NECK ULTRASONOGRAPHY FOR THE EVALUATION OF THE ETIOLOGY OF ADULT UNILATERAL VOCAL FOLD PARALYSIS

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Abstract: Background. An extralaryngeal neoplasm involving the vagus nerve and recurrent laryngeal nerve must be excluded when adult unilateral vocal fold paralysis is diagnosed.

Methods. Between 2004 and 2009, 53 adult patients with unilateral vocal fold paralysis received neck ultrasonography. Patients with laryngeal/hypopharyngeal cancer or with previously known cancers of the head and neck, thyroid, esophagus or lung, or with known etiology or trauma were excluded from this study.

Results. We included 26 men and 27 women. Ultrasonography revealed 16 patients (30%) having subclinical tumors, including thyroid papillary carcinoma in 7 patients, vagus nerve schwannoma in 2 patients, nodular goiter in 2 patients, malignant nodes in the lower neck in 4 patients, which were metastasized from lung cancer in 3 patients, esophageal cancer in 1 patient, and cervical esophageal cancer in 1 patient.

Conclusion. Neck ultrasonography is useful to detect subclinical neoplasia, causing unilateral vocal fold paralysis. Thyroid cancer is the most common neoplastic etiology of adult unilateral vocal fold paralysis. © 2011 Wiley Periodicals, Inc. Head Neck 34: 643–648, 2012

Keywords: ultrasound; thyroid cancer; recurrent laryngeal nerve; vagus nerve, esophageal cancer; lung cancer

Vocal fold paralysis is not uncommon in clinical practice.1,2 In adult patients, most vocal fold paralysis presents unilaterally, and 26% to 48% are caused by surgical procedures, such as thyroid, carotid, and heart surgeries.2–5 About 16% to 21% of vocal fold paralysis is idiopathic without apparent cause.3–5 With the exception of laryngeal or hypopharyngeal cancer, about 12% to 32% of unilateral vocal fold paralyses are related to clinically undetected tumors in the skull base, neck, thyroid gland, mediastinum, or lung.3–5 This is because the recurrent laryngeal nerve responsible for the movement of the vocal folds originates from the vagus nerve, which travels from the brainstem through the skull base into the carotid sheath of the neck, branches upward around the subclavian artery in the right side and the aortic arch in the left side to the tracheoesophageal groove and then enters the larynx at the cricothyroid junction.3–5 Because most of these subclinical tumors are malignant and may be locoregionally advanced with major nerve involvement, patients will die of the disease if misdiagnosed.

Because of different incidences of cancers in different countries, the most common neoplastic causes of unilateral vocal fold paralysis vary by country. Nevertheless, malignancies of the thyroid gland, lung, and esophagus are the most common.3–5 Therefore, several diagnostic tests such as chest X-ray, CT, and MRI from the skull base to the chest are frequently used to detect these subclinical tumors.6 However, their utilities in clinical practice are still debated. Because a high-resolution ultrasound examination can show the thyroid gland, tracheoesophageal groove, cervical vagus nerve,7 the supraclavicular regions, and the part of the cervical esophagus very clearly,8,9 an ultrasound examination can exclude thyroid cancer and can potentially reveal the presence of tumors involving the vagus nerve in the neck and the recurrent laryngeal nerve in the tracheoesophageal groove. In addition, fine-needle aspiration or core needle biopsy can be done with ultrasound guidance for obtaining cytological or histopathologic diagnoses at the same time.10

In this study, we used ultrasound examination as the first tool to evaluate the thyroid gland, the
tracheoesophageal groove, the entire jugular chain, and the supraclavicular regions to exclude the pathologic lesions in the thyroid gland, the lesions along the tracheoesophageal groove and the cervical portion of the vagus nerve, and the lesions in the supraclavicular regions that extend from the infracavicular regions such as for lung and esophageal cancers.

**PATIENTS AND METHODS**

Patients older than 20 years old who had been newly diagnosed with unilateral vocal fold paralysis without known causes at the Department of Otolaryngology of the National Taiwan University Hospital between May 2004 and December 2009 were enrolled in this study. This study was reviewed and approved by the institutional review board at the National Taiwan University Hospital. The exclusion criterion included patients with primary laryngeal/hypopharyngeal cancer or with previously known cancers mentioned in the exclusion criterion, 158 patients with known iatrogenic etiology, 59 patients with relevant trauma that caused vocal fold paralysis, and 37 patients without evaluation of causes of vocal fold paralysis, a total of 53 adult patients with unilateral vocal fold paralysis without apparent causes were included in this study. The clinical data and the final diagnoses of these 53 patients are shown in Table 1. They included 26 male patients and 27 female patients. Their ages ranged from 22 to 88 years old, with a median age of 62 years. Vocal fold paralysis occurred in the right side in 15 patients (28%) and in the left side in 38 patients (72%). Among these 53 patients, ultrasound examination found that 16 patients (30%) had ultrasonographically significant tumors in the neck, which included 9 lesions in the thyroid gland (Figure 1), 3 lesions in the supraclavicular region (Figure 2), 1 lesion in the lower jugular chain (Figure 3), 1 infiltrative lesion posteriorly to the thyroid gland (Figure 3), and 2 fusiform lesions located between the common/ internal carotid artery and internal jugular vein (Figure 4). Of the 9 nodular lesions in the thyroid gland, 7 lesions were papillary carcinomas and the other 2 lesions were benign nodular hyperplasia, confirmed by cytologic examination obtained from fine-needle aspiration under ultrasound guidance or pathologic examination of surgical specimen. The 3 lesions in the supraclavicular regions were malignant lymph nodes, which were squamous cell carcinoma confirmed by cytologic examination and metastasized from lung cancer revealed by subsequent chest CT. The malignant lymph nodes in the lower jugular chain and the ill-defined lesion posterior to the thyroid gland were squamous cell carcinoma also confirmed by cytologic examination and originated from esophageal cancer, which was demonstrated by transnasal esophagogastroduodenoscopy and subsequent chest CT (Figure 3). The 2 lesions between the carotid artery and internal jugular vein originated from the cervical vagus nerve. One of them was confirmed by surgery, and the other was stable in regular follow-ups for 3 years. Regarding the results of the other examinations, chest CT revealed 2 esophageal tumors and 3 lung tumors and esophagram/esophagogastroduodenoscopy revealed 2 esophageal tumors in total.

Comparing the clinical parameters between patients with and without subclinical neoplastic causes for vocal fold paralysis (Table 2A), there were

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>62 y (22–88)</td>
</tr>
<tr>
<td>Sex M:F</td>
<td>26:27</td>
</tr>
<tr>
<td>Side of vocal paralysis</td>
<td></td>
</tr>
<tr>
<td>Right side</td>
<td>15 (28%)</td>
</tr>
<tr>
<td>Left side</td>
<td>38 (72%)</td>
</tr>
<tr>
<td>Causes of vocal fold paralysis</td>
<td></td>
</tr>
<tr>
<td>Neoplasm causes</td>
<td>16 (30%)</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Esophageal cancer</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Thyroid benign tumor</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Vagus nerve schwannoma</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>37 (70%)</td>
</tr>
</tbody>
</table>

*Abbreviations: M, male; F, female.*
no statistically significant differences in age \( (p = .63) \), sex \( (p = .24) \), and affected side of vocal fold paralysis \( (p = .75) \). Comparing these 3 clinical parameters between the patients with thyroid neoplasm and with non-thyroid neoplasm (Table 2B), there were no statistically significant differences in age \( (p = .79) \), sex \( (p = .15) \), and affected side of vocal fold paralysis \( (p = 1.00) \).

**DISCUSSION**

Unilateral vocal fold paralysis may be due to intralaryngeal causes such as laryngeal/hypopharyngeal cancer, or other neoplastic causes that paralyze the recurrent laryngeal nerve or the upstream vagus nerve (which runs from the brainstem and skull base to the neck and upper mediastinum), such as skull...
base tumor, thyroid cancer, lung cancer, esophageal cancer, and metastases to the mediastinum.3–5 Despite that the occurrence of subclinical neoplasm resulting in unilateral vocal fold paralysis is decreased to around 15% in the recent decades with the early diagnosis of cancers, imaging studies for the detection of these subclinical tumors are still suggested because these underlying causes are potentially lethal if misdiagnosed.3–5 Despite great variability in clinical practice among otolaryngologists, chest X-ray, CT of the chest with/without the neck, and MRI from the skull base to the chest are the most common imaging studies for the detection of the subclinical tumors that are responsible for vocal fold paralysis.6

MRI has a good differential power for the diagnosis of tumors in the brainstem and the skull base, but the subclinical tumors in these regions, which are responsible for unilateral vocal fold paralysis in adult patients, are quite rare. In addition, thyroid cancer is

FIGURE 3. Case 1 (A–C). (A) On ultrasonography with transverse view, an ill-defined, heterogenous hypoechoic solid lesion “T” was located posteriorinferior to the right thyroid gland and abutted the trachea. (B) Transnasal esophagogastrroduodenoscopy (EGD) revealed an ulcerative tumor in the cervical esophagus, which was confirmed as esophageal cancer. (C) CT scan revealed a large tumor “T” in the lower anterior neck posterior to the thyroid gland and the trachea, which was compatible with ultrasound findings. Case 2 (D–F). (D) A round, enlarged, heterogeneously hypoechoic lymph node “T” with mixed capsular and punctate vascular pattern was noted in the lower jugular chain (level IV). (E) Transnasal EGD revealed a protruding tumor in the upper esophagus. (C) CT scan finding was compatible with ultrasound findings. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIGURE 4. (A) On ultrasonography with transverse view, a round, well-defined, hypoechoic, solid tumor “T” was located between the internal jugular vein “V” and the common carotid artery “A” of the right side of the neck. (B) On ultrasonography with longitudinal view, a fusiform solid tumor “T” was continued with the vagus nerve “VN” on the upper end. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
1 of the most common neoplastic causes of adult unilateral vocal fold paralysis; however, MRI is less helpful for the differential diagnosis of thyroid tumors. From a recent evidence-based medicine review for radiographic testing, MRI is not supported by the literature for the evaluation of adult unilateral vocal fold paralysis compared with the CT scan. A CT scan of the chest can demonstrate tumors in the lung and mediastinum very well and seems to be supported by a moderate amount of level IV literature; however, a CT scan of the neck is of questionable utility in the differential diagnosis of thyroid tumors and causes radiation exposure of the patients.

Ultrasonography is the most sensitive and accurate imaging study for the differential diagnosis of thyroid tumors compared with thyroid scintigraphy, CT, and MRI. In general, a thyroid tumor with hypoechoic or marked hypoechoic, ill-defined margins, microcalcification or macrocalcification, and taller than wide appearance is highly suspicious for malignancy. Despite the fact that the recurrent laryngeal nerve is not visible on ultrasonography even with a 14 MHz transducer, ultrasonography can show very clearly the plane between the thyroid gland and the cervical esophagus, where the recurrent laryngeal nerve is located. Therefore, ultrasonography can reveal any tumors in this region that may involve the recurrent laryngeal nerve. From this series, we found 9 thyroid tumors (Figure 1) and 1 cervical esophageal cancer (Figure 3) abutting or blurring this plane, which may imply compression or invasion of the recurrent laryngeal nerve. Specifically, for the thyroid tumors in this series, all showed a deep location in the posterior part of the thyroid lobe, near or abutting the trachea and the esophagus, which may be the reason why the initial presentation was unilateral vocal fold paralysis, rather than palpable anterior neck mass.

As suggested by other investigators, besides the thyroid gland, ultrasonography can check the other neck regions. Despite the fact that structures in the neck are complex, higher-frequency transducers in the range of 7 to 14 MHz applied in neck ultrasonography successfully offer an optimal visualization of the anatomy of the neck region, especially the cervical spaces anteriorly to the prevertebral fascia, and an optimal resolution of lesions smaller than 3 mm. Therefore, on ultrasonography, the lymph node–rich cervical spaces in the supraclavicular region and along the carotid artery and internal jugular vein can be seen very well. In addition, ultrasonography also demonstrates the cervical vagus nerve, which is shown as a small oval to round hypoechoic spot of 2 to 3 mm in the axial view located between the common carotid artery and the internal jugular vein below the carotid bifurcation (level III and level IV) and lateral to the internal carotid artery above the carotid bifurcation (level II). Therefore, any abnormal lesions along the jugular chain directly involving the cervical vagus nerve can be seen very well. The space-occupying hypoechoic well-defined lesion between and splaying the carotid artery and the internal jugular vein in the axial view and with a fusiform shape connecting to the vagus nerve in the longitudinal view should be considered as a neoplasm of vagus nerve origin, such as vagus nerve schwannoma with hypovascularity or normal vascularity, and paraganglioma of the vagus nerve if marked hypervascularity within the tumor shown by Doppler ultrasound imaging. Sometimes malignancies below the clavicle, such as lung, breast, and esophageal cancers, metastasize to the supraclavicular region or the jugular chain in the neck, which can also be detected on ultrasonography of the neck. In addition, the cervical esophagus can be seen through the thyroid gland window, especially in the left side. A head turning of 45 degrees bilaterally with mild flexion of the neck is a useful maneuver for a comprehensive ultrasound examination of the cervical esophagus. On ultrasonography, the cervical esophagus seems like a multi-layer tubular structure beneath the thyroid gland and the trachea. Any abnormal lesions in the cervical esophagus with extraluminal extension can be seen by ultrasonography as well. Therefore, high-resolution ultrasonography can evaluate the thyroid gland, supraclavicular region, the entire jugular chain, and cervical vagus nerve to exclude pathologic lesions in the thyroid gland such as thyroid cancer, to exclude metastatic lesions from below the clavicle such as lung, breast, or esophageal cancer, and to exclude any diseases involving the cervical vagus nerve.
Fine-needle aspiration or core needle biopsy of the suspicious lesion for cytologic or pathologic examination under ultrasound guidance done simultaneously is one of the advantages of ultrasonography over other imaging studies. With the exception of schwannoma, fine-needle aspiration cytologic examination is a very useful method to distinguish between malignant and benign lesions in the thyroid gland and the neck. Furthermore, it is also able to detect papillary carcinoma, squamous cell carcinoma, and adenocarcinoma with high accuracy, which is helpful for determining the origin of a malignancy. Therefore, high-resolution ultrasonography of the thyroid gland and the neck with guided aspiration cytology/biopsy is a good comprehensive imaging study for the evaluation of neoplastic causes of adult unilateral vocal fold paralysis.

Some have advocated a site or sex-specific evaluation of suspicious malignancies as a cause of adult unilateral vocal fold paralysis. However, in this case series, we did not note any differences in age, sex, or side of vocal fold paralysis for patients with subclinical tumors compared with those without subclinical tumors. Because ultrasonography of the thyroid and the neck is not difficult or time-consuming, and it can be performed in the clinic office, we recommend that all patients with vocal fold paralysis receive ultrasonography of the thyroid gland and the neck as the first-line imaging study, especially when the patient has no history of surgery or trauma despite the still small case number.

Despite the fact that ultrasonography of the neck has many advantages over other imaging studies, ultrasonography still has some limitations. First, the upper part of the level II neck may be too deep, and there are too many interfaces between tissues for a high-resolution ultrasound wave to pass. Therefore, a CT or MRI of the skull base may be needed if the skull base lesion is still concerned. Second, not all infraclavicular lesions involving the recurrent laryngeal nerve in the thoracic level have metastatic lesions in the neck. Therefore, a chest X-ray is still suggested at a minimum as the first-line imaging study along with ultrasonography of the neck to exclude obvious lesions in the thorax. Taking together, CT scan or MRI from the brainstem, skull base to the chest may be performed to definitely exclude all possible occult tumors responsible for vocal fold paralysis when ultrasonography as the first-line modality dose not revealed any significant lesion in the neck.

CONCLUSION

About 30% of adult unilateral vocal fold paralysis without apparent cause is caused by subclinical tumors. Ultrasonography is a useful tool to detect subclinical neoplasia in the thyroid gland and the neck, which can cause unilateral vocal fold paralysis. In this case series, thyroid papillary carcinoma involving the recurrent laryngeal nerve was the most common neoplastic etiology of adult unilateral vocal fold paralysis.

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REFERENCES