UNKNOWN PRIMARY CARCINOMA HEAD & NECK- INCIDENCE IN METASTATIC CERVICAL LYMPHADENOPATHY AT A TERTIARY CARE HOSPITAL

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Abstract

Objective: To find the incidence of unknown primary carcinoma head & neck in patients presenting with metastatic cervical lymphadenopathy.

Methodology: This case-control study was conducted at the Department of ENT, Head & Neck Surgery, Pakistan Institute of Medical Sciences, Islamabad. The duration of the study was three years from April 2013 to April 2016. A total of 86 patients were included in the study. Detailed history, examination, laboratory tests, imaging studies, endoscopies and biopsies of patients included in the study were performed. The frequency of patients with no primary lesion was noted.

Results: 86 cases were included in our study. Obvious lesions were found in 67.4% patients, while in 32.5%, no primary lesion was found after complete workup. Nasopharynx was the most frequent primary site involved. Level II nodes were the most frequent neck nodes involved. 7% of patients remained undiagnosed after complete workup.

Conclusion: The incidence of unknown primary carcinoma was found to be seven percent among the patients who presented with metastatic cervical lymphadenopathy.

Key Words: Unknown Primary, Neck Metastasis, Cervical lymphadenopathy, Neck nodes, Squamous cell carcinoma, Incidence, Head & Neck

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Introduction

Several etiologies are being involved in the metastatic neck lymphadenopathy, which is a joint clinical presentation. These etiologies range from benign self-limiting reactive hyperplasia to malignant conditions.¹ It accounts for 2-9% of head & neck malignancies and commonly occurs to nodal level II & III. Squamous cell carcinoma is the most common histological tumor type. Pathophysiology of unknown primary carcinoma is the same as that of known carcinoma of head & neck.

The neck and head regions have an enormously loaded lymphatic drainage. Both superficial and deep, the neck is accompanied by various lymph node groups.²³ Various body parts are studied for lymphatic drainage comprising nose, face, scalp, nasopharynx, sinuses, salivary gland, and upper aero-digestive tract.⁴ The knowledge of regional drainage of a specific group of the lymph node is inevitable for ENT surgeons.⁵ A diagnostic dilemma is observed in patients having persistent lymph node enlargement.⁶ Routine lab investigations or clinical grounds alone cannot be sufficient for its diagnosis.⁷
Meaningful treatment can only be started after a definite diagnosis based on a series of investigations. These investigations may include clinical history, physical examination, laboratory investigations, various imaging studies, endoscopies, biopsies and FNAC (fine needle aspiration cytology). FNAC is supposed to be the first line and most reliable and accurate investigation for metastatic cervical lymphadenopathy. Unnecessary surgical procedures are avoided by using FNAC. However, in some selective cases, a surgical biopsy is still required in order to decide. In spite of development in the diagnostic workup for malignancies, investigations are sometimes unable to find a primary site of origin for several patients with metastatic cancer. This is often referred to as occult primary or unknown primary carcinoma. Identification of the primary tumor has important clinical implications when a patient presents with a UPC. Localization allows for decreased morbidity, targeted therapy, and improved survival. The diagnostic investigation remains paramount, considering that treatment outcomes depend on whether the primary tumor is detected in UPCs. Transoral laser microsurgery and transoral robotic surgery, are surgical methods touted to increase the detection of primary tumors.

In the current study number of cases with metastatic cervical lymphadenopathy with no known primary site at presentation and after complete workup was noted. The objective of this study was to evaluate the frequency of unknown primary carcinoma in patients presenting with metastatic cervical lymphadenopathy.

**Materials and Methods**

This study was conducted at the Department of ENT, Head and Neck Surgery, Pakistan Institute of Medical Sciences, Islamabad. It was a case-control study, and the duration of the study was three years from April 2013 to April 2016.

All patients presenting to ENT OPD whom complaint of cervical lymphadenopathy with no other ENT related symptom and has metastatic neck disease confirmed on FNAC or biopsy were included in the study. Lymphomas, infective pathologies, patients with recurrent disease, post-radiotherapy, post-chemotherapy, oral cavity tumors, suprACLAVICULAR nodes secondary to breast, lung, and abdominal pathologies, all these cases were excluded from the study.

After written informed consent, a detailed history was taken, a thorough physical and ENT examination, especially screening the oral cavity, oropharynx, larynx, nose, and nasopharynx was carried out. Methodical neck assessment for lymph nodes was carried out. If more than one lymph node was enlarged, their number and level were also recorded. Routine investigations included FBC, ESR, Ultra Sound neck and X-Ray chest were done. Radiologic investigations, CT scan/ MRI, were done. Panendoscopies were carried out, including nasopharyngoscopy, direct laryngoscopy, pharyngoesophagoscopy, and bronchoscopy. Where lesion/ mass was found, a biopsy was taken from that site. In cases where there was no visible lesion, biopsies from putative sites were taken, i.e. Nasopharynx, Pyriform sinus, Base of the tongue, and Tonsils (tonsillectomy). In the case of pyriform, biopsies were taken from both sides. Wedge biopsies were taken from the base of the tongue, and bilateral tonsillectomies were done.

**RESULTS**

We included 86 cases in our study, with a male/female ratio 52:34, respectively. The age range was between 30-70, with a mean age of 54. Visible lesions were found in 58 (67.4%) patients, while in the rest (32.5%), no lesion/ abnormality of mucosa was found after complete workup. Nasopharynx was the most frequent primary site involved, followed by pyriform sinus in all patients (Table I). In patients with no obvious lesion, nasopharynx was still the most frequent site involved, followed by tonsils (Table I). In 6 (7%) cases, we did not find primary lesion after complete workup (Table I).

**Figure 1: Frequency of UPC and site distribution**
Unknown Primary Carcinoma Head & Neck- Incidence....  

Table I: Frequency of various primary head & neck sites involved

<table>
<thead>
<tr>
<th>Site</th>
<th>Obvious lesion</th>
<th>No obvious lesion</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharynx</td>
<td>18</td>
<td>09</td>
<td>27</td>
<td>31.4%</td>
</tr>
<tr>
<td>Pyriform sinus</td>
<td>16</td>
<td>03</td>
<td>19</td>
<td>22.1%</td>
</tr>
<tr>
<td>Tonsils</td>
<td>09</td>
<td>07</td>
<td>16</td>
<td>18.6%</td>
</tr>
<tr>
<td>Base of tongue</td>
<td>06</td>
<td>03</td>
<td>09</td>
<td>10.4%</td>
</tr>
<tr>
<td>Supraglottis</td>
<td>05</td>
<td>00</td>
<td>05</td>
<td>5.8%</td>
</tr>
<tr>
<td>Post cricoid</td>
<td>03</td>
<td>00</td>
<td>03</td>
<td>3.5%</td>
</tr>
<tr>
<td>Post. Pharyngeal wall</td>
<td>01</td>
<td>00</td>
<td>01</td>
<td>1.1%</td>
</tr>
<tr>
<td>No Evidence</td>
<td>00</td>
<td>06</td>
<td>06</td>
<td>7%</td>
</tr>
<tr>
<td>Total No of Cases</td>
<td>58</td>
<td>28</td>
<td>86</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table II: Number of unilateral, bilateral and contralateral metastatic cervical lymphadenopathy cases

<table>
<thead>
<tr>
<th>Laterality</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral</td>
<td>73</td>
<td>84.9%</td>
</tr>
<tr>
<td>Bilateral</td>
<td>11</td>
<td>12.8%</td>
</tr>
<tr>
<td>Contralateral</td>
<td>02</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

Table III: Case distribution according to neck level involved

<table>
<thead>
<tr>
<th>Neck Level</th>
<th>No of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>02</td>
<td>2.3%</td>
</tr>
<tr>
<td>II</td>
<td>44</td>
<td>51.1%</td>
</tr>
<tr>
<td>III</td>
<td>30</td>
<td>34.8%</td>
</tr>
<tr>
<td>IV</td>
<td>04</td>
<td>4.6%</td>
</tr>
<tr>
<td>V</td>
<td>06</td>
<td>7%</td>
</tr>
</tbody>
</table>

Table IV: Number of cases and N-stage at presentation

<table>
<thead>
<tr>
<th>N-Stage</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>25</td>
<td>29%</td>
</tr>
<tr>
<td>N2</td>
<td>58</td>
<td>67.5%</td>
</tr>
<tr>
<td>N3</td>
<td>03</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

Patients with unilateral neck node/ nodes were 73 (84.8%), while 11 (12.8%) presented with bilateral metastatic neck disease. Two (2.3%) patients presented with left-sided neck node and carcinoma were found on the contralateral side of tonsil (Table II). Among 11 cases of bilateral metastatic neck disease, 6 (54.5%) were primarily from the nasopharynx, 2 (18.1%) each from the base of the tongue, and post cricoid region and 1 (9.1%) from supraglottis. 48 (55.8%) cases presented with left-sided metastatic neck disease while 25 (29%) with right-sided.

Level II lymph nodes were the most frequently, 44 cases (51.1%), involved lymph nodes followed by level III, 30 cases (34.8%) (Table III). Most of the patients presented with N2 cervical lymphadenopathy, i.e. 58 (67.4%) patients, 25 (29%) presented with N1, and 3 (3.5%) patients with N3 disease (Table IV).

The frequency of unknown primary carcinoma was 6 (7%) in all cases after complete workup (figure 1).

**DISCUSSION**

The unknown primary presenting with metastatic carcinoma is an unusual scenario and accounts for 2-3% of patients with head and neck region malignancy, according to Motz K et al. In our study, the incidence of unknown primary was 7% in all patients presenting with metastatic cervical lymphadenopathy. Muller von der et al., in his study, mentioned that metastatic cervical lymphadenopathy commonly occurs to level II and III. In our study, out of 86 patients, metastasis to levels II and III was (51.1%) and (34.8%) respectively. Of 86 patients, male to female ratio was 52:34 (60.5%;39.5%) which is similar to other studies done by Suresh et al. and Pepper et al. Obvious lesions were found in 58 patients while in the rest, no lesion/ abnormality of mucosa was found after complete workup. These results are in accordance with the work done by some other researchers, i.e. Adesuwa et al. Nasopharynx was the most frequent primary site involved followed by pyriform sinus in all patients. Khan et al. also recorded similar findings.

Computed tomography and magnetic resonance imaging of the head & neck has diagnostic value and will identify a primary lesion in many cases. In our study, both these investigations helped diagnose the cases. PET-CT was not included in our study consid-
erating unavailability, costly nature of investigation, controversial, and heterogeneity of results between individual studies. According to Fogarty et al. 25. FDG-PET did not add significantly to conventional comprehensive investigations.

All patients presenting with cervical lymphadenopathy should be seen thoroughly; a detailed history and examination should be done. Personal history including drinking, smoking, sniff, paan, betel nuts chewing, should be ruled out. All head & neck regions, including scalp, upper respiratory and digestive tracts, ears, and nose, should be examined in detail. Special consideration of the anatomical distribution of lymphatics should be taken. As different neck levels are associated with different regions in terms of lymphatics, so regions related to particular lymph nodes should be evaluated. Fine needle aspiration cytology of abnormal lymph nodes should be performed to see the nature of the lesion. It can be done under ultrasound guidance. If results are not sure, then ultrasound-guided core biopsy or open biopsy may be required. It is considered that in metastatic squamous cell carcinoma if definitive treatment is undertaken soon afterward, excision biopsy will not compromise the outcome.12,13

Panendoscopies should be performed, which include nasopharyngoscopy, direct laryngoscopy, esophagoscopy, and bronchoscopy. If a lesion is found, a biopsy from the lesion has to be taken and sent for histopathological analysis. Treatment should be planned according to the histopathology report. If there is no primary lesion after all the workup, then biopsies from the base of the tongue, nasopharynx, pyriform fossae, and tonsils should be taken. The nasopharynx is of great importance as these cases have the potential to spread to cervical lymph nodes at an early stage. Tonsillotomy is recommended as this is the site for about 25% of tumors.14-16 In routine ipsilateral tonsillotomy to nodal involvement has been recommended; however, the contralateral spread may be as high as 10% from occult lesions, so bilateral tonsillotomy has better diagnostic yield. Many occult primaries of tongue base are submucosal, and biopsy is challenging to perform. A wedge biopsy should be performed to get a better yield. In our study, we performed bilateral tonsillectomies, and it increased the diagnostic yield. Similarly, with a wedge biopsy, the diagnostic yield was improved.

CONCLUSION

The incidence of unknown primary carcinoma was found to be seven percent among the patients who presented with metastatic cervical lymphadenopathy.

References


