Clinical Research

Analysis of cervical and retropharyngeal lymph node metastases in the patients with hypopharyngeal carcinoma with computed tomography and magnetic resonance imaging

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[Abstract] Background and Objective: Hypopharyngeal carcinoma has a high risk for early regional lymphatic dissemination. However, reports about regional lymph node metastases, especially retropharyngeal lymph node metastases, are rare. This research explored the spread of hypopharyngeal carcinoma, especially metastases of the retropharyngeal lymph nodes by studying computed tomography (CT) and magnetic resonance imaging (MRI) images. Methods: The CT/MRI images of 88 patients with pathologically confirmed hypopharyngeal carcinomas that were performed at our hospital between August 2000 and March 2009 were analyzed retrospectively. The interrelations among local stage and lymph nodes in various regions were analyzed by χ² test and multivariate logistical regression. Results: The rate of regional lymph node metastasis for all patients was 73.9%, and the highest rates of positive lymph nodes were at levels IIa (61.4%), IIb (44.3%), and III (37.5%). Metastases to levels I, IV, V, and VI were rare, as were retropharyngeal lymph-node metastases, which were always combined with metastases at levels II and III. Univariate analysis showed that level-IV metastases correlated to metastases at levels Ib and III; retropharyngeal lymph node metastases were correlated to level IIb and bilateral cervical lymph node metastases. Multivariate analysis showed that level-VI metastases correlated to level IV and that retropharyngeal lymph-node metastases correlated to bilateral cervical lymph node metastases. Conclusions: Regional lymph node metastases in patients with hypopharyngeal carcinoma follow some regulations, and skip metastasis is rare. The highest rates of positive lymph nodes are at levels II and III. Bilateral lymph node metastases may be a risk factor for retropharyngeal lymph node metastases.

Key words: Hypopharyngeal neoplasm, cervical neoplasm/lymph node, retropharyngeal lymph node, CT, MRI

Hypopharyngeal carcinoma has a substantially poorer prognosis of all malignant tumors of the head and neck, with metastasis to regional lymph nodes even at early stages. However, the metastatic profile of regional lymph nodes in hypopharyngeal carcinoma is only generally reported in the published reports of head-and-neck tumors1,2. Dedicated studies about regional lymph node metastasis in patients with hypopharyngeal carcinoma are hardly seen, and research on retropharyngeal lymph node metastasis is even rarer. Therefore, by analyzing computed tomography (CT) and magnetic resonance imaging (MRI) data, our study investigated cervical and retropharyngeal lymph node metastases and their correlations in patients with hypopharyngeal carcinoma to provide an evidence basis for clinical treatments.

Material and Methods

Clinical data

By searching the system of medical chart data at our hospital, data on 207 patients with pathologically confirmed hypopharyngeal carcinoma between August 2000 and March 2009 were collected. Among these patients, 114 had pretreatment CT data and another 11 had pretreatment MRI data. Among the 114 patients with pretreatment CT, 6 patients had other concomitant head-and-neck tumors and 31 had an inadequate scanning range. After excluding the patient data mentioned above, 77 patients with CT data and an adequate...
scanning range and 11 patients with MRI data were included in the study. These cases included 66 patients with pyriform sinus carcinomas, 20 with posterior hypopharyngeal wall carcinomas, and 2 with postcricoid carcinomas. Of these patients, 84 were men, 4 were women, and they were aged between 25 years and 79 years, with a median age of 55 years. Regarding the pathologic profiles, the cancer was rated as squamous epithelial carcinoma in 68 patients and as carcinoma in situ in 20 patients. According to the 2002 tumor-node-metastasis (TNM) staging system of the International Union Against Cancer (UICC), the T and N staging of 88 patients is detailed in Table 1.

Table 1 T and N stage distribution of 88 patients with hypopharyngeal carcinoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>0</td>
<td>8</td>
<td>3</td>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>N1</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>N2</td>
<td>2</td>
<td>7</td>
<td>8</td>
<td>33</td>
<td>50</td>
</tr>
<tr>
<td>N3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>19</td>
<td>14</td>
<td>52</td>
<td>88</td>
</tr>
</tbody>
</table>

Scanning
During CT scanning, the patient was in a supine position, with the neck bending backward to ensure that the cervical vertebra were parallel to the examination couch. The patient was told to breathe normally when scanning from the skull base to the clavicular head was performed.

Of these patients, 7 were immediately given contrast-enhanced scanning by the bi-spiral scanner Elscint Twin Flash CT. Both the slice gap and thickness were 5 mm, with a pitch of 1:1.

In the other 70 patients, plain scanning and intravenous contrast-enhanced scanning were given in a routine fashion by PHILIPS Brilliance 16 CT. After the plain scanning, contrast-enhanced scanning was performed on the same slices. Both the slice gap and thickness were 5 mm and reconstruction slice thickness was 2 mm. After reconstruction and fusion, the images were reviewed and analyzed by DICOM software.

A total of 11 patients were given MRI scanning. Scanning was performed using a SE sequence transversely, sagittally, and coronally. The scanning range started from the base of the skull and ended at the lower margin of the clavicular head. Variables for the scanning were: $T_1$WI TR/TE = 400–600/15–25 ms; $T_2$WI TR/TE = 1800–3000/90–150 ms; slice thickness/slice gap = 5 mm/0.5 mm. All the patients were given 0.1 mmol/kg of Gd-DTPA via intravenous injection after plain scanning. Then contrast-enhanced $T_1$WI scanning was performed transversely, sagittally, and coronally on the same slices as in the plain scanning. Images were reviewed and measured by DICOM software.

Image reviewing and diagnosis
In this study, the images were reviewed by two to three clinical physicians together with imaging specialists. Tumor site and the scope of involvement were observed and the staging was determined. Diagnostic criteria for metastatic lymph nodes were: (1) on transversal images, the maximum diameters were $\geq 5$ mm for retropharyngeal lymph nodes, $\geq 11$ mm on level IIa, and $\geq 10$ mm on other levels; (2) on enhanced scanning, the boundary of the lymph node was circularly enhanced, along with the central necrotic area, regardless of the size of the lymph nodes; (3) lymph nodes were either confluent or showed more than 3 lymph nodes in the lymph drainage area of the primary tumor, and the diameters of these lymph nodes were between 8–10 mm on the transversal image; and (4) extracapsular invasion of lymph nodes was present.

Statistical methods
The correlations between lymph-node metastases in the various levels were tested by $\chi^2$ test and logistic multivariate analysis. $P < 0.05$ indicated statistical significance. All the statistical analyses were performed with SPSS15.0 software.

Figure 1 CT images of the lymph node metastases of hypopharyngeal carcinoma
A, enhanced CT shows the left retropharyngeal lymph node (3 mm × 3 mm) in front of the carotid sheath; B, enhanced CT shows the bilateral retropharyngeal lymph node intumesce (11 mm × 10 mm) with ring reinforcement; C, enhanced CT shows bilateral level-IIa lymph node intumesce, the sizes are 9 mm × 11 mm and 9 mm × 9 mm, respectively.
Results

Metastasis in regional lymph nodes

Among the 88 patients with hypopharyngeal carcinoma, the incidence of cervical lymph-node metastasis was 73.9% (65/88). The most frequently seen metastatic sites were levels IIa and IIb. The distribution of lymph-node metastases in different cervical levels is shown in Table 2.

Table 2 The distribution of regional lymph node metastases in 88 patients with hypopharyngeal carcinoma

<table>
<thead>
<tr>
<th>Level</th>
<th>Lymph node metastasis [patient No. (%)]</th>
<th>Combined with the other level metastasis [patient No. (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ib</td>
<td>3 (3.4)</td>
<td>3 (100.0)</td>
</tr>
<tr>
<td>IIa</td>
<td>54 (61.4)</td>
<td>42 (77.8)</td>
</tr>
<tr>
<td>IIb</td>
<td>39 (44.3)</td>
<td>36 (92.3)</td>
</tr>
<tr>
<td>III</td>
<td>33 (37.5)</td>
<td>30 (90.9)</td>
</tr>
<tr>
<td>IV</td>
<td>8 (9.1)</td>
<td>8 (100.0)</td>
</tr>
<tr>
<td>Va</td>
<td>2 (2.3)</td>
<td>2 (100.0)</td>
</tr>
<tr>
<td>Vb</td>
<td>1 (1.1)</td>
<td>1 (100.0)</td>
</tr>
<tr>
<td>VI</td>
<td>5 (5.7)</td>
<td>5 (100.0)</td>
</tr>
<tr>
<td>Retropharyngeal</td>
<td>12 (13.6)</td>
<td>12 (100.0)</td>
</tr>
</tbody>
</table>

Analysis of the correlations between lymph node metastases of different levels

Since patients in our study had mostly locally advanced disease, with less frequent occurrences of disease at early stages (T1 and T2), stages T1 and T2 were combined as local early-stage disease, and stages T3 and T4 were considered local advanced-stage disease. Included in the statistical analyses were local staging, bilateral cervical lymph-node metastasis, and lymph-node metastases at various levels.

The $\chi^2$ test showed a significant correlation between level IIb and both bilateral cervical lymph node metastasis and retropharyngeal lymph node metastasis ($P = 0.021$ and $P = 0.028$, respectively), and between level Ib and lymph node metastases at levels III and IV ($P = 0.021$ and $P = 0.001$, respectively).

Logistic multivariate analysis showed a significant correlation between bilateral cervical lymph node metastasis and retropharyngeal lymph node metastasis ($P = 0.016, OR = 4.846, 95\% CI = 1.348–17.420$). Level-VI lymph node metastasis was significantly correlated to level-IV lymph node metastasis ($P = 0.033, OR = 8.556, 95\% CI = 1.190–61.512$).

Discussion

Metastasis in the cervical lymph nodes is extremely common in patients with hypopharyngeal carcinoma. Previous data mainly derive from pathologic analysis on surgical samples, but large-scale case reports have been rare. In addition, since the retropharyngeal lymph nodes are generally not included in the lymph-node dissection for hypopharyngeal carcinoma, study reports about these are even rarer.

With the progress in modern imaging in recent years, CT and MRI have been widely used in detecting and diagnosing malignant tumors of the head and neck. Relevant studies suggest that CT and MRI can clearly reveal the condition of cervical lymph nodes, and their accuracy in determining metastasis therein can be as much as 80%–90%. At present, CT- or MRI-based evaluations of regional lymph node metastasis in patients with hypopharyngeal carcinoma is a considerably reliable and feasible method.

Our study revealed that the incidence of lymph node metastasis in patients with hypopharyngeal carcinoma was 73.9%, and that lymph node metastasis at the various levels was not correlated to local staging, which was consistent with the published literature. This suggested that, for hypopharyngeal carcinoma, metastasis could occur even at early stages, and thus patients with both early-stage and advanced disease should be given preventive treatment for metastasis at regional lymph nodes.

Some scientists have also studied the pattern and distribution of metastasis in the cervical lymph nodes of patients with hypopharyngeal carcinoma. Candela et al. summarized the data from Memorial Sloan-Kettering Cancer Center and demonstrated that level-I and level-V lymph node involvement was always accompanied by lymph-node involvement at other levels. Moreover, only one (0.3%) patient had skip metastasis. Buckley et al. suggested that level-I and level-V lymph node metastasis was not common even in N+ patients. Yu et al. analyzed the surgical samples from the radical neck dissections of 32 patients with laryngeal carcinoma and 18 patients with hypopharyngeal carcinoma (that is, a total of 50 patients) whose cervical lymph node metastasis was confirmed by palpation, CT scanning, or both, and found that cervical lymph node metastasis was mainly distributed at levels II and III, less frequently at levels IV and VI, and rarely at levels I and V. Shah found that, in patients with cN0 disease, pN+ was only seen at levels II and III, and lymph nodes at levels I and V were not found to be involved. In patients with cN1–cN3 disease, pN+ lymph nodes could be found at levels I-V, but mostly at levels II and III. The French Head and Neck Study Group 18 studied 313 patients from 12 hospitals and demonstrated that upper cervical metastasis was most common (55%), followed by midcervical (28%), and lower cervical metastasis (17%). In addition, some scientists also reported that cervical lymph node metastasis was mainly distributed at levels II and III in patients with N0 hypopharyngeal carcinomas and at levels II, III, and IV in patients with N+ disease. It is therefore considered that patients with N+ disease should be treated with radical cervical lymph-node dissection, while patients with N0 disease can be treated with regional (levels II and III) lymph-node dissection.

Among the patients in this study, the highest incidence of lymph node metastasis was seen at levels IIa, IIb, and III (61.4%, 44.3%, and 37.5%, respectively). Of patients with lymph node metastasis, the incidence at level IIa was 83.1% and level IIb was...
of the posterior pharyngeal wall, accounting for 30.0% of all carcinomas of the posterior pharyngeal wall. Another 6 patients had pyriform sinus carcinomas, accounting for 9.2% of all pyriform sinus carcinomas. All the retropharyngeal lymph node metastasis was seen in patients with N2 disease and was accompanied by lymph node metastasis at other cervical levels. Univariate analysis showed significant correlations between retropharyngeal lymph node metastasis and level-IIb and bilateral cervical lymph node metastasis, while multivariate analysis suggested significant correlations between bilateral cervical lymph node metastasis and retropharyngeal lymph node metastasis. This indicated bilateral cervical lymph node metastasis was a risk factor for retropharyngeal lymph node metastasis. But some scientists have also suggested that retropharyngeal lymph node metastasis could occur even in patients with hypopharyngeal carcinoma without lymph node metastasis at other cervical levels. This idea was based on the published studies by Mancuso et al. and Hasegawa et al. In 1983, Mancuso reported that, among 11 patients with retropharyngeal lymph node metastasis, 2 had hypopharyngeal carcinomas, 1 had T4N3 disease with deep superior cervical lymph node metastasis, 1 had retropharyngeal lymph-node recurrence after total laryngectomy for hypopharyngeal carcinoma, without lymph node metastasis at other cervical levels. However, local tumor conditions and regional invasion at the time of first diagnosis were not specified in the study report. Another patient with retropharyngeal lymph node metastasis but no metastasis at other cervical lymph nodes in the study was a breast cancer survivor. In 1994, Hasegawa reported that one out of two patients with pN0 oropharyngeal carcinoma had positive retropharyngeal lymph nodes, but none of the three patients with pN0 hypopharyngeal carcinoma had positive retropharyngeal lymph nodes. It was also noted in the study report that no retropharyngeal lymph node metastasis was found in patients with cN0 disease. The authors believe this evidence is not enough to support that retropharyngeal lymph node metastasis can be found even in patients with hypopharyngeal carcinoma without lymph node metastasis at other cervical levels.

In conclusion, regional lymph node metastasis can be seen even in the early stages of hypopharyngeal carcinoma, with certain metastatic patterns but rarely skip metastasis. The highest incidence of lymph node metastasis is seen at levels II and III, but no patients with lymph node metastasis solely in levels I, IV, V, or VI, or the retropharyngeal area were found. Bilateral cervical lymph node metastasis may be a risk factor for retropharyngeal lymph node metastasis. The study results have certain implications for selecting the scope of clinical treatment for patients with hypopharyngeal carcinoma and shall encourage further investigation.

References


