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Lymph node metastasis in suprasternal space in pathological node–positive papillary thyroid carcinoma

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ABSTRACT

Background: The objective of the current study was to investigate the clinical significance of the suprasternal space lymph node (SSLN) in pathological node-positive (pN+) papillary thyroid carcinoma (PTC) patients.

Method: One hundred and forty patients with pN + PTC who underwent neck dissection were enrolled into this study. SSLN was resected and used as a specimen to investigate the relationship of SSLN with several clinicopathological parameters.

Results: The metastasis rate of SSLN was 20.7%. On univariate analysis, we found that SSLN metastasis was significantly associated with primary cancer site (inferior portion), strap muscle invasion, level III metastasis, Level IV metastasis and lymph node metastasis between sternocleidomastoid and sternohyoid muscles. On multivariate analysis, primary cancer site (inferior portion), strap muscle invasion, Level IV metastasis and lymph node metastasis between sternocleidomastoid and sternohyoid muscles were independent risk factors for SSLN metastasis of PTC.

Conclusion: For pN + PTC patients, special attention should be paid to the issue of SSLN metastasis.

Introduction

Papillary thyroid carcinoma (PTC) accounts for nearly 90% of thyroid malignancies, but with good prognosis, despite an increase in incidence over the past decades [1]. Up to 90% of PTC patients have pathological proven lymph node metastasis [2]. The suprasternal space lymph node (SSLN) has not been sufficiently investigated based on the prevailing literature [3,4]. In the current study, we define SSLN as follows: its anterior boundary consisting of superficial layers of the investing layers of the deep cervical fascia; its posterior consisting of deep layers of the investing layers of the deep cervical fascia and the strap muscles; its superior consisting of upper intersection of superficial and deep layers of the investing layers of the deep cervical fascia; its inferiors consisting of the suprasternal notch (SN) and its external boundary comprising of vertical line of sternoclavicular joint (Figs. 1 and 2). Anatomically, SSLN is located anterior to the strap muscles and does not belong to level VI, since level VI is anterior to the superficial layer of the deep cervical fascia which is the posterior to the strap muscle [5]. Therefore, it is an easily overlooked anatomical area during selective neck and modified neck dissection. However, dissection of SSLN is a routine procedure for obtaining pathological SSLN specimen in our department. So far, only few studies have been performed to investigate the association of clinicopathological parameters and SSLN in PTC patients. In the present study, our aim was to investigate the association between SSLN and clinicopathological features of pathologically node positive (pN+) PTC patients.

Materials and methods

From January 2015 and September 2017, 140 pN + PTC patients who underwent surgeries in the Department of General Surgery, Nanfang Hospital, Southern Medical University were enrolled in this study. All data were extracted from the Pan-cancer database of our department [6–8]. In our institution, patients with clinically positive neck lymph nodes indicated by preoperative imaging or physical examination would receive neck dissections. The standard surgical protocol in the study comprised total thyroidectomy plus

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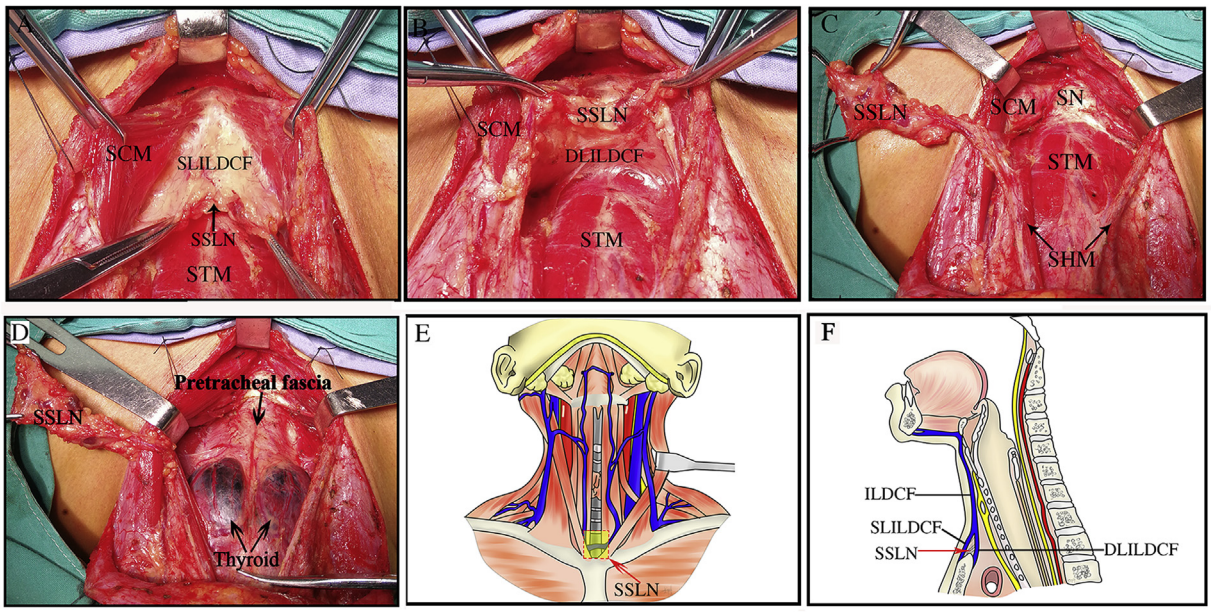

Fig. 1. SSLN coverage area. (A) A superior view of SSLN; (B) A posterior view of SSLN; (C) SSLN was completely resected before dissecting strap muscles; (D) SSLN was resected while thyroid capsule and pretracheal fascia remained intact [thyroid gland was black-stained by nanoparticle carbon]; (E and F) Anatomical diagram of SSLN. SSLN, suprasternal space lymph node; SCM, sternocleidomastoid muscle; SLILDCF, superficial layers of the investing layers of the deep cervical fascia; DLIDCF, deep layers of the investing layers of the deep cervical fascia; SHM, sternohyoid muscle; STM, sternothyroid muscle; SN, suprasternal notch.

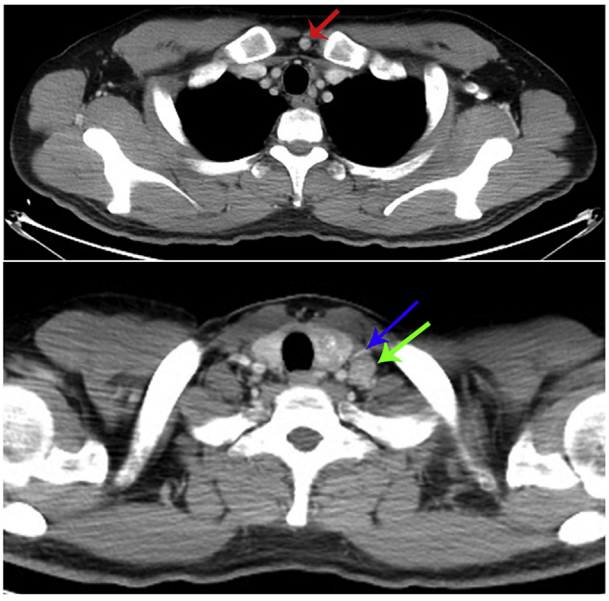

Fig. 2. A CT scan showing enhanced SSLN in PTC in 1 case. SSLN was enhanced (red arrow); lymph node on left neck of Level IV was enhanced (green arrow) which is near the internal jugular vein (blue arrow). CT, computed tomography; SSLN, suprasternal space lymph node.

central neck dissection plus selective or modified radical neck dissection. SSLN was resected and separated as an independent specimen. The inclusion criteria for the patients were as follows: (1) papillary thyroid carcinoma patients with the standard surgical protocol; (2) cervical lymph nodes were PTC metastases proved by postoperative pathology review; (3) the SSLN was resected and separated as a separate specimen by the surgeon; (4) no prior history of radioactive iodine (RAI) treatment, radiotherapy or chemotherapy or neck surgery; (5) the medical history was completely recorded. The informed consents were obtained from all the patients. This study was approved by the ethical review board of Nanfang Hospital, Southern Medical University. All pathological specimens were reviewed by the same experienced pathologists. The site of primary tumor was categorized as upper, middle, or lower third based on the results of preoperative imaging with a longitudinal view. In multifocal cases, the analysis was based on the dominant tumor. All clinical stages were reclassified based on the 8th American-Joint Cancer Classification Tumor-Node-Metastasis (AJCC TNM) staging system. All patients were followed up every 3–5 months postoperatively. Patients with proven histology/cytology results or suspicious lesion according to imaging studies were defined as recurrence [9].

All clinicopathological features, including age, gender, primary tumor site, diameters of the primary tumor, strap muscle invasion, central neck lymph node metastasis, lateral neck lymph node metastasis, lymph node metastasis between sternocleidomastoid and sternohyoid muscles, and initial or re-operative treatment, were analyzed to explore the relationship with SSLN. The chi-square or Fisher's exact test were used as appropriate. Multivariate logistic regression analysis was performed to identify risk factors for SSLN metastasis of PTC. $P < 0.05$ was considered as statistically significant. All statistical analysis was performed using SPSS 22.0 (IBM Corporation, Armonk, New York, USA).

Result

All patients underwent a successful surgical treatment, and no recurrence was observed during postoperative follow-up with a median period of 23 months (range, 12–44). Postoperative pathological examination revealed that 29 patients (20.7%) were pN1a and 111 patients (79.3%) were pN1b. The median number of total resected lymph nodes in level II, III, IV, Vb, VI and lymph node metastasis between sternocleidomastoid and sternohyoid muscles were 5 (range, 3–7), 6 (range, 4–10), 12 (range, 6–15), 8 (range, 5–9), 6 (range, 4–18) and 3 (range, 0–4), respectively. The median number of SSLN was 2 (range, 0–5). The metastasis rate of SSLN was

Table 1
Relationship between SSLN and clinicopathologic features of 140 PTC patients.

Variables	SSLN		OR(95%CI)	P value
	Positive (n = 29)	Negative (n = 111)		
Gender				0.81
Male	9	32	1.21(0.69–2.68)	
Female	20	79		
Age				0.72
<55	12	50	0.86(0.23–1.28)	
≥55	17	61		
Diameter of neoplasm				0.33
<1 cm	6	15	1.10(0.46–2.21)	
≥1 cm	23	96		
Site of neoplasm				0.01*
Inferior portion	14	27	5.16(2.11–12.60)	
Upper-Middle portion	15	84		
Strap muscle invasion				0.02*
Yes	6	7	3.87(1.19–12.61)	
No	23	104		
Reoperation				0.31
Yes	10	28	1.89(0.78–3.31)	
No	19	83		
Level II metastasis				0.47
Yes	12	38	1.12(0.69–1.99)	
No	17	73		
Level III metastasis				
Yes	25	75	3.13(1.01–9.64)	0.04*
No	4	36		
Level IV metastasis				0.01*
Yes	25	68	3.80(1.24–11.70)	
No	4	43		
Level VI metastasis				0.11
Yes	23	100	1.76(0.89–2.67)	
No	6	11		
Level Vb metastasis				0.29
Yes	11	31	1.26(0.79–3.35)	
No	18	80		
LNSS metastasis				<0.001*
Yes	22	14	25.93(9.16–73.38)	
No	7	97		

Abbreviation: SSLN, suprasternal space lymph node; PTC, papillary thyroid carcinoma; LNSS, lymph node between sternocleidomastoid and sternohyoid muscle; OR, odd ratio; CI, confidence interval; *, statistically significance.

20.7% (29/140) in this cohort, and the central neck lymph node metastasis rate was 87.9% (123/140). As shown in Table 1, we analyzed the relationship between SSLN metastasis and clinicopathological features of 140 PTC patients. We found that SSLN metastasis was significantly associated with primary cancer site (inferior portion, $P = 0.01$), strap muscle invasion ($P = 0.02$), level III metastasis ($P = 0.04$), Level IV metastasis ($P = 0.01$) and lymph node metastasis between sternocleidomastoid and sternohyoid muscles ($P < 0.001$). However, no significant association was identified between SSLN metastasis and gender, age, the diameter of neoplasm, reoperation, level II, level Vb and level VI metastasis.

To identify risk factors for SSLN metastasis of PTC, variables with statistically significant differences were included in a multivariate model (Table 2). We found the following risk factors for SSLN metastasis: primary cancer site (inferior portion) with an OR (95% confidence interval [CI]): 1.34 (1.03–3.19); strap muscle invasion with an OR (95% CI): 1.03 (1.01–2.84); Level IV metastasis with OR (95% CI): 1.78 (1.15–3.36); and LNSS metastasis with an OR: 3.97 (1.92–5.87).

Table 2
Multivariate analysis of the risk factors for SSLN metastasis for PTC.

Variables	OR(95%CI)	P value
Site of neoplasm	1.34(1.03–3.19)	0.04*
Strap muscle invasion	1.03(1.01–2.84)	0.04*
Level III metastasis	1.11(0.78–1.56)	0.56
Level IV metastasis	1.78(1.15–3.36)	0.02*
LNSS metastasis	3.97(1.92–5.87)	<0.001*

Abbreviation: SSLN, suprasternal space lymph node; PTC, papillary thyroid carcinoma; LNSS, lymph node between sternocleidomastoid and sternohyoid muscle; OR, odd ratio; CI, confidence interval; *, statistical significance.

Discussion

The suprasternal space, also called the space of Burns, consists of superficial and deep layers of the investing layers of the deep cervical fascia above the manubrium of the sternum [10]. It has little areolar tissue and few lymph nodes. The rate of lymph node metastasis of thyroid or head and neck cancer in suprasternal space has been investigated by few studies [3,4]. In their description of the lymph node between sternocleidomastoid and sternohyoid muscles in clinically node-positive PTC patients, Sun et al. [4] mentioned that lymph node between sternocleidomastoid and sternohyoid muscles is a part of the suprasternal space. Homma et al. [3] reported 2 cases of PTC patients with lymph node metastasis between sternocleidomastoid and sternohyoid muscles. In our medical practice, we found that the medial edge of the sternohyoid muscle is an anatomical boundary between SSLN and lymph node between sternocleidomastoid and sternohyoid muscles. Therefore, we defined SSLN as a distinct area from lymph node between sternocleidomastoid and sternohyoid muscles and suprasternal space in the current study. To the best of our

knowledge, this is the first cohort involved study focusing on the correlation between SSLN metastasis and the clinicopathological parameters of PTC patients.

Central neck compartment (level VI) lymph nodes are the most commonly affected nodal regions in PTC patients, which include prelaryngeal, pretracheal, and tracheoesophageal groove node basins [11–14]. In this study, we did not found any significant association between SSLN and level VI metastasis. Anatomically, SSLN is located anterior to the strap muscles and does not belong to level VI [5], and surgeons can remove this part before dissecting thyroid capsule and pretracheal fascia (Fig. 1D). Furthermore, the internal border of level III and IV is the antero-lateral border of the sternocleidomastoid muscle (SCM). Thus, SSLN located inside of the internal border is not covered by the lateral neck areas. Therefore, like the lymph nodes between sternocleidomastoid and sternohyoid muscles, SSLN can not be included in the standard anatomical subdivision of neck areas, and to some extent, may easily be overlooked when patients are undergoing neck dissection.

In the current study, we found that the SSLN was associated with level IV and lymph nodes between sternocleidomastoid and sternohyoid muscles metastasis in the multivariate analysis. However, level VI was not associated with SSLN metastasis in the univariate analysis. Sun et al. [4] reported that lymph node metastasis between sternocleidomastoid and sternohyoid muscles is caused by the increasing tumor load after lateral neck metastasis or the communication between the superficial or deep anterior cervical chain and the deep lateral cervical chain. Homma et al. [3] speculated that the fibrofatty tissues, including metastasis from level IV, may gradually spread into lymph nodes between sternocleidomastoid and sternohyoid muscles and SSLN little by little due to the daily motion of the neck. We also found that the tumors located at the inferior portion of thyroid had a higher SSLN metastasis rate compared with those located at the upper or middle portion of the thyroid. These results indicate that SSLN is more frequently associated along with level IV due to jugular lymphatic vessels crossing many levels originating from the inferior thyroid gland, which is consistent with previous studies, including that of Sun et al. [4].

We observed that strap muscle invasion was also an independent risk factor for SSLN metastasis of PTC in the multivariate analysis. We postulate that the spread of invasion of lymphatic drainage on the superficial level of the strap muscle may be an alternative route of SSLN metastasis.

Among the 140 patients, the metastasis rate of SSLN was 20.7%, which is similar to the metastasis rate of lymph node between sternocleidomastoid and sternohyoid muscles (22.6% among 115 patients) reported by Sun et al. [4]. Moreover, we found that SSLN was significantly associated with lymph node metastasis between sternocleidomastoid and sternohyoid muscles in this cohort. We speculate that the communicating branches of anterior jugular vein and external jugular vein which crossed lymph node between sternocleidomastoid and sternohyoid muscles and SSLN may explain this finding. Besides, reoperation was not associated with SSLN metastasis indicating that it was not caused by implantation. Taken together, we believe that the resection of SSLN should be considered for pN + PTC, especially for patients with suspected level IV metastatic lesions, neoplasm site in the inferior portion of the thyroid gland, and strap muscle invasion.

There are several limitations to the current study. First, the retrospective nature of the study may lead to some inevitable bias. Second, because this study involved a small sample size of patients from a single-institution with a short period of follow-up, the results may not accurately reflect the prognostic value of SSLN in PTC patients. A prospectively designed study with a larger cohort enrolled and long time follow-up period is warranted to further evaluate the clinical significance of SSLN in PTC patients.

Conclusion

In summary, we investigated, for the first time, the association of SSLN metastasis with the clinicopathological features of pN + PTC patients. For PTC patients with suspected level IV metastatic lesions, tumor site in the inferior portion of the thyroid gland or strap muscle invasion, greater attention should be paid to the issue of SSLN metastasis.

Conflicts of interests

All authors declared no potential conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2019.07.034.

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