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A DESCRIPTIVE STUDY OF MRI IN ORAL CANCER PATIENTS AT A TERTIARY CARE HOSPITAL IN JAIPUR.

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ABSTRACT:

Aim: To describe the observations of MRI in oral cancer patients as per Tumor size, Depth of tumor invasion, Bone involvement and T-staging assuming histopathology as gold standard.

Material & methods: 70 patients with biopsy proven oral cancer with clinical stage at or below T4a were included in this hospital based descriptive type of observational study. All patient underwent clinical and MRI examination. MRI was performed on PHILIPS INGENIA 3 TESLA MRI. Images were interpreted as per tumor size, depth of tumor invasion, bone involvement and the tumor was staged for size (T) under TNM staging criteria of carcinoma oral cavity. All patients underwent surgery and the final diagnosis was made by histopathology. Statistical analysis was applied to find out the Sensitivity, Specificity, Accuracy, PPV and NPV of MRI. Agreement of association was inferred by kappa statistics. Correlation was inferred by Pearson's Correlation coefficient. P-value < 0.05 was taken as significant.

Results: Accuracy of MRI for T- staging in oral cancer patients was 82.85%. Kappa value for MRI data was 0.75. Average depth of invasion calculated on MRI was 8.48mm and by histopathology was 6.90mm.Pearsons correlation coefficient was 0.988. Shrinkage factor was 0.81. Sensitivity, specificity, accuracy, PPV and NPV of MRI in predicting bone invasion was 92.3%, 90.90%, 91.42%, 85.71% and 95.23% respectively.

Conclusion: MRI tumor staging helps to plan appropriate therapy. Depth of invasion in oral malignancies can be measured reliably on MRI which helps in predicting cervical lymph nodal metastasis which can be used as an important supportive tool in deciding type of neck dissection and prognosis of patient.

Keywords: Depth of tumor invasion, Oral Cancer, T-Stage.

Introduction

Oral cancer is the 12th most common cancer globally and the 8th most common in developing countries.[1]The incidence of oral cancer in Indian males is 13% of all malignancies and is the third most common cancer in Indian females.[2]

Squamous cell carcinomas amount to more than 90% of malignant tumours of the oral cavity. Squamous cell carcinoma of lower gingivo buccal complex and tongue are the most common cancer in the Indian sub-continent due to tobacco chewing and alcohol abuse and have been described as Indian oral cancer.[3] Increased incidence of oral squamous cell carcinoma in Indian population is rampant because of habit

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like use of tobacco, tobacco with lime, or tobacco with betel-nut and alcohol.[4]

The prognosis of carcinoma of the oral cavity is influenced by variety of factors such as degree of cellular differentiation, size, location, presence of infiltration into the bony tissue, immune response, age, gender, patients, socio economic status and the presence of cervical lymph node metastasis, the latter being considered the most important factor when determining the prognosis.[5-7] The overall five-year survival rates for cancers of the tongue and oral cavity are around 50%.

The value of imaging in the staging of oral squamous cell carcinoma (OSCC) is in judging operability, assessment of the prognostic characteristics and dimensions of the primary tumor, depth of tumor invasion, the presence of cervical lymph node metastasis, detection of bone infiltration and diagnosis of synchronous primary tumours.[8] Surgical planning depends on tumor invasion: the surgeon needs to know the extent of tumor invasion to achieve adequate surgical clearance.

Owing to superior soft tissue contrast capability and non-involvement of any biological risk to the patient, MRI is the imaging modality of choice in local assessment of oral cavity.[9-11]The choice of appropriate treatment for patients with oral cancer depends largely on accurate pre-treatment staging. Magnetic resonance imaging (MRI) can produce excellent-quality images and direct multi planar formats without ionizing radiation.

This study evaluated the squamous cell carcinomas of the oral cavity (oral tongue and gingivo-buccal complex) on the basis of their appearance, soft tissue and/or bone extent, depth of tumor invasion and T-staging assuming histopathology as gold standard.

MATERIAL AND METHODS

This Hospital based Descriptive type of Observational Study was conducted in the Department of Radio-diagnosis and Modern imaging, ENT, Oncosurgery and Pathology of S.M.S. Medical College, Jaipur from march 2017 to February 2018 after approval from institutional Research Review Board.

Sample size of 70 patients with biopsy proven oral cancer at or below clinical stage T4a according to TNM staging classification were included in study following appropriate consent.

INCLUSION CRITERIA:-

1. All biopsy proven patients (in patients or out patients) of oral cancer at or below clinical stage T4a referred to the department of Radio-diagnosis for MRI examination.
2. Both male and female patients.
3. Patients who gave appropriate informed and written consent for MRI, Neck Dissection and Histopathological examination.

EXCLUSION CRITERIA:-

1. Claustrophobic patients.
2. Patients with metallic implants, pacemakers.
3. Patients of oral cancer with clinical staging greater than T4a.
4. Malignancies other than tongue and gingivo-buccal in location.

Patients who were not willing to have MRI, Neck Dissection and Histopathological examination.

METHOD OF DATA COLLECTION

All patients underwent clinical and MRI examination. All patients underwent surgery and the final diagnosis was made by histopathology.

MRI PROTOCOL:-

MRI Machine – PHILIPS INGENIA 3 TESLA was used. Position of Patient – supine on the MRI table and head coil was applied. Routine T1WI (Axial and coronal spin echo T1W), T2WI (Axial, coronal and sagittal fast spin echo T2W), Short Tau Inversion Recovery (STIR) sequences, Axial diffusion-weighted sequence followed by post contrast axial T1W sequences were taken.

INTERPRETATION OF IMAGES

SIZE

Axial and coronal T2WI were used for measuring the size of lesion. The lesion appears slightly hyper intense on T2WI when compared with T1W images which appears isointense to surrounding mucosa and can predict large size of the lesion. Maximum three dimensional size is taken on axial and coronal images. Lesion was staged for size (T) under TNM staging criteria of carcinoma oral cavity.

DEPTH OF INVASION

Axial gadolinium-enhanced T1-weighted sequence was used to measure depth of invasion for tongue and buccal sub-sites where tumours lie vertically and hence reflected in a medial to lateral dimension.

A horizontal line joining the two tumour–mucosa junctions was drawn as a reference line. We measured the depth of invasion by drawing perpendicular lines from the reference line to the point of maximal tumour projection and invasion and then calculated the greatest radiologically determined tumour thickness by adding these two parameters. (**Fig1**)

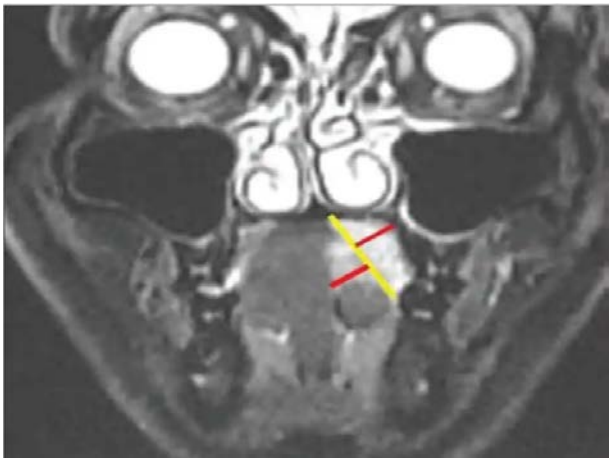

Fig. 1: Coronal STIR image showing left tongue carcinoma. Yellow line represent reference line drawn between the two tumour mucosa junctions. Perpendicular measurements (red lines) on either side to the point of maximal tumor projection are added to get tumor thickness.

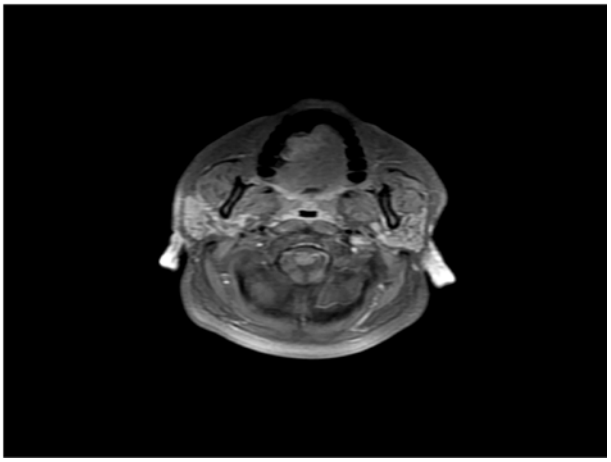

Fig. 2: Calculating depth of invasion (red line) in right lateral border of carcinoma tongue after drawing reference line(black line).White line represents exophytic mass which is ignored

BONE INVASION

MRI diagnostic criteria we used for the evaluation of the infiltration of mandibular bone were :- (1) Lack of the typical hypo intense signal of cortical bone on T1 which is replaced by the signal intensity of the tumour, useful to determinate the cortical invasion. (2) Presence of enhancement after Gd- DTPA administration, in order to demonstrate the marrow involvement.

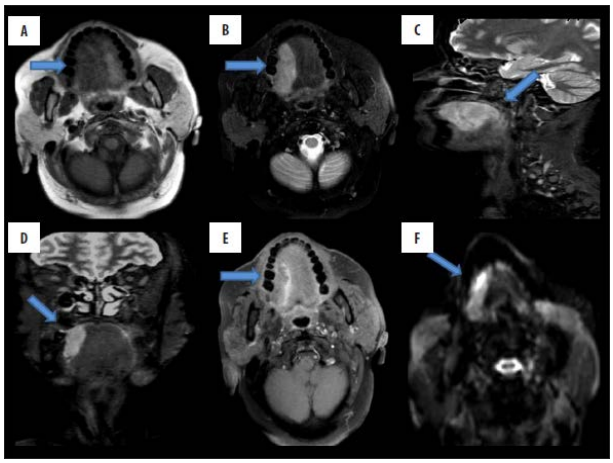

Fig. 3: Shows a mass lesion with soft tissue signal intensity involving the right lateral border of tongue , appearing isointense on T1W images (A), hyperintense on T2W (B), STIR sagittal (C),STIR coronal images (D),extending posteriorly to involve the posterior margin of the tongue, showing mild contrast enhancement on post-contrast T1W images (E) and restriction on diffusion weighted images (F)

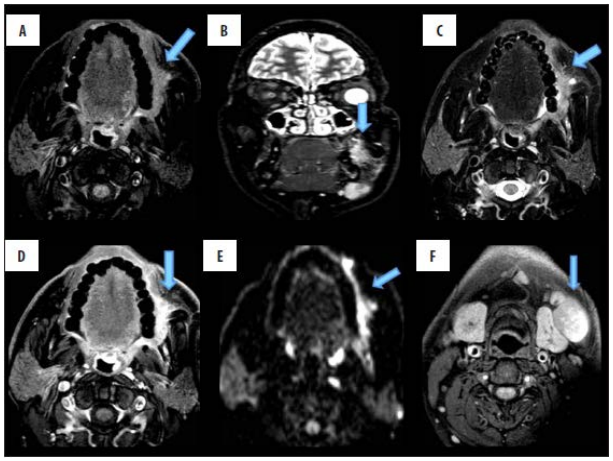

Fig. 4: Shows a mass lesion with ill-defined soft tissue signal intensity, involving the buccal mucosa on the left side, opposite the second, third molars, appearing isointense on T1W **(A),** hyperintense on STIR coronal **(B),** T2W **(C)** images, extending to the left retro molar trigone with loss of fat planes with the buccinator muscle, showing minimal enhancement **(D)** and restriction on DWI **(E). (F)** shows enlarged lymph nodes at levels Ib ,II on both sides.

STATISTICAL ANALYSIS

Statistical analysis was applied to find out the Sensitivity, Specificity, Accuracy, PPV and NPV of MRI. Agreement of association was inferred by kappa statistics. Correlation was inferred by Pearson's Correlation coefficient. P-value < 0.05 was taken as significant.

RESULTS

Most commonly affected age group was of 30-39 years (35.71%), followed by 40-49years (27.14%).OSCC was more commonly seen in males (78.57%) compared to females (21.43%). Buccal mucosa was the most frequently involved site, accounting for 61.42% cases, followed by tongue 34.29% and gingivo-buccal sulcus in 4.29% cases.Socio-economic status of the patients was calculated based on Kuppuswamy's socio-economic status scale. Most of the patients fall under class IV (41.42%) followed by class V (34.28%) and class III (24.28%). In the present study, most of the patients had poorly differentiated (37.14%), followed by well differentiated (31.42%), and moderately differentiated (31.42%) primary tumor.

MRI T stage when compared histopathologically results in 82.85% accuracy rate. Kappa value for MRI data was 0.75 showed strong agreement of association. Average depth of invasion calculated on MRI was 8.48mm and by histopathology was 6.90mm.Pearsons correlation coefficient was 0.988. Shrinkage factor was 0.81 in the present study.

83.33% of patients with depth of invasion greater than 9mm showed evidence of cervical lymph nodal metastasis at one or another levels while 50% cases with depth of invasion greater than 3mm but less than 9mm showed cervical lymph nodal metastasis. No evidence of cervical lymph nodal metastasis in cases in which depth of invasion was less than 3mm was noted.

Sensitivity, specificity, accuracy, PPV and NPV of MRI in predicting bone invasion was 92.3%, 90.90%, 91.42%,85.71% and 95.23% respectively when compared histopathologically.

DISCUSSION

The oral squamous cell carcinoma (OSCC) is one of the rapidly growing oral cancers in the literature of oncology and it is the 6th most common cancer in the world. Tobacco and heavy alcohol is the predominant cause of oral cancers. Tobacco alone covers 90% of all oral cancers. The five year survival rate of oral cancer is 68% in early stage and 27% in the late stage.[12]

The Indian subcontinent has one of the highest incidences of oral cancer in the world; mainly due to the high prevalence of chewing a combination of smokeless tobacco and areca nut[13]

In most countries around the world, oral cancer is more common in males than in females; likewise,in the present study, the incidence of oral squamous cell carcinoma was seen more in males (78.57 %). This can be explained by the fact that the incidence of chewing tobacco and betel nut is higher among males. This study is in accordance with the study of Chaturvedi et al.[2]

The risk of developing oral cancer increases with age and the majority of cases occur in

people aged 4th to 6th decade of life. In the present study, we observed that in patients with OSCC the mean age was 45.41 years and the most commonly involved age group was 30-39 years accounting for 35.71% followed by age group of 40-49 years (27.14%).

A point to note is that 2 cases out of 70 were in between age group 20-29 years. The youngest patient was 20 years old. A study by Hashmi GS et al [83] reported observations showing greater incidence of OSCC within 4th – 5th decade of life. Recently Chaturvedi et al[2] in their study stated the mean age of 45.11 years in patients with OSCC.

Site of oral squamous cell carcinoma has bearing on overall outcome of disease like malignancy of tongue and floor of mouth behave more aggressively when compared with buccal or labial mucosa malignancy. In the present study, most common involved site was buccal mucosa 43(61.42%) followed by tongue 24(34.29%) and gingiva-buccal sulcus 3(4.29%). This finding were similar to the study done by Chaturvedi et al.[2] They mention that, higher involvement of buccal mucosa in Indian population is related to a peculiar habit of placing the smokeless tobacco/areca nut product in the lower buccal vestibule.

Differentiation of tumor has direct impact on prognosis and survival of the patient. In the present study, most of the patients were poorly differentiated (37.14%), followed by well differentiated (31.42%), and moderately differentiated (31.42%). This study was in accordance with Zhou et al, [14] Chaturvedi et al[2] and Sachin Sarode et al [15] who reported similar observations.

In addition to major risk factors for oral cancer (tobacco, alcohol and betel quid use), socio-economic status is also an important risk factor. In the present study, socio-economic status of the patients was calculated based on kuppuswamy's socio-economic status scale.

Most of the patients fall under class IV (41.42%) followed by class V (34.28%) and class III (24.28%).This is in accordance with the S. Wanrnakulasuriya et al.[16]They identified low socio-economic status as an independent variable associated with increased cancer risk.

Correct pre-operative staging is fundamental for proper therapeutic planning. Accuracy rate for T staging based on MRI examination when compared with Histopathological examination came out to be 82.85%.MRI under estimated 1 case of T2 stage and 4 cases of T3 stage and 4 cases of T4 stage while overestimated 3 cases of T3 stage. Similar accuracy of MRI was also seen in study done by A.Vidri et al[17] predicting T stage accuracy of MRI examination of 82%. Tumor size is an important TNM staging parameter in many solid cancers, and the largest tumor diameter has been used for many years in the AJCC and UICC TNM staging systems. Solid cancer is, however, a three-dimensional structure in which cancer cells spread in different planes at various rates to invade the surrounding structures. Owing to the unequal rate of cancer spread in different planes and the presence of tumor necrosis, tumor will never conform to a perfect spherical shape. The largest tumor diameter therefore cannot reflect perfectly the total tumor volume and total number of cancer cells.

Literature reveals that, of all the prognostic parameters that have been evaluated, tumor thickness and depth of invasion have emerged as the best predictors for cervical nodal metastasis. As stated by Moore et al[18]depth of invasion and tumor thickness are not the same, and a distinction has to be made, even though many authors use these two terms synonymously. ''Depth of invasion'' means the extent of cancer growth into the tissue beneath an epithelial surface. Cases in which the epithelium is destroyed, some investigators reconstruct a surface line and measure from this line. However, the depth of invasion is sometimes expressed by referring to the microscopic, anatomic deep structures that are reached, rather than by referring to objective micrometre measurements in millimetres. On the other hand, thickness concerns the entire tumor mass; an objective parameter is needed, and it can be obtained using an ocular micrometre. The proximity to blood vessels and lymphatics is what determines an increased risk

of nodal metastases developing in as much as it facilitates the tumour's ability to expand. Therefore, it might be better to take into consideration the actual mass that is present beneath the theoretical reconstruction of a basement membrane (depth of invasion) rather than the thickness of the entire tumor.

There is a significant role of imaging in predicting depth of tumour invasion. Various studies showed role of MRI in predicting depth of tumour invasion. Tetsumura A et al (2001),[19] Iwai et al,[20] Paul Lam et al.[21] According to them the radiologic tumor thickness as measured on contrast-enhanced T1-weighted images had significant correlation with histologic tumor thickness. This study observed the similar findings with a mean radiological tumour thickness of 8.48mm and histological tumour thickness of 6.90mm.The Pearson's Correlation Coefficient(R) was calculated and its value came out to be 0.988 (p-value of 0.00001).Paul Lam et al [21] showed almost similar Pearson's Correlation Coefficient value (R)-0.938.

MRI showed slightly greater thickness when compared to histological thickness. The possible cause of the discrepancy between the histologic and radiologic thicknesses may be due to the shrinkage of specimen during formalin fixation despite the immediate stretching and pinning of specimen on a foam board. Shrinkage factor for the present study came out to be 0.81.

In the present study prediction of lymph nodal metastasis was done based on radiological tumour thickness calculated on contrast-enhanced T1-weighted images and then was compared with the Histopathological nodal status. These lymph nodal metastasis was divided according to proposed tumor thickness staging classifications. These included stage I (tumor</=3 mm), stage II (> 3 mm but <9mm) and stage III (> 9 mm).38 patients out of 70 patients showed metastasis to the cervical lymph nodes according to radiological tumour thickness. A total of 10 cases showed depth of invasion </= 3mm (Stage I),out of which no patient showed metastatic cervical lymphadenopathy.36 cases showed tumour thickness between 3 and 9mm,out of which 18 patients (50%) were positive for metastasis to cervical lymph nodes. 24 cases showed tumour thickness >9mm with a 20 patients (83%) were positive for metastatic lymphadenopathy. According to Anthony Po Wing Yuenet al[22] , tumor of up to 3 mm thickness had 10% nodal metastasis, tumor thickness of more than 3 mm and upto 9 mm had 50% nodal metastasis, tumor of more than 9 mm had 65% nodal metastasis. However Paul Lam et al[21] uses similar tumour thickness staging classification and found 9% for stage I,21% for stage II and 45% for stage III.

In the present study, the depth of invasion is directly proportional to the cervical lymph node metastasis. The statistically significant value is indicative of progressive increase in lymph node metastasis with increase in the depth of tumor invasion. The probable reason could be that the thick tumors, which invade more deeply, have access to wider lymphatics in which tumor emboli can form more readily than in the small-caliber lymphatics of superficial areas.

The evaluation of either the depth or the extension of the invasion of both the soft tissue and the bone adjacent to the lesion is necessary to well stage the oral-cavity tumours. Clinical assessment of mandibular invasion is possible by either evaluating clinical symptoms and signs or bimanually assessing the mobility of the tumour in relation to the mandible[23]. However, the clinical examination always requires an imaging correlation. Antonello Vidiri et al[24] and Maryam Koopaie et al[25] compared computed tomography and magnetic resonance imaging in the evaluation of the mandibular invasion by squamous cell carcinomas (SCC) of the oral cavity and showed better sensitivity ,specificity and accuracy of MRI in prediction of bone invasion by oral squamous cell malignancies. In the present study, we reported a total of 28 out of 70 cases positive for bone invasion considering the probable tumour invasion of either cortical and/or medullary components involvement. Post-operative histopathology reveals 24 cases positive for bone invasion. MRI had given false positive results in 4 cases and missed 2 cases that were positive for bone invasion giving a

sensitivity of 92.3%, specificity of 90.90% and accuracy of 91.42%.PPV and NPV was 85.71% and 95.23% respectively

CONCLUSION

MRI tumor staging helps to plan appropriate therapy. Depth of invasion in oral malignancies can be measured reliably on MRI which helps in predicting cervical lymph nodal metastasis which can be used as an important supportive tool in deciding type of neck dissection and prognosis of patient.

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