



Cervical Lymph Nodes: A Hotbed for Metastasis of Malignancy

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Abstract

Aim and Objectives: Aim of this study was to find semblance between cervical lymph node metastasis and various malignancies. Objectives were to estimate the incidence of neck node metastasis (NNM) from primary head and neck malignancies and incidence of metastatic involvement of supraclavicular lymph node from malignancies other than head and neck region.

Materials and Methods: Retrospective data was obtained from Hospital Management Software system from March 2012 to March 2017. 4000 patients were analysed and based on inclusion and exclusion criteria 68 patients were identified with clinically palpable cervical lymph nodes without the presence of obvious primary lesion anywhere in the body.

Results: 41.7% patients had lung cancer as a primary malignancy, 17.64% had breast carcinoma and 20.58% patients were with head and neck malignancy other than oral cavity malignancy. 7.3% of patients had primary malignancy in cervix. 2.94% patients had endometrial malignancy and renal malignancy each. Primary malignancies of gall bladder, pancreas, skin, prostate and vagina constituted 1.47% for each type.

Conclusion: Understanding the pertinence of cervical lymph nodes specially supraclavicular lymph nodes with different primary tumor sites will help us to plan interdisciplinary management of patients and also to correlate with prognosis of patient.

Keywords: Neck node; Metastasis; Distant primary; Lymphatics

Introduction

Cervical lymph node metastasis most commonly develop from oral cavity malignancies but, not always. Apart from oral malignancies, squamous cell carcinoma of the upper aerodigestive tract, salivary gland malignancies, thyroid cancers and skin cancers of head and neck region can portend as cervical nodal metastasis [1]. Lymphoma and tuberculosis also expresses in cervical lymph nodes, so they should always be taken into consideration as a differential diagnosis. Besides all this, infraclavicular malignancies can also present as neck node metastasis. Thus cervical nodal metastasis in absence of obvious primary on head and neck examination should alarm physician to suspect for distant primary tumor. Prompt diagnostic evaluation of such patients would amend the prognosis to some extent. Incidence of neck node metastasis from distant primary site is about 1% which includes breast, lung, gastrointestinal tract, genitourinary tract and sometimes central nervous system malignancies. This retrospective study is aimed at finding incidence and correlation between supraclavicular lymph node and malignancies originating from lung, breast, renal cell carcinoma, endometrium etc. Till date there are no reported studies where incidence of metastasis to cervical lymph nodes from distant primary site is compared.

Materials and Methods

Retrospective data was obtained from Hospital Management Software system from March 2012 to March 2017. After screening records of 4000 patients, 68 patients were identified with cervical lymph node metastasis without the primary malignancy of oral cavity. Based on the available data patients with cervical lymphadenopathy were categorized into 13 groups comprising of head and neck malignancy other than oral cavity primary, lung, breast, gall bladder, vagina, endometrium, cervix, prostate, skin, pancreas, kidney, tuberculosis and lymphomas (Hodgkins and Non Hodgkins). Patients with final diagnosis of lymphoma and tuberculosis were excluded from study. Incidence and distribution of expression of cervical lymph node metastasis was studied in all patients.

The data was tabulated in Microsoft excel software 2013 and subjected for statistical analysis

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Table 1: Frequency distribution of primary cancers.

Type of Primary	N	%
Lung	28	41.17
Breast	12	17.64
Head and Neck	14	20.58
Cervix	5	7.3
Endometrium	2	2.94
Kidney	2	2.94
Gall Bladder	1	1.47
Pancreas	1	1.47
Skin	1	1.47
Prostrate	1	1.47
Vagina	1	1.47
Total	68	100

using IBM SPSS 23 (IBM Inc, Chicago). Descriptive for mean age, Frequencies and percentages for categorical data was done. One sample T Test was done to evaluate the significance of the data.

Results

Out of 68 patients 41.7% (n=28) patients had lung primary, 17.64% (n=12) had breast carcinoma, 20.58% (n=14) patients were with head and neck malignancy other than oral cavity malignancy. 7.3% of patients had primary malignancy in cervix (n=5). 2.94% patients had endometrial and renal malignancy each (n=2). Primary malignancies of gall bladder, pancreas, skin, prostate and vagina constituted 1.47% for each type (n=1) (Table 1).

Our data suggested that primary tumor from lung has higher predilection rate 26.4 %, followed by breast which is 11.32%. Figure 1 is showing distribution of neck node metastasis from distant primary sites. There is statistically significant difference in the side of involvement of metastatic cervical lymph nodes ($p < 0.001$). Left supraclavicular node (L-SCLN) metastasis is more predominant (45.58%; n=31), followed by right supraclavicular node metastasis (R-SCLN) (27.95%; n=15). Figure 2 is showing comparison of levels of cervical lymph node involvement. Level I lymph node metastasis was found in carcinoma of breast, larynx and tonsils (4.41%; n=3). Metastatic involvement of level II lymph nodes (7.35%; n=5) was lung, prostate, breast and skin malignancy. Level III lymph node metastasis was found in one case of carcinoma breast (1.47%; n=1). Level IV involvement (20.58%; n=14) was seen with primary malignancies of gall bladder, renal cells, lung, breast, cervix and nasopharynx. R-SCLN metastasis was also found in patients with lung primary (8.82%; n=6), carcinoma of vagina (1.4%; n=1) and carcinoma cervix (1.4%; n=1) patients. Table 2 shows comparative distribution of expression of metastatic disease in cervical lymph nodes. P-value of < 0.001 was highly indicative of statistically significant difference in the distribution of expression of metastatic disease among the cervical lymph nodes.

Discussion

Several theories have been put forth to understand the lymphatic pathway of neck region, still the exact pathway remains controversial. In this retrospective study, we have analysed 4000 patient in last 5 years; of which 150 patients were diagnosed as unknown primary with neck node metastasis, but patients with hodgkins lymphoma and pulmonary koch's were excluded hence total number of patients

Table 2: Comparison of metastatic involvement of cervical lymph nodes from distant primary.

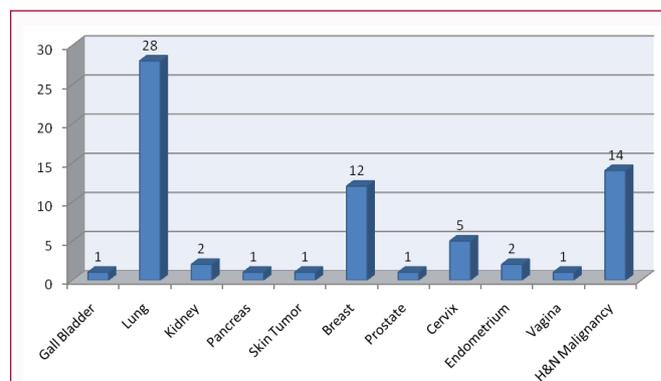
Level	No. of Patients (n)	No. of Patients (%)
I	3	4.41
II	5	7.35
III	1	1.47
IV	14	20.58
SCLN-L	31	45.58
SCLN-R	14	22.05
Total:	68	100
P value	0.001**	

** : Highly significant ($P < 0.001$)

analysed were 68. Neck Node Metastasis (NNM) from malignancies other than head and neck region is complex and intriguing to study. Malignancies arising from oral cavity, lateral part of nasal cavity usually present level IB lymphadenopathy. Malignancies involving nasopharynx, oropharynx, hypopharynx, and larynx present level II Lymph node metastasis. Salivary gland malignancies especially parotid glands are associated with level II neck node metastasis. Level IA i.e. submental nodal metastasis is often associated with malignancies from anterior oral cavity, anterior nasal cavity. In our study 20.58% patients presented with supraclavicular lymph node enlargement, which had primary tumor in head and neck region.

Primary tumours other than head neck region have different mechanism of metastasis. Anatomic location and function of thoracic duct plays important in spread of metastatic disease from infraclavicular primary sites. It lies at the junction of the left subclavian vein and Internal Jugular Veins (IJV). The duct enters the thorax through the aortic opening of the diaphragm and travels superiorly in the posterior mediastinum. Lymphatic flow toward the left neck begins in the superior mediastinum. Thus left supraclavicular lymph nodes receive lymphatic drainage from thorax, abdomen and pelvis [2].

Lymphatic system of breast constitutes axillary lymph nodes and internal mammary nodes. Sometimes breast lymph is also drained into supraclavicular, cephalic, posterior, intercostals, sub-diaphragmatic and sub peritoneal lymph nodes. Occasionally lymphatic vessels may travel along the cutaneous branches of intercostal vessels towards the posterior intercostal lymph nodes situated near the rib head, from where lymphatic flow travels towards the thoracic duct. Tanis et al. suggested that the superficial lymphatic vessels from breast

**Figure 1:** Overall incidence of distribution of distant primary with neck node metastasis.

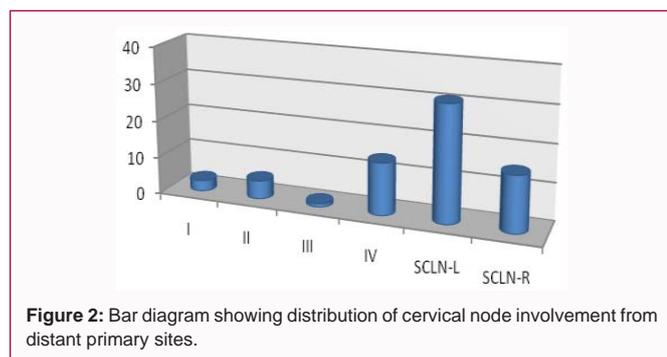


Figure 2: Bar diagram showing distribution of cervical node involvement from distant primary sites.

are sometimes situated more superiorly thus they may drain into supraclavicular lymph nodes. Although the incidence of carcinoma breast metastasizing to neck is low (2.3% to 4.3%) [3-6]. It is considered to be the most common primary malignancy metastasizing to cervical lymph nodes. In our study breast carcinoma is third most common malignancy to metastasizing to cervical lymph nodes. 17.64% (n=12) patients had cervical lymph node metastasis with left SCLN, level V, level II, level I and level III involvement in descending order.

Amongst all lung cancers only large cell carcinoma and adenocarcinoma can metastasize to supraclavicular lymph nodes. Metastatic supraclavicular lymph nodes involvement by pulmonary malignancies is straight away categorized as N3 and is considered to be stage IIIB disease, where as involvement of other cervical lymph nodes is classified as M1 and considered as stage IV disease [7]. Davis et al. [8] reported 1.5% to 32% incidence of neck node metastasis from lung primary. In our study, involvement of cervical lymph node from lung cancer was 41.17%. We observed lung to be the commonest malignancy to express in cervical lymph nodes. Maximum involvement was seen in left SCLN, followed by right SCLN, level IV, level II and level V in descending order. There was no patient with level I involvement from lung malignancy.

Renal Cell Carcinoma (RCC) rarely shows neck node metastasis, reported incidence is only 1% [9]. In our study 1% (n=2) patients had cervical lymph node metastasis from renal cell carcinoma. Overall incidence of distant metastasis in renal cell carcinoma (RCC) is 30% to 40% [10]. It metastasizes to lungs (76%), regional lymph nodes (66%), bone (42%), and liver (41%) [11] and 1.5 to 3.5% to cervical lymph nodes [12]. The mechanism of metastasis to head and neck region can be explained by Batson's paraspinal plexus consisting of valve-less venous anastomosis with prevertebral, vertebral, and epidural systems which result in little resistance to the spread of tumor emboli. Vertebral venous plexus bypasses the pulmonary venous system hence results in head and neck region metastasis without involvement of lung [12-14]. We had one case with level IV lymphadenopathy and other one was with left SCLN.

Cervical and uterine cancer metastasizes to para-aortic, mediastinal and supraclavicular nodes and also to lungs, liver and skeleton. Batson's plexus was first proposed to explain metastasis of disease to head and neck region but more recently vider et al pointed out that the vertebral venous system may be more significant pathway for tumor spread when there is obstruction of pelvic vein, as seen in pelvic malignancy. Fisher and fisher tumor cells traverse the lymph nodes and gain access to venous system via lymphatico-venous communication within nodes or via thoracic duct [15]. In our study percentage of cervical and uterine cancer metastasizing to cervical nodes was 2.94% each and the residence for metastasis was level IV,

V and left SCLN.

Carcinoma of the prostate is common malignancy affecting elderly men. It may spread by local extension, lymphatic or haematogenous dissemination [16]. Reported incidence of prostate cancer metastasizing to supraclavicular lymph nodes is in $\leq 0.5\%$ of cases [17,18]. There were 1.47% (n=1) patients who had prostatic malignancy and presented with supraclavicular lymphadenopathy in this study. So it is recommended to consider prostate cancer as a differential diagnosis in cases of unknown primary with neck node metastasis. Testicular cancers can also rarely metastasizes to cervical region incidence being 2.6% to 4.5%, with a neck swelling as prominent feature in 5% of cases [19]. In our study we have not found any case of testicular cancer and supraclavicular lymph node metastasis.

Gall bladder cancer rarely metastasizes to head and neck region, which was also reflected in our study with percentage of 1.47%. Metastasis from cutaneous malignancies to head and neck region is less than 1% [20]. We have found 1.47% incidence of cervical metastasis from cutaneous malignancy.

Our data suggested that primary tumor from lung has higher predilection rate 26.4 % for cervical lymph node metastasis, followed by breast (11.32%). Highest incidence of cervical lymph node metastasis is seen in LSCLN followed by R SCLN and Level LN's.

Conclusion

Cervical lymph nodes are byway for metastasis from various distant primary sites. Though the incidence is less, one should inscribe about distant primary in order to plan interdisciplinary management at the earliest and to improve the prognostic outcomes in tern reflecting into improved quality of life to the patient.

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