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Original Article

Radiology Section

Differentiating Benign and Malignant Metastatic Cervical Lymph Nodes by Diffusion Weighted MRI Sequence

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ABSTRACT

Introduction: The metastasis to the regional cervical lymph nodes is associated with an increase in nuclear to cytoplasmic ratio leading to reduction in water diffusivity and micro circulation of the node.

Aim: To analyze the potential role of diffusion-weighted imaging to differentiate benign and malignant lymph nodes in oral squamous cell carcinoma.

Materials and Methods: The diffusion-weighted imaging, T1 and T2-weighted MR sequences were performed on biopsy proven squamous cell carcinomas(47 cases) involving oral tongue and/or gingivo-buccal region with cervical lymphadenopathy. The apparent diffusion coefficient [ADC] was measured by using two b factors (500 and 1000 s/mm^2).

Results: On diffusion images, 26/47 patients with malignant lymph nodes showed restricted diffusion on DWI with low signal intensity on ADC maps. Whereas all patients with benign nodes showed no restricted diffusion.The ADC was significantly greater in metastatic lymph nodes [0.82×10^{-3}mm^2/s, $p< 0.01$] than in benign lymphadenopathy [1.21×10^{-3}mm^2/s]

Conclusion: Diffusion-weighted imaging helps in discriminating malignant from benign lymph nodes resulting from oral cavity squamous cell carcinomas. A minimum threshold value of ADC should be kept in mind to identify malignant lymph nodes after taking an appropriate region of interest.

Keywords: Apparent diffusion coefficient, Lymphadenopathy, Perfusion, Squamous cell carcinomas

INTRODUCTION

The detection of cervical nodes metastasis is an important indicator for the prognosis and the treatment of head and neck tumors [1]. Parameters like shape, size, extra-capsular spread and an abnormal inner architecture were used for diagnosing benign and/or malignant metastatic lymph node and size was being the most used one parameter. The presence of central necrosis is the most reliable sign of malignity [2]. However, several reports showed that such conventional parameters are not sufficient to discriminate benign from malignant lesions [3,4].

Recently diffusion-weighted imaging with Magnetic Resonance was introduced. This MR imaging technique analyzes motion of intracellular water: with every change in the water protons movements a variation of signal intensity is produced in diffusion-weighted sequences and as a consequence on Apparent diffusion coefficient [ADC] maps [5]. ADCs values changes according to microstructures and pathophysiologic states which are intrinsic to different tissues, obtained by measuring amount of restricted diffusion after drawing appropriate region of interest in a series of diffusion-weighted MR images [6].

The motion is disturbed by macromolecules, intracellular organelles, and fibers in the tissues [7]. As showed in many studies, metastatic nodes present a reduction of diffusivity, which attributes to hypercellularity, leading to an increased nuclear-to-cytoplasmatic ratio and to perfusion [6]. This reduces the extracellular matrix & the diffusion space of water protons in the extra and intracellular dimensions, with a resultant decrease in ADCs [1]. This procedure provides different information about diseased tissues which can be very well seen on diffusion weighted sequence of MRI.

Hence, our study aim to discriminate between benign and malignant lymph nodal metastasis secondary to squamous cell carcinomas of tongue and gingivo-buccal region.

MATERIALS AND METHODS

Prospective type of study was conducted in Acharya Vinobha Bhave rural hospital Sawangi, [Meghe] in Wardha District of Maharashtra state India from August 2013 to February 2015 certified by ethical Department of University. All biopsy proven cases of squamous cell carcinomas of oral tongue and gingivo-buccal region was undergone MRI were included

in the study and Claustrophobic, patients with metallic implants, other cancers of the oral cavity and patients not willing for MRI were excluded. MR imaging was performed on consecutive patients with oral tongue and/or gingivo-buccal squamous cell carcinoma with enlarged neck nodes following appropriate consent. Our study was performed on 47 patients (18 females and 29 males with an average age of 53 years) with enlarged neck nodes. All 47 patients were below stage IVa according to TNM staging classification and were operated thereafter and post operative samples were then sent for histopathological examination. The study cohort included 21 patient with benign lymphadenopathy and 26 patients with malignant lymphadenopathy.

MR TECHNIQUE AND IMAGE ANALYSIS

All the studies were performed by 1.5-T superconductive scanner (BRIVO MR 355 1.5 TESLA GE MRI).We first performed routine T1WI, T2WI sequences and then diffusion-weighted imaging on these patients. We removed those patients whose MR images were poor in quality due to low signal to-noise ratios particularly in small nodes or because of artifacts. The diffusion-sensitizing gradients were applied with a b factor of 0.500 and 1000s/mm^2 per axis in each patient. The ADC value was automatically reconstructed by a standard software imager. The nodal ADC value was obtained by defining a region of interest (ROI) covering all the pathologic nodes and averaging the results. In the study we chose only the largest abnormal adenopathies with exclusion of necrotic areas.

IMAGE ANALYSES

During the MR studies, we evaluated the quality of diffusion-weighted MR images and determined whether they were acceptable for further analyses. We paid special attention to susceptibility artifacts image distortion, the chemical shift artifacts severity and ghosts in the phase-encoding direction.

RESULTS

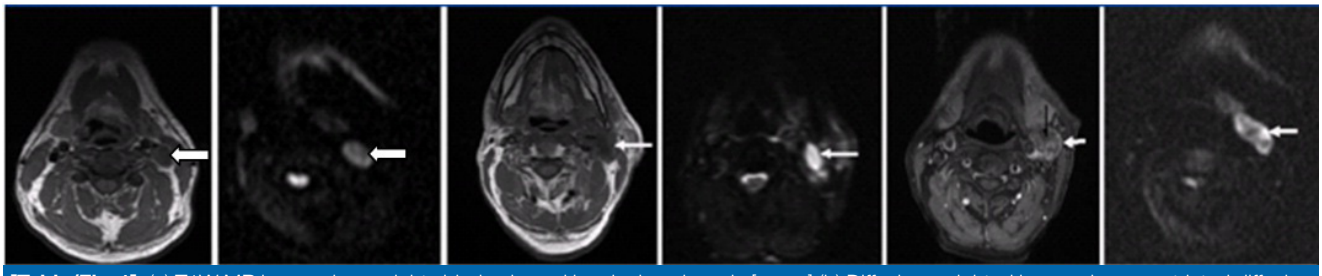
On DWI images in 21/47 cases lymph nodes showed low signal intensity [b=1000], whereas on the ADC maps it presented high signal. However malignant disease appeared hyper intense on diffusion images [Table/Fig-1- 3] and showed low signal intensity on ADC maps. The mean ADC value [Table/Fig-4] of metastatic and lymphomatous nodes was about 0.82×10^{-3}mm^2/s [range: 0.599×10^{-3}–1.020×10^{-3}mm^2/s],lower than the mean value of benign nodes 1.21×10^{-3}mm^2/s [range: 1.020×10^{-3}–1.414×10^{-3}mm^2/s]; this difference was statistically significant [$p < 0.01$]. The best threshold value in our study was calculated and came out to be 1.01×10^{-3}mm^2/s for differentiating malignant from benign nodes.

DISCUSSION

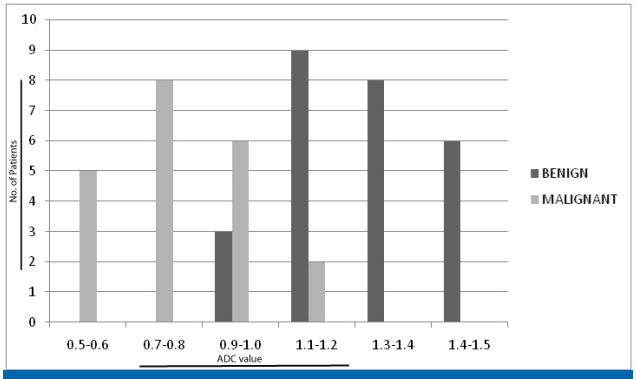
The presence of cervical metastatic nodal disease is a major prognostic determinant for patient with oral cavity cancer, significantly reducing patient survival [1]. The evaluation of cervical nodes is important for diagnosis and staging of malignant diseases and also for planning treatment and follow-up.

Metastasis to the regional cervical lymph nodes are the tumour implants that discontinues from the primary tumour. The invasiveness of malignant tumours permits them to penetrate in to the vessels, lymphatic system and other body cavities , providing the opportunity to spread. The possible mechanism by which regional and distant spread can occur are embolic spread from node to node, permeation of internodal lymphatics of direct extranodal spread resulting in fused cavities that drains directly to distant lymph nodes via long range pathway or direct spread

Brownian motion is the term given to the free diffusion of random thermal motion of molecules measured and expressed as a diffusion coefficient. In biologic tissues, totally free diffusion of molecules does not exist due to cell membranes or molecular boundaries which cause restriction. In the human body, when diffusion is measured, it includes the component of the other kind of micro motion and which is called as perfusion [8]. The translational diffusion extent of molecules measured in the human body is the apparent diffusion coefficient [ADC]. Apparent diffusion coefficient



[Table/Fig-1]: (a) T1W MR image shows right sided enlarged jugular lymph node [arrow] (b) Diffusion weighted image shows restricted diffusion in the lymph node [arrow]. **[Table/Fig-2]:** (a) TIW MR image shows left upper jugular enlarged lymph nodes (b) DWI shows left upper jugular enlarged lymph nodes [arrow] showing restricted diffusion [arrow] **[Table/Fig-3]:** (a) Contrast enhance T1W MR image shows enlarged left submandibular lymph nodes [white arrow] with non-enhancing necrotic component [black arrow] (b) DWI shows enlarged left submandibular lymph nodes [arrow] showing restricted diffusion



[Table/Fig-4]: Chart showing distribution of ADC values among the examined patients

varies according to the microstructures and pathophysiologic states that are intrinsic to different tissues. These changes in Apparent diffusion coefficient values can be obtained by measuring signal intensity in a series of diffusion-weighted MR images.

To our knowledge, DW-MRI sequence has been used to differentiate malignant from benign lesions in several former studies [9]. In line with these prior studies the results of our study demonstrate a significant difference of ADC values between benign and malignant lymph nodes in 47cases of oral squamous cell carcinomas in which 21 cases among them shows restricted diffusion. However, there was a slight overlap of ADC values between benign and malignant lymph nodes in our study seen in 5 patients [10].

The best threshold value calculated was $1.01\times10^{-3}mm^2/s$ for differentiating malignant from benign nodes with a sensitivity of 97% and specificity of 91.1%. Both Chang et al., and Wang et al., reported a threshold value of $1.22\times10^{-3}mm^2/s$, with a sensitivity of 91% and a specificity of 93%, accordingly with our results [6,11]. Razek et al., in a recent study reported metastatic mean ADC value lower than benign ones, with a cut-off value of $1.38\times10^{-3}mm^2/s$, obtaining a sensitivity of 98% and a specificity of 88% [12]. The mean ADC value calculated for malignant and benign metastatic lymph nodes were $0.82\times10^{-3}mm^2/s$ and $1.21\times10^{-3}mm^2/s$ respectively comparable to another study demonstrating a statistically significant difference between the mean ADC values in the benign and malignant lesions $1.505x10^{-3}mm^2/s$ and $1.071^{-3}mm^2/s$ respectively with an ADC threshold values of $1.33x10^{-3}mm^2/s$ for the differentiation between benign and malignant head and neck lesions [9].

In our study we some time came across with the subcentimtric nodal metastasis which leads to partial volume effect when drawing ROI in these lymph nodes leading to significant false positive results [13] and potential bias in image interpretation. Therefore such lymph nodes with a maximum short axial Diameter of 1 cm were excluded.

Sometimes, unexpectedly large ADC values were noted in large malignant lymph nodes secondary to intranodal necrosis or leading to underestimation of lesion extent [14]. To avoid this we kept ROIs on the solid portions of target lymph nodes, away from the necrotic components.

Although our study did not assess the effect of combining DW imaging with TSE MRI on diagnostic accuracy, it is judicious to summarize that the high sensitivity of conventional MR sequences for necrosis or liquefaction may help to prevent necrosis-induced false negative rate of DW-MRI [15].

Finally after comparing with previously reported literatures and our own experience, we found better sensitivities and specificities were obtained using DW-MRI than CT or conventional MRI in staging cervical lymph node metastasis [16].

CONCLUSION

Malignant cervical lymph nodes from oral cavity cancers shows restricted diffusion and appear hyper intense on diffusion weighted imaging identifying a threshold ADC value equal to $1.01\times10^{3}mm^2/s$ between malignant and benign lymph nodes though several studies shows variation of threshold values concluding that diffusion weighted imaging could be considered as an important supportive tool for the diagnosis of enlarged cervical lymphadenopathies in oral cavity cancer.

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