intubated and was placed at a head down position. The larynx and posterior wall of the oropharynx were elevated medially, and the posterior belly of the digastric muscle was elevated superiorly. The superior ganglion of the sympathetic trunk and internal carotid artery were identified in the retropharyngeal space (Fig. 1a). Retropharyngeal tissues, including RPLN, were then dissected along the prevertebral fascia and sympathetic trunk. Recently, to put

the operative field in the bright field, an endoscope was used in combination with transcervical approach (Fig. 1b).

Results

Among 16 patients, 7 underwent RPLN dissection as the initial surgery, while the remaining 9 underwent RPLN dissection as a salvage surgery. RPLN metastases were detected by contrast-enhanced computed tomography and/or magnetic resonance imaging in all seven patients who underwent initial surgery. Among them, RPLN metastases were identified by positron emission tomography combined with CT (PET-CT) in two patients. In contrast, all patients who underwent salvage surgery were referred to our institution during follow-up at the other hospitals. The summary of clinical features and functional and oncological outcomes of patients who underwent RPLN dissection as initial surgery and as salvage surgery are shown in Tables 1 and 2, respectively. All patients had simultaneous or previous LN metastasis in the upper jugular chain. RPLN metastases were identified in the ipsilateral LN in 15 patients, and bilateral LN in one patient. A patient with bilateral RPLN metastases (case 15) underwent ipsilateral dissection to prevent death due to bleeding from the metastatic LN and airway obstruction. However, dissection of the contralateral RPLN was delayed to avoid possible postoperative severe swallowing dysfunction since contralateral metastatic RPLNs were small and asymptomatic (Fig. 2). The aforementioned transcervical approach was applied for RPLN dissection in all patients and no patient required mandibulotomy. Postoperative

Table 1 Clinical features and outcome of cases with initial surgery

| Case | Age/gender | TNM | Primary location | Metastasis size/location | Concurrent treatment | RAI | Recurrence | Complication | Status (follow-up period) |
|------|------------|------------|------------------|--------------------------|----------------------|-----|------------|------------------------------------|---------------------------|
| 1 | 83/F | T4a N1b M0 | R. whole | 7 mm/R | TT + bil. ND + Tra | – | DM | Dysphagia (1 M) tracheal stoma | AWD (7 Y) |
| 2 | 57/M | T3 N1b M0 | Bil. multiple | 20 mm/R | TT + bil. ND + MD | – | RPLN | Dysphagia (2 M) | AWD (7 Y) |
| 3 | 46/F | T1b N1b M0 | R. upper | 14 mm/R | TT + ND | + | – | Dysphagia (2 W) | NED (5 Y) |
| 4 | 69/M | T2 N1b M1 | R. middle | 11 mm/L | TT + bil. ND | + | – | Dysphagia (2 W) VC paralysis (4M) | AWD (5 Y) |
| 5 | 72/F | T3 N1b M0 | R. upper | 15 mm/R | TT + ND | – | – | Dysphagia (2 W) SP paralysis (1 M) | NED (5 Y) |
| 6 | 58/F | T3 N1b M0 | R. upper | 20 mm/R | TT + ND | – | – | – | NED (5 Y) |
| 7 | 68/M | T2 N1b M0 | L. upper–middle | 20 mm/L | TT + ND | + | – | Dysphagia (2 W) VC paralysis (3 M) | NED (15 M) |

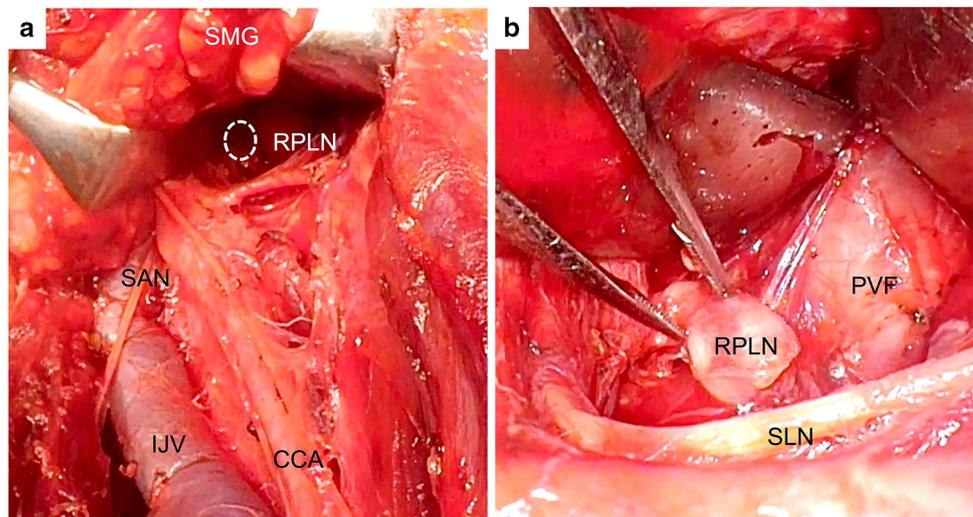
R right, L left, TT total thyroidectomy, bil bilateral, ND neck dissection, Tra tracheal resection, MD mediastinal dissection, DM distant metastasis, RPLN retropharyngeal node, VC vocal cord, SP soft palate, NED no evidence of disease, AWD alive with disease, Y year, M month, W week

Table 2 Clinical features and outcome of cases with salvage surgery

| Case | Age/gender | TNM | Previous treatment (interval) | Metastasis size/location | Concurrent treatment | RAI | Recurrence | Complication (duration) | Status (follow-up period) |
|------|------------|------------|-------------------------------|--------------------------|----------------------|-----|------------|---|---------------------------|
| 8 | 72/F | rT0 N1b M1 | TT+ND (9 Y) | 40 mm/L | ND | + | RPLN+DM | Dysphagia (2 M) | DOD (11 Y) |
| 9 | 72/F | rT0 N1b M0 | HT (11 Y) | 22 mm/L | CT+ND | + | RPLN+DM | VC paralysis (2 M) | |
| 10 | 59/M | rT0 N1b M0 | ST (16 Y) | 20 mm/R | CT+ND | + | – | Dysphagia (2 W) | NED (11 Y) |
| 11 | 73/F | rT0 N1b M0 | TT (16 Y) | 21 mm/L | ND | + | – | – | NED (39 M) |
| 12 | 52/F | rT0 N1b M0 | TT+ND (9 Y) | 8 mm/R | ND | – | LN | VC paralysis (12 M) | AWD (10 M) |
| 13 | 57/F | rT2 N1b M0 | HT (3 Y) | 23 mm/L | CT+ND | + | – | Dysphagia (2 W) SP paralysis (1.5 M) | NED (6 Y) |
| 14 | 70/F | rT0 N1b M0 | TT (5 Y) | 14 mm/R | ND | + | LN | – | NED (5 Y) |
| 15 | 67/F | rT0 N1b M1 | HT (14 Y), CT (11 Y) | 23 mm, 10 mm (bil) | ND | – | LN | Dysphagia (2 W) | AWD (45 M) |
| 16 | 58/F | rT0 N1b M0 | HT (20 Y), CT (16 Y) | 10 mm (R) | bil ND | + | RPLN | – | AWD (53 M) |

R right, L left, TT total thyroidectomy, HT hemithyroidectomy, ST subtotal thyroidectomy, bil bilateral, ND neck dissection, CT complete thyroidectomy, DM distant metastasis, RPLN retropharyngeal node, VC vocal cord, SP soft palate, DOD death of disease, NED no evidence of disease, AWD alive with disease, Y year, M month, W week

Fig. 1 Intraoperative findings in right RPLN dissection. **a** The larynx and posterior wall of the oropharynx were elevated medially, and the posterior belly of the digastric muscle was elevated superiorly. RPLN were identified in the retropharyngeal space. SMG submandibular gland, SAN spinal accessory nerve, IJV internal jugular vein, CCA common carotid artery. **b** Retropharyngeal tissues were dissected along the prevertebral fascia and sympathetic trunk. SLN superior laryngeal nerve, PVF prevertebral fascia



pathological examinations revealed an isolated RPLN metastasis of papillary thyroid carcinoma in all patients. Three patients with initial surgery and seven patients with salvage surgery underwent postoperative radioactive iodine therapy (RAI).

Eleven patients showed temporary dysphagia, but eight patients recovered within 3 weeks after surgery and the other three patients recovered within 2 months (Table 3). Four patients showed temporary vocal cord paralysis due to intraoperative injury of the recurrent laryngeal nerve during

primary tumor resection (three patients) and vagal nerve injury during RPLN dissection (one patient). They recovered within 1 year after surgery. No patients showed other severe complications. Oral intake was initiated on postoperative day (POD) 1–40 (median 7.5 days). Eleven patients required feeding through a nasogastric tube. However, as the oral intake increased, the nasogastric tube was removed from POD 3 to 60 (median 17 days) in all patients. All patients successfully recovered their swallowing function and took normal oral intake from POD 1 to 60 (median 17 days).

Fig. 2 Presentation of the patient with bilateral RPLN metastases (case 15). **a** Flexible fiberoscopy revealed the protrusion of lateral pharyngeal wall. **b** Chest CT revealed multiple lung metastases. **c, d** RPLN metastasis of the right side with the risk of pharyngeal bleeding (arrow)

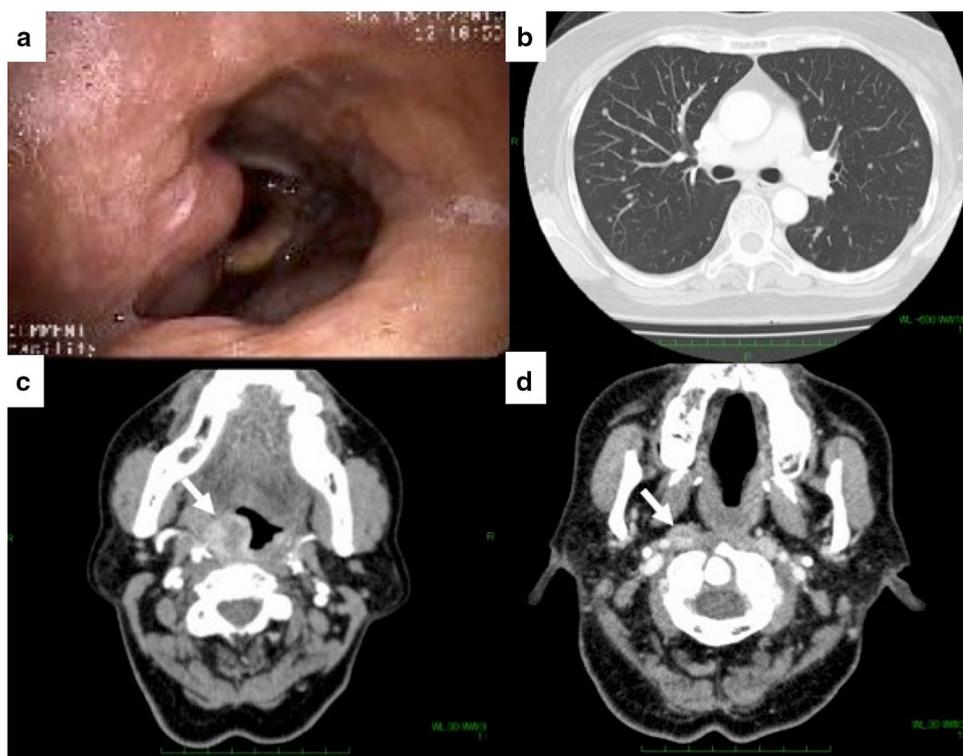


Table 3 Recovery period of postoperative swallowing function

| | Start oral intake (day) | Normal diet intake (day) | Tube feeding period (day) |
|----------------|-------------------------|--------------------------|---------------------------|
| <i>Case 11</i> | <i>1</i> | <i>1</i> | <i>0</i> |
| <i>Case 14</i> | <i>1</i> | <i>1</i> | <i>0</i> |
| Case 6 | 3 | 5 | 0 |
| <i>Case 16</i> | <i>3</i> | <i>5</i> | <i>0</i> |
| <i>Case 9</i> | <i>7</i> | <i>17</i> | <i>0</i> |
| <i>Case 12</i> | <i>5</i> | <i>10</i> | <i>3</i> |
| Case 5 | 2 | 11 | 8 |
| Case 4 | 8 | 22 | 10 |
| Case 10 | 7 | 15 | 14 |
| Case 15 | 10 | 20 | 14 |
| Case 3 | 15 | 17 | 16 |
| Case 13 | 14 | 22 | 17 |
| Case 7 | 11 | 23 | 20 |
| Case 1 | 10 | 54 | 41 |
| Case 2 | 18 | 57 | 49 |
| Case 8 | 40 | 60 | 60 |
| Median | 7.5 | 17 | 12 |

Italic values: cases with salvage surgery (cases 8–16)

Bold: tube feeding periods ≥ 2 weeks (cases 1, 2, 3, 7, 8, 10, 13 and 15)

The median follow-up period after RPLN dissection was 57 (range 10–132) months. Four patients (25%) showed recurrence in the retropharyngeal space (one patient who underwent initial surgery and three patients who underwent salvage surgery). Three patients (19%) showed lateral neck LN metastasis, and another three patients (19%) had distant metastasis. Two patients who underwent salvage RPLN dissection died of the disease due to distant metastasis, and six patients (three patients who underwent initial surgery and three patients who underwent salvage surgery) with distant metastasis and/or persistent locoregional disease survived. The remaining eight patients (50%) were found to have no evidence of the disease (Tables 1, 2).

Discussion

PTC often metastasizes to the central and lateral neck LNs, but it rarely affects the RPLN [1–10]. In 1970, MaCormack reported RPLN metastases in 7 of 313 (2.24%) patients with thyroid carcinoma [1]. However, in a recent large series, Desuter reported that only 0.43% (3/696) of PTC had RPLN metastasis and Wang reported 25 (0.43%) patients (22 patients with PTC) in a series of 5381 patients with thyroid cancer [5, 9].

Three types of presentation of RPLN metastasis were identified: (1) nodal relapse in the RPLN after previous surgical treatment, (2) cervical and parapharyngeal node

involvement as the initial presentation of PTC, and (3) RPLN metastasis as the only nodal involvement at first diagnosis [5, 13, 14]. In our cohort, each type of presentation was found in nine (56%), seven (44%), and zero patients, respectively. Rouvière described the direct lymphatic connection between the thyroid and lateral RPLN in approximately 20% of the anatomic subjects, mainly arising from the posterior aspect of the superior pole of the thyroid [15]. In this study, although four of seven patients with RPLN metastasis at first diagnosis presented tumor in the superior pole of the thyroid, all seven patients had multiple lateral cervical LN metastases. Furthermore, nine patients with recurrent RPLN metastasis after prior surgery had also multiple lateral cervical LN metastases. These results suggest that alteration in the direction of the lymphatic drainage to the retrograde fashion by neck dissection and/or metastatic cervical LNs results in the unusual metastasis to the RPLN, as we previously reported [7].

RPLN metastasis is not necessarily immediately life-threatening, but with progression, it may cause formidable symptoms such as intolerable neck pain, syncope, and/or lower cranial nerve paralysis resulting in poor quality of life. Moreover, RPLN metastasis occasionally involves critical structures, such as the internal carotid artery and jugular vein [8, 10]. McCormack et al. reported that the cause of death among patients with RPLN metastasis was skull base invasion and bleeding from the pharynx [1]. In the present series, one patient presented bleeding from metastatic RPLN invading the oropharyngeal wall. To prevent death due to blood loss and airway obstruction, the ipsilateral metastatic RPLN was surgically resected, and the defect of the pharyngeal wall was reconstructed using radial forearm free flap.

The cervical approach provides a wide exposure of the retropharyngeal space, but the morbidity of such an extensive approach is rarely justified in the treatment of metastatic differentiated thyroid cancer. In terms of the functional outcome after RPLN dissection, a high incidence of postoperative subjective swallowing difficulties ranging from 36 to 68% has been reported among patients who had RPLN dissection for thyroid cancer, possibly due to paralysis of the glossopharyngeal nerve damaged by RPLN dissection [7–10]. Wang et al. reported that 2 (8%) of 25 patients developed permanent dysphagia and Moritani reported that 4 (18%) of 22 patients showed palatal weakness. However, the present study demonstrated that RPLN dissection via a transcervical approach for RPLN metastases of PTC using our surgical technique provided acceptable functional and long-term oncological outcomes. Although temporary swallowing dysfunction and hoarseness were observed in several patients, they eventually resolved in all patients.

Recently, the trans-oral approach to isolated PTC metastases to RPLN has been reported. Some head and neck surgeons reported ultrasonography-guided trans-oral resection

of isolated RPLN metastasis without severe complications [16, 17]. On the contrary, Moore et al. and Goepfert et al. successfully performed trans-oral robot-assisted surgery (TORS) for RPLN metastasis of the recurrent PTC [18, 19]. The trans-oral approach is less invasive and allows adequate access for the excision of an isolated metastatic RPLN from an oncological point and avoids the potential morbidity of other approaches (transcervical or transmandibular). This method is thought to be suitable especially for patients with obesity and patients after neck dissection. However, TORS is limited by its cost, system availability, need for extra training, and the loss of tactile feedback. At present, there are several options for the treatment of metastatic RPLN, including watchful observation, RAI, external irradiation, and more recently tyrosine kinase inhibitors other than surgical extirpation. The indication for surgical resection of RPLN metastasis is controversial. The decision as to whether surgical or non-surgical management of RPLN metastasis will be made depends on the type and extent of the disease, the size of RPLN, as well as patient characteristics such as age, performance status, and comorbidities. However, long-term remission is hardly expected with these non-surgical treatments [20–22]. Two out of seven patients who underwent salvage surgery followed by RAI were relapsed to RPLN. In addition, external radiation and molecular-targeted drug treatment have a risk of complications such as carotid artery rupture when surgery becomes difficult during follow-up. Taken together, our present results suggest that surgical extirpation should be considered the first choice of treatment for RPLN metastasis from PTC.

This study has several limitations. First, we included a relatively small number of patients with RPLN metastasis of PTC who was treated with surgical resection with or without RAI. Therefore, we could not compare the oncological outcomes with those of patients who received other treatment options including watchful observation, RAI alone. Second, the retrospective nature of this analysis introduces some selection biases. We believe that a large number of studies and the uniformity of the surgical approach will lead to robust observations in the future. Lastly, the mean overall follow-up of approximately 5 years might be considered relatively short in the setting of differentiated thyroid cancer, and thus we believe that long-term observation is still necessary.

Conclusion

Although transcervical approach for RPLN metastases of PTC provided acceptable functional and oncological outcomes, half of the patients with RPLN metastasis have had distant metastasis and/or persistent locoregional disease. Indications of surgery for patients with RPLN metastasis

need to be performed carefully in consideration of patients' prognosis and quality of life.

Compliance with ethical standards

Conflict of interest All authors have no conflict of interests to be disclosed on this work.

Ethical approval The study was conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. Ethical approval was obtained from the Ethics Committee of the Kobe University Hospital (#190195) prior to enrolment.

Informed consent Informed consent was obtained from all individual participants included in the study.

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