Diagnostic Efficacy of Computed Tomography in Detecting Cervical Metastases in Clinically N₀ Head and Neck Squamous Cell Carcinoma

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Abstract The search for a single non-invasive highly accurate diagnostic modality for identification of cervical metastasis in head and neck squamous cell carcinoma (HNSCC) is yet to bear fruit. Thirty proven cases of HNSCC with no palpable neck nodes were selected, requiring surgery for the primary tumour. Detailed clinical evaluation and contrast enhanced computed tomography (CECT) scans were done. Patients underwent elective neck dissection along with surgery for the primary tumour. Specimens were sent for histopathological examination (HPE), considered gold standard. Results of CECT were compared with HPE. Clinical examination had a NPV of 80 % and CECT had a sensitivity, specificity, PPV, NPV, and accuracy of 83, 75, 45.5, 94.7, and 76.7 % respectively. A CECT may be added to the initial assessment of a patient of HNSCC, allowing for earlier diagnosis of nodal metastasis that may allow for a better chance at survival.

Keywords Head and neck squamous cell carcinoma · Cervical lymph node · Metastasis · Clinically node negative · Computed tomography

Introduction

Head and neck squamous cell carcinomas (HNSCC) are an important source of morbidity and mortality in the world, more so in the Indian populace, being the second most

common form of cancer in India, with a frequently aggressive behaviour and a strong correlation with tobacco use [1]. Cervical lymph node metastasis, reported as the most important mechanism of spread, is one of the most critical prognostic factors for staging tumors and deciding upon a management strategy [2, 3]. Diagnosis of cervical metastases may be effectuated by a number of methods, with histopathological examination of a head and neck dissection specimen considered the gold standard [4]. Clinical assessment by palpation is the most widely used method for detecting cervical metastases; however, both sensitivity and specificity of this method are low [5, 6]. The consequent risk of missing subclinical metastasis is the source of one of the greatest controversies in the history of head and neck oncology: whether or not to electively treat the clinically node negative neck. The search for a single non-invasive highly accurate diagnostic modality for the identification of cervical metastasis is yet to bear fruit. There is a paucity of scientific data from our country comparing the efficacy of different diagnostic modalities for detection of cervical metastases. It is our endeavour to shed further light on the existing controversy, focusing on the role of computed tomography for the detection of cervical metastases in a clinically N₀ neck in HNSCC.

Materials and Methods

A prospective study was conducted in the Department of Otorhinolaryngology—Head and Neck Surgery, Loknayak Hospital between December 2012 and February 2014. A total of 30 patients of all age groups and both sexes were selected based on the presence of histologically proven HNSCC with a clinically N₀ neck, and the primary tumor being treated with surgery as the primary treatment

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modality. Patients were excluded if they had any significant palpable cervical lymphadenopathy, evidence of distant metastasis, history of irradiation of head and neck, undergone surgery for head and neck malignancy in the past, known allergy to iodinated contrast media, and if they were pregnant. A detailed history and thorough general physical and otolaryngological examination were conducted. The tumor was staged and treatment was planned based on the histopathological report of the preoperative biopsy. Each patient underwent a routine haematological and biochemical workup for surgery, in addition to a chest radiograph and abdominal ultrasound to screen for distant metastases. A contrast enhanced computed tomography (CECT) scan of the primary site along with the neck was carried out for each subject with a Siemens Definition AS Plus 128 slice Computerised Tomography scanner. Spiral acquisition was done at 5 mm thickness from the primary lesion and regional lymph nodes, and reconstructed at 1 mm. A bolus infusion of 1 ml/kg non-ionic iodine based contrast iohexol was administered and the scan was initiated as soon as the intravenous bolus was completed. Criteria for considering a node to be positive on CECT scan are as follows: size greater than 1 cm, spherical shape, three or more lymph nodes in the first drainage area, rim enhancement, central necrosis, and extracapsular spread (Fig. 1). Any node detected as metastatic on CECT was documented according to the location, number, size and relation to surrounding structures. All patients under study underwent an elective neck dissection along with surgical excision of the primary tumour. A total of 30 neck dissections were performed with no case of bilateral

dissection. Tissue in each neck dissection specimen was fixed in formalin, embedded in paraffin, sectioned, and stained with haematoxylin and eosin. The pathologist examined the nodes microscopically. The standard of reference for node positivity was presence of tumor at histopathological examination. The pathologist was blinded with respect to the computed tomography scan report.

The data was taken in terms of range, mean and standard deviation for qualitative data, and in terms of frequency and percentage for quantitative data and the results were analysed in proportions using SPSS statistical software. Results of clinical examination and computed tomography were analysed vis-à-vis histopathological results of neck dissection specimens with respect to sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy.

Sensitivity was the percentage of histopathologically proven node positive necks that were correctly interpreted by imaging as positive for disease, defined as $(\text{Number of true positive necks}) \times 100 / (\text{number of true positive} + \text{false negative necks})$, where true positive were the necks correctly diagnosed as node positive on imaging and false negative were necks diagnosed as normal, but with pathological evidence of nodal metastasis. Specificity was the percentage of necks with histopathologically proven absence of metastatic neck disease correctly interpreted as negative for disease on imaging, defined as $(\text{number of true negative necks}) \times 100 / (\text{number of true negative} + \text{false positive necks})$, where true negative is a neck correctly detected as node negative on imaging, and false positive a neck diagnosed as node positive on imaging with absence of metastatic nodal disease on histopathology. NPV was the percentage of necks interpreted as node negative on imaging that were histopathologically proven to be node negative, defined as $(\text{number of true negative necks}) \times 100 / (\text{number of true negative} + \text{false negative necks})$ and PPV is the percentage of necks interpreted as node positive that were histopathologically proven to be node positive, defined as $(\text{number of true positive necks}) \times 100 / (\text{number of true positive} + \text{false positive necks})$. Accuracy is the overall ability of the investigating modality to correctly diagnose a neck as positive or negative for metastatic disease, defined as $(\text{number of true positive} + \text{true negative necks}) \times 100 / (\text{total number of patients who underwent scanning})$.

Fig. 1 Radiologically malignant lymph node on CECT; the arrow indicates a malignant lymph node that is greater than 1 cm in size, appears spherical in shape, with a peripheral rim enhancement

Results

Hundred and fifty one patients of proven head and neck cancer attending the outpatient department between December 2012 and February 2014 were screened, with an average age of 47.30 years and a sex ratio of 1.70

Table 1 Distribution of primary according to site and T stage

Primary site	T ₁	T ₂	T ₃	T ₄	Total	Percentage
Buccal mucosa	2	4	4	0	10	33.3
Larynx	0	2	6	1	9	30
Tongue	1	2	3	0	6	20
Undeterminable oral cavity	0	0	2	0	2	6.7
Lower alveolus	0	2	0	0	2	6.7
Lip	0	1	0	0	1	3.3

favouring males. Of these, 30 individuals matched the inclusion criteria mentioned previously, ranging from 20 to 72 years in age, with a mean age of 48.47 years and a male:female ratio of 1.73:1. The distribution of the primary site is as is shown in Table 1, with buccal mucosa being the commonest site, followed by larynx, tongue, lower alveolus, undeterminable oral cavity, and lip, in that order. Majority of study subjects presented with stage T₃ laryngeal and stage T₁ or T₂ oral cavity primaries.

All 30 subjects were staged according to the TNM staging system [7], and were posted for surgical excision of the primary tumour along with an elective neck dissection. Time gap between presentation to the outpatient department and surgery was no more than 1 month for any case. Of these, 14 underwent a Supraomohyoid neck dissection (level I–III), six underwent an extended Supraomohyoid neck dissection (level I–IV), six underwent a central neck dissection (level VI), three underwent an anterolateral neck dissection (level II–IV, VI), and one patient underwent a modified radical neck dissection (level I–V).

On clinical assessment, all 30 cases were node negative. In 24 of these, histopathological evidence corroborated with the findings of clinical examination. In 20 % cases, the patients were upstaged from a clinically N₀ to a histopathologically N₊ neck, with evidence of microscopic metastases. The NPV of clinical examination, thus, was 80 %, as is shown in Table 2.

Table 3 compares the results of computed tomography and histopathology. Computed tomography upstaged 11 of the 30 clinically N₀ necks to a clinico-radiologically N₊ neck. Of these, five were correctly upstaged, and six incorrectly, with a PPV of 45.5 %. CT correctly diagnosed five out of six histopathologically proven nodal metastases, with a sensitivity of 83.3 %. Out of the 24 cases that

Table 2 Clinical examination vis-à-vis histopathological examination

Clinically N ₀	30
Histopathologically N ₊	6
True negative	24
False negative	6
Negative predictive value	80 %

Table 3 Computed tomography vis-à-vis histopathological examination

	HPE N ₊	HPE N ₀	Total
CT N ₊	5	6	11
CT N ₀	1	18	19
Total	6	24	

CT computed tomography, HPE histopathological examination

showed no histopathological evidence of nodal metastasis, 18 were correctly diagnosed as N₀ by CT, with a specificity of 75 % and a NPV of 94.7 %. CT, thus, diagnosed the presence or absence of nodal metastases with an accuracy of 76.7 %.

Discussion

The presence of cervical metastases reflects the aggressive nature of HNSCC. The management of cervical metastatic disease has, historically, been a controversial topic, more so in the case of the clinically N₀ neck. It is a recognized fact that cervical metastases is the most important prognostic factor in HNSCC, showing a 50 % reduction in five-year survival rates for ipsilateral nodal metastases, and a 75 % reduction in case of bilateral metastases [8–11]. Thus the evaluation of the neck nodes for metastases is paramount in the management of cases of HNSCC.

Palpation, the most widely used method for assessment of nodal metastases, demonstrates a large variation of findings amongst examiners. The false negative rate for palpation in our study was 20 %, lower than that reported in literature, where reported rates varied between 27 and 38 % [6, 12, 13]. This inconstancy in findings has been attributed to variables determining the reliability of clinical examination, namely the experience of the examiner, individual variability in anatomy of the neck, as well as any previous treatment modality to the neck in the form of surgery or radiotherapy [4]. Despite this variability in reported rates, it is safe to assume that palpation is a less-than-ideal method of detection of nodal metastases, with an overall high false negative rate and a low specificity and sensitivity.

This inaccuracy of palpation to detect nodal metastases paved the way for studies evaluating other diagnostic means for detection of metastases to cervical lymph nodes, and today we have a battery of tests at our disposal, not the least of which is computed tomography. In this study, CT yielded a sensitivity, specificity PPV, NPV and accuracy of 83.3, 75, 45.5, 94.7, and 76.7 %, respectively. The sensitivity results obtained in this study were similar, with specificity results somewhat lower, when compared to other studies, where sensitivity of 77.5–82.09 %, and specificity of 85.71–96 %, have been reported [11, 14–16]. The PPV and NPV were similar to those reported by Rottey et al. (53.9 and 82.9 %, respectively), while markedly different from those reported by Watkinson et al., Anand et al., and Haberal et al. (81–94.5 and 60–85 %, respectively) [11, 15, 17, 18]. The diagnostic accuracy of CT in this study is comparable to that reported by Rottey et al., Feinmesser et al., and Moreau et al. (75.3–81 %), with a higher accuracy, ranging from 83 to 90 %, reported by Merritt et al., Thakur et al., Haberal et al., Lenz et al., and Friedman et al. [11, 13, 14, 17, 19, 20].

This great variability in results of computed tomography may be attributed to the heterogeneity of the groups being studied, the criteria applied for node positivity, as well as the differences in the thickness of sections, and amount and method of contrast infusion. However, computed tomography still scores a place above clinical assessment as a diagnostic test for evaluation of the neck for nodal metastases, with higher accuracy, specificity, as well as greater reliability than the latter. Thus, it is our recommendation that a CECT be included in the initial evaluation of the patient, allowing a more accurate staging of disease at diagnosis that may lead to a more appropriate management protocol. That said, given the fallacies in the currently available methods of assessment, there is still a need for future research into the development of a single, non-invasive, readily available, and relatively inexpensive diagnostic modality for the identification of cervical metastases.

Compliance with Ethical Standards Written informed consent was obtained from all individual participants in their preferred language for inclusion in the study. All procedures performed in the study were in accordance with the ethical standards of the institutional ethics committee.

Conflict of interest The above research has not been funded by any organization, and all authors have declared that they have no conflict of interest.

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