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Clinicoradiological and Histopathological Comparative Study of Nodal Metastasis in Head and Neck Cancers.

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ABSTRACT

Background: Detection of regional lymph nodes in head and neck cancers greatly modifies the staging, treatment and prognosis of the patient and helps in planning the management of these patients. **Methods:** A prospective study was conducted in the Department of E.N.T., S.M.G.S. Hospital, G.M.C. Jammu, in collaboration with the Department of Radio diagnosis and Imaging, G.M.C. Jammu & Department of Radiation Oncology GMC, Srinagar from 2008 to 2012 in which patients attending / admitted in the Department of E.N.T., with cancer of head and neck, were assessed for lymph node metastasis (at different levels). 16 patients, all cases of squamous cell carcinoma head and neck, underwent appropriate neck dissections. The patients were examined clinically as well as with ultrasonography for detection of various enlarged lymph nodes at different levels. Computed tomography and magnetic resonance imaging were done, wherever indicated. Patients were subjected to fine needle aspiration cytology in cases of palpable lymph nodes. The removed lymph nodes were examined histopathologically. **Results:** The findings of clinical, radiological and histopathological studies were compared. We concluded that clinical palpation should be supplemented by ultrasonography in every case of head and neck cancer. However, since computed tomography picks up lymph nodes missed by ultrasonography in a significant number, is important in imaging primary tumour and picks up necrosis and extracapsular spread at the most, it should be included in each case of head and neck cancer. **Conclusion:** Magnetic resonance imaging being equivalent to computed tomography in picking up the nodes, but lagging behind the criteria such as picking up of nodal necrosis and extra capsular spread of lymph nodes, and is too costly, so may be included as an imaging modality wherever computed tomography is contraindicated.

Keywords: Head & Neck Surgery, Lymphadenopathy, Oncology.

INTRODUCTION

Lymphatic metastasis is the most important mechanism in the spread of head and neck squamous cell carcinomas.[1] The rate of metastasis probably reflects the aggressiveness of the primary tumor and is an important prognostic indicator.[2]

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Presence or absence of regional lymph nodes in head and neck cancers greatly modifies the staging, treatment and prognosis of the patient. Detection of neck node is of paramount importance preoperatively in planning the management of these patients. Failure to detect disease in the neck may directly affect the prognosis.[3] The presence of metastatic cervical lymph nodes in head and neck malignancy can lead to a drop in survival rate to nearly 50%. There are various modalities used to detect regional nodal metastasis like clinical evaluation, ultrasonography, ultrasonography-guided fine-needle aspiration, computed tomography, magnetic resonance imaging, single photon emission computed tomography, 18 fluorine deoxyglucose-positron emission tomography and colour Doppler ultrasonography, and all of them vary in detecting the nodal metastases with respect to sensitivity, specificity, accuracy and predictive values. The advent of high-resolution systems and specific contrast media, fine-cut computed tomography scanning has

allowed the detection of pathological cervical nodes of smaller size that may be missed by clinical examination.[4]

MATERIALS AND METHODS

A prospective study was conducted in the Department of E.N.T., S.M.G.S. Hospital, G.M.C. Jammu, in collaboration with the Department of Radiodiagnosis and Imaging, G.M.C. Jammu and Department of Radiation Oncology GMC, Srinagar from 2008 to 2012 in which patients attending / admitted in the Department of E.N.T., with cancer of head and neck, were assessed for lymph node metastasis (at different levels). 16 patients, all cases of squamous cell carcinoma head and neck, underwent appropriate neck dissections. The patients were examined clinically as well as with ultrasonography for detection of various enlarged lymph nodes at different levels. Computed tomography and magnetic resonance imaging were done, wherever indicated. Patients were subjected to fine needle aspiration cytology in cases of palpable lymph nodes. The removed lymph nodes were examined histopathologically. The findings of clinical, radiological and histopathological studies were compared. The patients with residual or recurrent disease were not included in this study. Besides the systemic examination, otorhinolaryngological, head and neck examination was done. The primary tumour was assessed and staged clinically. The palpable lymph nodes were documented according to the number, size, site, consistency, and mobility. The site was recorded according to the level of the lymph nodes in the neck.

After the clinical examination of cervical lymph node, patients were subjected to ultrasound examination with 7-12 MHz probe and computerized tomography (plain followed by contrast) with axial sections of 3-5 mm thickness from the base of the skull to C-6 vertebra. Characteristics of lymph nodes found were recorded in terms of various parameters like size, shape, density, extracapsular spread, central necrosis and peripheral rim enhancement. The lymph node was diagnosed as positive for metastasis if the following criteria were met: lymph node with size greater than 1 cm except for level II, where lymph node greater than 1.5 cm was considered positive, central necrosis and peripheral rim enhancement after intravenous contrast, three or more lymph nodes in the primary drainage area, round shape on ultrasonography, extracapsular spread and carotid artery invasion. Images taken by ultrasonography and computed tomography were assessed by the radiologist without the knowledge of the histopathology. Selective patients underwent plain, magnetic resonance imaging followed by infusion contrast and the characteristics found were recorded in terms of various parameters given above as on computed tomography. The results were calculated in terms of sensitivity, specificity, positive predicted value, negative predictive value and accuracy for each modality used.

Criteria used for True/False Positives/Negatives: True Positives included nodes detected as positive on clinical/ ultrasound/computed tomography and magnetic resonance imaging and confirmed positive on histopathological examination. False Positives included nodes detected as positive on clinical/ ultrasound, computed tomography and magnetic resonance imaging and found to be negative on histopathological examination. False Negatives included nodes detected as negative on clinical/ ultrasound, computed tomography and magnetic resonance imaging and found to be positive on histopathological examination. True Negatives included nodes detected as negative on clinical/ ultrasound/ computed tomography and magnetic resonance imaging and confirmed negative on histopathological examination.

RESULTS

A total of 16 cases of head and neck squamous cell carcinoma with cervical lymphadenopathy were included in the study. A total of 16 neck dissections were performed. We observed that maximum number of cases were of laryngeal origin (50%), oropharynx (31.25%), hypopharynx (12.5%) and unknown primary (6.25%), with a male to female ratio of 4.3:1 and with the maximum cases in the age group of 56-60 years (31.25%) years. A total number of 96 lymph nodes were dissected out. Out of which, 33 (34.37%) were diagnosed as malignant, while 63 (65.63%) were non-malignant on histopathological examination. Computed tomography detected only 73 lymph nodes, the highest of all the modalities.

On clinical examination, ultrasonography, computed tomography and magnetic resonance imaging (done only in 9 patients), 19, 26, 73 and 42 lymph nodes were detected respectively. The distribution of lymph nodes as per levels of the neck is shown in [Table 1].

On clinical examination, 11 (57.89%) cervical nodes were considered to have metastatic spread, out of which 9 (81.81%) were true positives, 7 (77.77%) had nodal size greater than 1.5 cm and 2 (22.22%) had size less than 1.5 cm, and 2 (18.18%) were false positives, one (50.00%) had size less than 1.5 cm and one (50.00%) had greater than 1.5 cm. Eight (42.10%) nodes were considered negative on palpation, out of which 5 (62.5%) were true negatives, of which 1 (20.00%) had size greater than 1.5 cm and 4 (80.00%) had size less

than 1.5 cm and 3 (37.5%) were false negatives all had size greater than 1.5 cm.

Table 1: Number of lymph nodes detected as per palpation ultrasonography, computed tomography and magnetic resonance imaging at different levels of neck.

Level of lymph nodes	Palpation		Ultrasonography		Computed tomography		Magnetic resonance imaging	
	(No.)	(%)	(No.)	(%)	(No.)	(%)	(No.)	(%)
I	2	10.5%	3	11.53%	4	5.47%	4	9.5%
II	6	31.5%	7	26.92%	24	32.87%	12	28.57%
III	11	57.8%	14	53.84%	39	53.42%	20	47.61%
IV	—	—	1	3.84%	3	4.10%	3	7.14%
V	—	—	1	3.84%	3	4.10%	3	7.14%
VI	—	—	—	—	—	—	—	—
Total	19	100%	26	100%	73	100%	42	100%

Table 2: Statistical results of different modalities.

Modality	Clinical examination	Sonography	CT Scan	MRI
Sensitivity	75%	85.71%	82.14%	88.88%
Specificity	71.42%	75%	91.11%	87.5%
Positive predictive value	81.81%	80%	85.18%	84.21%
Negative predictive value	62.5%	81.81%	89.13%	91.30%
Accuracy	73.68%	80.76%	87.67%	88.09%

Of the 26 nodes detected on ultrasonography, 12 (80%) were true positives and 3 (20%) were false positives. 9 (81.81%), were true negatives and 2 (18.18%) were false negatives as shown in [Table 3]. Size of the nodes detected ranged from 0.7 × 0.4 cm to 5.7 × 3.8 cm, 14 (53.84%) were found positive for malignancy on histopathological examination, out of these 10 (71.42%) were round and 4 (28.58%) were oval, had an axial diameter of > 1.2 cm, 8(57.14%) were hypo-echoic and 6(42.85%) were hyper-echoic, 10 (71.42%) showed no necrosis, while 4 (28.57%) showed necrosis, 11 (78.57%) did not showed ECS while 3 (21.42%) showed ECS whereas 12 (46.15%) nodes were found negative on histopathological examination on sonography; of these, 8 (66.66%) were oval and 4 (33.33%) were round, 5 (41.66%) were hyper-echoic and 7(58.33%) were hypo-echoic, all 12 (100%) had no necrosis and ECS with only 2 nodes found in relation to the carotid sheath were found pressing on the internal jugular vein which was confirmed as tumor invasion of the vein on histopathological examination.

Table 3: Comparison of clinico-radiological examination with pathological results.

Palpation	Pathological Report		Total No. (%)
	Positive No. (%)	Negative No. (%)	
Positive	9 (81.81%)	2 (18.18%)	11 (57.89%)
Negative	3 (37.5%)	5 (62.5%)	8 (42.10%)
Total	12	7	19
Ultrasonography			
Positive	12 (80%)	3 (20%)	15 (57.69%)
Negative	2 (18.18%)	9 (81.81%)	11 (42.31%)
Total	14 (53.84%)	12 (46.15%)	26 (42.30%)
Computed Tomography			
Positive	23(85.18%)	4(14.8%)	27(36.98%)
Negative	5(10.86%)	41(89.13%)	46(63.01%)
Total	28(38.35%)	45(61.64%)	73
Magnetic Resonance Imaging			
Positive	16(84.21%)	3(15.78%)	19(45.23%)
Negative	2(86.95%)	21(91.30%)	23(54.76%)
Total	18(42.85%)	24(57.145)	42

On computed tomography, 73 nodes were detected of which, 23 (85.18%) were true positives and 4 (14.8%) were false positives, 41 (89.13%) were true negatives and 5 (10.86%) were false negatives. The size of the nodes detected ranged from 0.5 × 0.3 cm to 5.7 × 3.8 cm, 1.1 cm size considered as positive and less than 0.5 cm as negative. On histopathological examination, the nodes which were positive were having axial diameter > 1.05 cm. Of the 73 nodes detected on computed tomography, 28(38.35%) were found positive for malignancy on histopathological examination, and

of these 23(82.14%) were round and rest were oval, 23(82.14%) were hypodense and 5(17.85%) were hyperdense, 21 (75%) had no necrosis, while 7(25%) showed necrosis, 5 (71.42%) were detected by computed tomography while 2 (28.57%) more were confirmed on histopathological examination, 21(75%) did not show ECS while 7 (25%) showed ECS, out of these 7 nodes 6(85.71%) were detected by computed tomography while one more was confirmed on histopathological examination, with only 3 nodes were pressing on the internal jugular vein which was confirmed as tumor invasion of the vein on histopathological examination. Forty-five nodes (61.64%) were found negative on histopathological examination, of these 36 (80%) were oval and 9 (20%) were round, 5 (11.11%) were hypodense and rest 40 (88.88%) were hyperdense, with no necrosis and ECS as shown in [Table 4].

Table 4: Nodal necrosis and extracapsular spread as detected by different modalities.

	Ultrasonography	CT Scan	MRI
Detected nodal necrosis	1 (25%)	5(25%)	2 50%)
Nodes negative for necrosis but positive on histopathological examination	3 (75%)	21(75%)	2 50%)
Detected nodal extra capsular spread	2 (66.66%)	6 85.71%)	4 80%)
Nodes negative for extra capsular spread but positive on histopathological examination	1 (33.33%)	1 (14.28%)	1 (20%)

On magnetic resonance imaging (done only in 9 patients), 42 nodes were detected, 16 (84.21%) were true positives and 3 (15.79) were false positives, 21 (91.30%) were true negatives and 2 (8.70%) were false negatives. The size of the nodes detected ranged from 0.5 × 0.3 cm to 5.7 × 3.8 cm, size greater than 1.05 cm considered positive for malignancy. On histopathological examination, all nodes positive for malignancy had an average axial diameter of > 1.06 cm. Of the 42 nodes detected on magnetic resonance imaging, 18 (42.85%) were found positive for malignancy on histopathological examination, 12 (66.66%) were round and rest 6 (33.33%) were oval, 14 (77.77%) had no necrosis, while 4 (23.22%) showed necrosis, 13 (72.22%) did not show ECS while 5 (27.77%) showed ECS of these five nodes 4 (80%) were detected by magnetic resonance imaging while 1 (20%) was confirmed on histopathological examination only 3 positive nodes were seen pressing on the internal jugular vein which was confirmed as tumor invasion of the vein on histopathological examination. Twenty-four (57.15%) nodes were found negative on histopathological examination, of these 18 (75%) were oval and 6 (25%) were round with no necrosis and ECS.

DISCUSSION

Various sites for head and neck cancers in order of their frequency are oral cancer, laryngeal cancer, nasopharyngeal cancer, nasal cavity and paranasal sinuses, salivary gland cancer, thyroid cancer, hypopharyngeal cancer and oropharyngeal cancer.[2] There is a significant relationship between age, smoking status and site of tumour. We found a male to female ratio of 3:1 in head and neck squamous cell carcinomas, which is in accordance with the present study, but can be as high as 10.5:1[5] The high incidence among males and the increased frequency of laryngeal site involvement in the present study may be attributed to increased amount of smoke and tobacco intake.

Since palpation picks up nodes of greater than 1 cm, many malignant nodes are missed by palpation, so under staging is there in many a cases. The reliability of palpation in cervical lymph node metastasis depends on the experience of the examiner, the anatomy of the individual neck, the fat and muscle present above the lymph node. Sometimes the bone e.g. Mandible present above the lymph node also influences the palpation. It was observed that palpation could not be relied upon for diagnosis, as it has low sensitivity, specificity and accuracy.

The minimal diameter in the axial plane was found to be the most accurate criteria for predicting malignant lymph node. The variation in size found in the present study may be attributed to different interpretation of clinician and radiologist. According to our study, all nodes positive for malignancy had an axial diameter > 1.1 cm on radiology which was comparable to [6, 7] (got) with corresponding figures of 0.7 and 0.9 cm respectively.

Whether lymph nodes are metastatic or not, is difficult to determine directly by ultrasound. However, the positive rate can be enhanced by evaluation of size, shape and boundary of the lymph node. According to some, ultrasound is indispensable for diagnosing cervical lymph node metastasis in malignant head and neck tumours[8], but some authors concluded that ultrasound did not add significantly to the information obtained by the simple neck palpation.[9] Ultrasound has certain advantages which include low cost as compared to computerized tomography, minimal stress to the patient, ease of application and repetition without radiation hazards. As stated by[10], we also felt that ultrasound provided information of an anatomic nature, including the detection of subclinical lymph

nodes, volumetric evaluation and determination of vascular connections, particularly the detection of carotid artery pressurization. High frequency ultrasonography imaging can detect most diseased nodes[11], and in many cases, distinguish benign or reactive from metastatic nodes.

A lot of variation is seen in the results of computerized tomography. These variations were due to the use of different parameters to consider a node positive for metastasis, the difference in the thickness of the section and amount or methods of contrast infusion i.e. bolus or continuous.

According to our study, we found that palpation picks only nodes of size > 1 cm, but with ultrasonography, computed tomography and magnetic resonance imaging, the nodes of smaller sizes as stated previously can be picked up. On palpation, we had 3 patients of N_3 stage, 5 patients of N_2 stage, 5 patients of N_1 stage and 3 patients of N0 stage. Computed tomography upgraded two (three) tumours from N_0 to N_1 and one each from N_0 to N_2 and N_1 to N_2, while magnetic resonance imaging upgraded one tumour from N_0 to N_1 and one from N_1 to N_2, whereas ultrasonography upgraded one tumour from N_0 to N_1 and one from N_1 to N_2. No patient was down staged in our study. Computed tomography or magnetic resonance imaging should be considered for the routine staging of neck in all head and neck malignancies.[12, 13]

In the present study, we found that maximum no. Of lymph nodes detected were at the level of level three in all the investigative modalities used, followed by level II and level I, the literature of which was not found. This can be attributed to more number of cases from the larynx and associated areas

Our study proves that the shape of the node is not that much reliable criterion to prove whether the node is malignant or not, as believed by some authors, though metastatic lymph nodes were considered round by some[6], while some reported reactive or benign nodes were oval.[11]

Ultrasonography can accurately diagnose echogenecity of the lymph node as seen in our study, but its reliability was poor to state that whether the lymph node is malignant or not[11] Some malignant nodes can show an-echoic picture due to necrosis or cystic changes. The positive rate can be higher for well delineated than poor delineated lymph nodes, but similar among the homogeneous, heterogeneous and reflective core patterns of internal echoes and whether a lymph node is metastatic or not is difficult to determine directly by ultrasound.[8] Hypodensity of a lymph node was helpful in pointing to malignancy of the lymph node to some extent in our study. Nodes measuring 10 mm or more with central low density were always malignant. [14] Central lucency and nodal confluence on computed tomography were highly reliable indicators of malignancy, whereas nodal size bore a less direct relationship.[15]

All nodes showing necrosis on US were positive for malignancy, absence of necrosis was seen in both benign and malignant nodes as studied by some [6] some were able to detect necrosis of 0.3 cm on nodes and this was only in metastatic nodes.[11] Non reacting nodes showed necrosis, though US was 40% sensitive in picking necrosis and radiological detection of necrosis 3 mm or more was found only in metastatic nodes.

Magnetic resonance imaging is inferior to computed tomography in identifying central necrosis or extra nodal tumor spread.[2] Computed tomography scanning still has an edge over magnetic resonance imaging for detecting cervical nodal involvement. Advances in magnetic resonance imaging technology (fast spin-echo imaging, fat suppression) have not yet surpassed the capacity of computed tomography scanning to identify lymph nodes and to define a nodal architecture. Central necrosis, as evaluated by unenhanced T1- and T2-weighted images, has been shown to provide an overall accuracy rate of 86-87% compared with computed tomography scanning, which has an accuracy rate of 91-96%. The use of newer contrast media, especially supramagnetic contrast media agents, hopefully will improve the sensitivity of magnetic resonance imaging.[4]

ECS can occur in smaller nodes. Approximately 40 to 60% of positive nodes showed extra capsular spread. Radiology was hundred percent accurate in detecting lymph nodal pressure over neck vessels. This was an improvement over clinical examination, which only labeled it positive without telling about pressure over vessel wall. It was found that the invasion of jugular vein by tumour is seen usually in massively enlarged nodes.[16] The wall of carotid was hypoechoic in 11/12 patients with surgically proved invasion of the artery[17] Palpation is less sensitive than computed tomography and ultrasonography in the detection of carotid artery involvement, hence the clinical suspicion of arterial invasion should be confirmed by either computed tomography or ultrasonography which have similar accuracy in the detection of carotid artery invasion [18]

The overall sensitivity of palpation, ultrasonography, computed tomography and magnetic resonance imaging in our study is 75%, 85.71%, 82.14% and 88.88% respectively as shown in [Table-2]. The study is helped by the similar results from many studies.[19-22] but some showed results different from the present study. It could be because of different criterion of parameters taken in the present study.[23]

The specificity in our study for palpation, ultrasonography, computed tomography and magnetic resonance imaging is 71.42 %, 75%,

91.11% and 87.5%, respectively, supported by[19, 22, 24] where as some found that specificity for palpation, ultrasonography and computed tomography was calculated as 95.5%, 83.0% and 83.6%, respectively.[23]

Positive predictive value for palpation, ultrasonography, computed tomography and magnetic resonance imaging were 81.81%, 80%, 85.18% and 84.21% respectively in our study, which is in accordance with different studies done by some[22,25] None of the above studies compared all the four modalities in a single study.

The negative predictive value for palpation, ultrasonography, computed tomography and magnetic resonance imaging were 62.5%, 81.1%, 89.13% and 91.30% respectively in our study, which is supported by[22, 25, 26] The overall accuracy in our study was 73.68%, 80.76%, 87.67% and 88.09% in clinical examination, ultrasonography, computed tomography and magnetic resonance imaging respectively. The results matched with many studies done in the past. [2, 6, 12, 19, 21]

CONCLUSION

Ultrasonography turned out to be a significant tool in our study as it is having high sensitivity as compared to computer tomography while it lagged behind computed tomography in terms of specificity, positive predictive value, negative predictive value and accuracy. As compared to magnetic resonance imaging, it lagged behind in every statistical result. It also has advantages of repeated use, less cost, ease of application and no radiation hazards, but it has disadvantage of not picking up the total number of nodes as deep nodes remain elusive to its imaging penetration and it has no role in detecting the primary head and neck tumor. There is always a risk of anaphylaxis due to contrast infusion, which is also true for both computed tomography and magnetic resonance imaging. On clinical examination, the minimum diameter of lymph node, which was picked up, was greater than 1 cm. This was major limitation of palpation, the other being diagnosing the primary site of head and neck cancer, necrosis of lymph nodes, extra capsular spread and pressure over major neck vessels. Though certain criteria like hardness, skin fixity and fixity to underlying structures can give some clue about malignancy. Computed tomography and magnetic resonance imaging appears to be the best modalities, as they detect maximum number of lymph nodes and were having high sensitivity, specificity, negative predictive value and positive predictive value but are costly and computed tomography also have radiation side-effects.

Necrosis is the most reliable radiological criteria. However, it is usually found in large metastatic lymph nodes. In this study, we found that computed tomography is the best modality for identifying necrosis. Contrast-enhanced magnetic resonance imaging even with fat suppression is still inferior to computed tomography. Computed tomography is slightly better than magnetic resonance imaging in staging both primary tumour and cervical lymph nodes, whereas clinical palpation and ultrasonography lagged far behind.

So, it is concluded that clinical palpation should be supplemented by ultrasonography in every case of head and neck cancer. However, since computed tomography picks up lymph nodes missed by ultrasonography in a significant number, is important in imaging primary tumour and picks up necrosis and extracapsular spread at the most, it should be included in each case of head and neck cancer. Magnetic resonance imaging being equivalent to computed tomography in picking up the nodes, but lagging behind the criteria such as picking up of nodal necrosis and extra capsular spread of lymph nodes, and is too costly, so may be included as an imaging modality wherever computed tomography is contraindicated.

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