Clinical, Radiological and Pathological Co-Relation of Mandibular Involvement in Cancers of Oral Cavity

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ABSTRACT

Introduction: In Head and neck squamous cell carcinoma (HNSCC), the clinical assessment of mandibular involvement is often inaccurate and unreliable. Involvement of mandible, upstage the disease to stage IV. Investigations like orthopantomogram, computed tomography (CT), magnetic resonance imaging (MRI), bone scintigraphy etc have been evaluated by different authors for involvement of mandible with wide variation in results. This has prompted us to correlate clinically, radiological, and pathological to formulate the appropriate protocol for evaluation of mandibular involvement.

Methods: It is a prospective and a retrospective study. In prospective part, all patients with clinical and radiological confirmation of mandibular involvement were undergone mandibulectomy. The histologic findings of mandibular bone involvement were then compared with the radiographic findings, along with tumor location, stage, and grade. For retrospective study, the medical records of patients, who had undergone mandibulectomy as a part of treatment of oral cavity cancers were analyzed and correlated.

Results: In the present study, the bone involvement was found in 69% clinically, 40.5% by Orthopantomogram, 39.6% by CT scan and 54% on MRI scan. The histological confirmation of bone involvement was evaluated in all the above cases. It was found that 22% of clinically positive, 46% of OPG positive patients, 52% of CT scan positive and 46% of MRI positive had invasion

Conclusion: There is no single modality of investigation which appears to have high specificity and sensitivity. Combination of different modalities increases the both sensitivity and specificity. In our study clinical examination along with high resolution CT scan has the acceptable sensitivity and specificity which may be applied for better results.

Keywords: Squamous Cell Carcinoma, Oral Cancer, Mandibular Invasion, Staging, Investigations

Introduction

Primary tumors of oral cavity may arise from the surface epithelium, minor salivary gland or sub mucosal soft tissue. They are grouped under two major headings- head and neck squamous cell carcinoma (HNSCC), accounting for about 90% of all head and neck tumor and glandular neoplasm, the majority arising in the thyroid [1]. The most common symptom of a patient with oral carcinoma is a persistent ulcer in the mouth, which may be associated with bleeding, slurred speech, dysphasia, and a neck mass. Neurological disturbances in the mandibular branch of the trigeminal nerve indicates perineural invasion and increasing pain in the mandible is often a sign of cortical invasion. Radiation of this pain to the ipsilateral ear (referred otalgia) is usually a symptom of paramandibular/ parapharyngeal muscle involvement [2] [3]. Involvement of mandible, upstages the disease to stage IV. At this stage, surgery followed by adjuvant treatment is the only option of cure. Resection of mandible not only increases the morbidity and mortality but

also hamper the quality of life. The methods of mandibular reconstruction with the invention of microvascular surgery and free bone graft has improved the quality of life as well as aesthetic results. But it requires expertise, prolonged surgical time and is not cost effective.

Therefore, detection of mandibular involvement is of primary importance. Various investigations like orthopantomogram, computer tomography (CT), magnetic resonance imaging (MRI), bone scintigraphy etc have been evaluated with wide variation in results. This has prompted us to correlate clinically, radiological, and pathologically the mandibular involvement and to formulate the appropriate protocol for its evaluation.

Material and methods

This study is a prospective and a retrospective study. Prospective study consists of 42 patients with histological diagnosis of squamous cell carcinoma, and has undergone mandibular resection as part of their treatment. Mandibular

resection was deemed necessary either because of the clinical or radiological diagnosis of bone invasion and in order to achieve a clear resection margin. Tumors were staged (clinical TNM stage groupings) according to the American Joint Committee on Cancer (7th edition). Small lesions were divided according to the site of origin like floor of mouth, lower alveolus, retromolar trigone etc. Those lesions which encompassed more than one site due to size were classified by the center of the lesion. For retrospective study also, 42 patients were included in the study.

Criteria of inclusion

1. Patients of squamous cell carcinoma of oral cavity.
2. Patients of oral cavity cancers in an operable stage.
3. Cancer nearer to or over the mandible.
4. Patients who have undergone any form of mandibulectomy.

Criteria of exclusion:

1. Patients with neo adjuvant chemotherapy or radio therapy
2. Patients with inoperable stage
3. Patients with operable oral cancers not willing for surgery or medically unfit for surgery
4. All patients were carefully examined clinically. Patients with clinical diagnosis of oral cancers were biopsied. The complete metastatic work up was done in patient with positive biopsy report. Patients with localized disease were assessed for need of mandibular resection as a part of treatment.
 - The clinical evidences of mandibular involvement include:
 - Small lesion over the alveolus/retro molar trigone
 - Large lesion with the epicenter on the alveolus
 - Extensive lesions engulfing alveolus
 - Clinical history of spontaneous loosening of tooth
 - Non healing ulcer after tooth extraction
 - Associated pain in absence of infection or inflammation
 - Pain/anesthesia/paresthesia over lower lip and cheek

These patients were subjected to radiological investigation like orthopantomogram, CT scan of face and neck, MRI scan with special attention to detect mandibular involvement. Patients received an OPG or MRI was analyzed by a single radiologist. Most of CT scan was done using 0.5cm cuts with 3D reconstruction of mandible. Mandible was

reported to be involved by the tumor radiologically if there is any evidence of superficial bony erosion, erosive or infiltrative cortical bone loss, widening of inferior alveolar canal.

All patients who were clinically and radiological positive for mandibular involvement were subjected to surgery including mandibular resection. Marginal mandibulectomy was done in patients who were negative of bone involvement, for adequate clear margin.

Under general anesthesia all patients were reexamined for the fixity of tumor and extent of tumor. After specimen was removed the periosteum of mandible along with the tumor was attempted to strip from the mandible and irregularity of bony surface were noted.

The resected tumors were fixed in 10% buffered formalin. The multiple sections were taken through the tumor at the center of bone invasion and were decalcified and processed for paraffin sectioning followed by staining with haematoxylin and eosin. Histologic examination of the sections was performed by onco-pathologist without knowledge of the radiological status. The presence of bone invasion was classified into two types: erosion and infiltration. In erosive bone invasion, the tumor advances as a compact, broad front into bone, such that the tumor-bone interface is well defined. There is loss of cortical continuity with inflamed fibro-connective tissue between the advancing tumor and receding cancellous bone. With infiltrative bone invasion, the tumor adopts a diffuse, irregular, infiltrating pattern, such that the tumor-bone interface is ill defined. There is loss of cortical continuity with inflamed fibro-connective tissue between the infiltrating tumor and cancellous bone, often with islands of unresorbed bone left behind the advancing tumor. Irrespective of pattern of bone involvement, it was reported positive if a single malignant cell was found inside the cancellous bone.

The histologic findings of mandibular bone involvement were then compared with the radiographic findings, along with tumor location, stage, and grade. The grading was done based on differentiation into well, moderate and poor.

Result and Discussion

The maximum incidences of cancer were reported at floor of mouth. In the present study, frequent site of involvement is at alveolus followed by buccogingival sulcus, and buccal mucosa. (Table-1). This can be due to specific habits of tobacco chewing and keeping the quid at bucco-gingival sulcus. In an institutional study conducted at Allahabad of Uttar Pradesh by Mehrotra et al revealed that the tongue was the most common site involved by the malignant

process [4]. The global incidence of cancer of head and neck neoplasms [5] is 6% and Head & neck cancers account for one fourth of male cancers in India [6,7].

On Retrospective analysis, the incidence of bone invasion was found in 6 patients (27%) with carcinoma alveolus whereas only 2 patients (5%) with carcinoma retromolar trigone and buccogingival sulcus. All patients underwent segmental mandibular resection. Of the 42 patients, 8 (19%) had histologic confirmation of mandibular bone invasion. Tumor differentiation was as follows; 1 (2%) poorly, 17 (40%) moderate, and 14 (33 %) well differentiated. The incidence of mandibular bone invasion was 14%, 35%, and 0% respectively (table-2).

On prospective analysis, all the pathologically bone positive for tumor infiltration were found in patients with carcinoma alveolus. However the incidence of bone invasion was 11 patients (55%) with alveolus cancer. 31 patients underwent segmental mandibular resection and in 11 patients' marginal mandibulectomy was done. Of the 42 patients, 11 (26%) had histologic confirmation of mandibular bone invasion. Tumor differentiation was as follows; 2 (5%) poorly, 17 (40%) moderate, and 13 (31%) well differentiated. The incidence of mandibular bone invasion was 50%, 35%, and 23% respectively.

Clinical examinations of all 42 patients (prospectively) were done and retrospectively records of all 42 patients were analyzed based on fixity, loosening of tooth, pain or neurological symptoms. Among them 58 patients (69%) were clinically positive for bone involvement and only 19 patients (32.8% of all clinical positive patients) have pathologically confirmed mandibular involvement (table-3 & 4). So the clinical evaluation has sensitivity of 94% and negative productive value of 96 % which reveals the highly sensitive and can predict the proportion of those with negative results which do not have the bony involvement. It is a very poor modality to predict true negative value and the proportion of positive test result that actually have bony involvement as specificity is only 38% and positive predictive value is 31%.

Orthopantogram was done in 74 patients and only 30 patients (40.5%) were found positive for mandibular involvement (table-5 & 6). Among them only 14 patients (46% of OPG positive patients) have pathologically confirmed mandibular involvement. So the sensitivity and specificity of orthopantogram is 78% and 70% respectively. It has a high negative predictive value i.e. 92% but with the positive productive value of 35%.

Computerized tomography was done in 53 patients to evaluate mandibular involvement and among them 21

patients (39.6%) had radiological evidences of mandibular involvement (table-7 & 8). Only 11 patients (52% of radiologically positive patients) have pathologically confirmed mandibular involvement. So the sensitivity and specificity of CT scan is 91% and 76% respectively. It has 53% Positive predictive value and 95% of negative predictive value.

24 patients were subjected to Magnetic resonance imaging (MRI) and 13 patients had the evidences of mandibular involvement i.e. 54%. Only 6 patients (46% of MRI positive patients) have pathologically confirmed mandibular involvement (table-9). It revealed 100% sensitivity whereas the specificity is only 60% with 46% of positive predictive value and 100% of negative predictive value.

The incidence of bone invasion was 27% with alveolus whereas only 5% were involved with retromolar trigone and buccogingival sulcus. Study from GCRI, Ahmedabad revealed the chances of bone involvement are higher if primary lesions were on retromolar trigone [8]. This may be due to less number of patients with lesions over retromolar trigone presented in the study and in maximum of these patients RMT was involved secondarily from primary over buccal mucosa or BG sulcus. And most of the patients in Ahmedabad study were gutaka/kheni eater who regularly placed the quid towards the RMT region.

20% had histologic confirmation of mandibular bone invasion by oral SCC in our study. Compared to the study Bahadur S et al, there is a 22% to 29% incidence of carcinoma invasion of mandibular bone on initial presentation [9]. Weisman and Kimmelman found one third of all oral tumors that invade bone failed to show any clinical indication of mandibular involvement [10].

Clinical evaluation is highly sensitive but not specific. In our study the sensitivity was 94% and negative productive value of 96% with Specificity of 38% and positive predictive value of 31%. Rao LP et al concluded that clinical impression of mandibular invasion showed a sensitivity of 96% and specificity of 65%, whereas radiological examination (OPG) had a sensitivity of 92% and specificity of 88% [11]. Various studies have shown clinical examination to have a sensitivity (positivity in disease of 30% to 60%), however, unpredictability lies in the high rate of false positive and false negative interpretations of 40% to 60%. and 10% to 30 % respectively [12].

The sensitivity and specificity of orthopantogram is found to be 78% and 70% respectively. It has a high negative predictive value i.e. 92% but with the positive productive value of 35%. According to Shaha et al the ability of

panoramic tomography to detect mandibular bone invasion by oral carcinoma has been examined by several studies which report a sensitivity of 60% to 64% [13]. These values of OPG in our study may be due to the fact that all OPGs were performed outside and came with the reports and were reevaluated by our Onco- radiologist so there may be some personal bias.

The sensitivity and specificity of CT scan is 91% and 76% respectively. It has 53% Positive predictive value and 95% of negative predictive value. Shaha et al observed diagnostic accuracy of CT scan as 68% and concluded that clinical examination was superior to CT for assessing for mandibular involvement and found CT to be "helpful in evaluating the primary tumor and the neck nodes, although its definite value in evaluation of the mandible was very limited [13]. Lane et al found the sensitivity of CT for bone involvement in RMT cancers was 50%, with a negative predictive value of 61.1%. The positive predictive value was 91.1%. These findings suggest that CT is a useful, but potentially inaccurate, predictor of bone invasion in the RMT [14].

In our study MRI scan revealed 100% sensitivity whereas the specificity is only 60% with 46% of positive predictive value and 100% of negative predictive value. Brown et al compared different imaging modalities in predicting invasion of the mandible [15]. After 5 of 35 cases, the MRI was no longer used on account of its generally poor quality. Evaluation of cortical bone involvement is difficult with MRI. The high intensity signal of marrow fat makes the MRI more useful in assessing the medullary spread of tumor [16]. MRI does however; give superior soft tissue contrast with minimal amalgam restoration artifact when compared to CT [17]. The high sensitivity and negative predictive value of MRI in our study may be due to less number of patients who underwent MRI.

Persistent low positive predictive value and specificity in all investigation in our study was recognized. This may be due to the fact that even in early bone erosion, radiological examination was considered positive. We have not considered the different pattern of radiological bone involvement. Pathologically though presence of single malignant cell in the cancellous part of bone was reported positive for bone involvement, these results may be due to the fact that in our hospital all the bones were grossed with ordinary saw, chisel and hammer.

It is observed that predicting bone (mandible) involvement in oral cancers remains a challenge for clinicians. No single modality of investigation appears to have high specificity

and sensitivity. Combination of different modalities increases the both sensitivity and specificity. Meticulous clinical evaluation as well as radiological evaluation is pre requisite to detect early bony involvement. A guide line for evaluation of mandible radiologically should be proposed for detection of true bony involvement. During histological examination extra effort should be put to detect bone involvement as pathological stage not only determine the adjuvant treatment but also predict the prognosis. Our study revealed clinical examination along with high resolution CT scan has the acceptable sensitivity and specificity which may be applied for better results.

Conclusion

There is no single modality of investigation which appears to have high specificity and sensitivity. Combination of different modalities increases the both sensitivity and specificity. In current study clinical examination along with high resolution CT scan has the acceptable sensitivity and specificity which may be applied for better results.

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