Diffusion weighted imaging in differentiation of cervical lymphadenopathy

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Introduction
Lymphadenopathy is an abnormal increase in size and/or altered consistency of the lymph nodes. Modern imaging modalities such as ultrasound, computed tomography and magnetic resonance imaging allowed reliable detection of cervical lymph nodes. However, the differentiation of benign and malignant lymph nodes remains a challenging job. Nowadays MRI technique of diffusion weighted imaging (DWI) and apparent diffusion coefficient mapping [ADC mapping], is in practice which is a non-invasive MRI technique. DWI can provide information about the lymph node biology and physiology and help us to differentiate benign from malignant lymph nodes.

Material and Methods
The present study was carried out in the tertiary hospital on 25 patients with enlarged cervical lymph nodes diagnosed clinically and confirmed on ultrasound. A detailed history was elicited from all the patients including relevant past and personal history. Thorough General Examination and Systemic Examination were carried out in every case. Basic laboratory investigations like Hb, TLC, DLC and chest radiograph or any other relevant investigation was done.

MR imaging was performed with the use of a 1.5-T MR (Achieva, Philips Medical Systems, Netherland B.V.) by using a standard head and neck coil. After localizer images in axial, coronal and sagittal planes, Conventional images were obtained including T1-weighted images (TR/TE 622/15) and T2-weighted fast spin echo images (3725/80) in the axial and coronal planes, with a section thickness of 3–4 mm, an intersection gap of 0.4 mm. Diffusion-weighted images were obtained in the axial plane, 3–4 mm slice thickness, 1 mm intersection gap, FOV 250 mm, TR/TE-3500/70 ms. The diffusion sensitizing gradient were applied in all three orthogonal planes (X, Y, Z) using b values (0 and 800).
Apparent diffusion coefficient (ADC) maps were automatically calculated by MRI machine software and included in the sequence. ADC maps generated from DWI sequence were used for the measurement of ADC values and MRI characterization and ADC values were recorded as per proforma attached. The ultrasound and MRI findings and ADC values were correlated with FNAC/Histo-pathological findings/clinical follow up.

**Results**

Following observations were made to accomplish aims and objectives of our study.

**Table No.1**: Distribution according to intensity of lymph nodes in MRI

| Intensity                  | Number of patients (n=25) | Percentage |
|----------------------------|---------------------------|------------|
| Homogenous signal intensity| 9                         | 36.0       |
| Heterogeneous signal intensity | 17                        | 64.0       |

**Table No 2**: Distribution of lymphnodes according to necrosis

|                                      | Number of patients (n=25) | Percentage |
|--------------------------------------|---------------------------|------------|
| Necrosis present                     | 8                         | 32.0       |
| Necrosis absent                      | 17                        | 68.0       |

**Table No.3**: Distribution of LN on the Diffusion weighted MRI finding (DWI)

| DWI finding                        | Number of patients (n=25) | Percentage |
|-------------------------------------|---------------------------|------------|
| LNs Showing restriction on DWI      | 19                        | 76.0       |
| LNs Not Showing restriction on DWI  | 6                         | 24.0       |

**Table No.4**: Distribution of ADC Value ($\times 10^{-3}\text{mm}^2/\text{s}$)

| ADC Value ($\times 10^{-3}\text{mm}^2/\text{s}$) | Number of patients (n=25) | Percentage |
|-------------------------------------------------|---------------------------|------------|
| $<1.0$                                           | 16                        | 64.0       |
| $>1.0$                                          | 9                         | 36.0       |

**Table No.5**: Distribution according to MRI Diagnosis

| MRI Diagnosis                                 | Number of patients (n=25) | Percentage |
|-----------------------------------------------|---------------------------|------------|
| Malignant                                     | 19                        | 76.0       |
| TB                                            | 4                         | 16.0       |
| Non-specific infective lymphadenopathy        | 2                         | 8.0        |

**Table No.6**: Distribution according to cytological diagnosis

|                                      | Number of patients (n=25) | Percentage (%) |
|--------------------------------------|---------------------------|----------------|
| Malignant                            | 18                        | 72.0           |
| TB                                   | 5                         | 20.0           |
| Infected etiology                    | 2                         | 8.0            |

**Table No.7**: Correlation of ADC Value on DWI with FNAC diagnosis

| FNAC Diagnosis                     | Number of patients (n=25) | Percentage | ADC Value ($\times 10^{-3}\text{mm}^2/\text{s}$) (Mean±SD) | Range | P value (Benign vs Malignant) |
|------------------------------------|---------------------------|------------|-----------------------------------------------------------|-------|-----------------------------|
| Benign                             | 7                         | 28.0       | 1.37±0.27 (Mean±SD)                                       | 1.08-1.61 | 0.0052                      |
| Hodgkin lymphoma                   | 3                         | 12.0       | 0.72±0.16 (Mean±SD)                                       | 0.7-0.76 | 0.0119                      |
| Non Hodgkin lymphoma               | 2                         | 8.0        | 0.69±0.07 (Mean±SD)                                       | 0.63-0.76 | 0.0026                      |
| Well Differentiated Metastatic Lymphnode | 8                         | 32.0       | 0.91±0.21 (Mean±SD)                                       | 0.58-1.2 | 0.0110                      |
| Poorly Differentiated Metastatic Lymphnode | 5                         | 20.0       | 0.93±0.19 (Mean±SD)                                       | 0.77-1.2 | 0.0052                      |
| Total                              | 25                        | 100.0      | 0.91±0.20 (Mean±SD)                                       | 0.58-1.61 |                             |

**Table No.8**: Correlation of MRI Diagnosis with cytological diagnosis

|                          | Malignant | Tubercular | Infective etiology |
|--------------------------|-----------|------------|--------------------|
| MRI Diagnosis            | 19        | 4          | 2                  |
| Cytological Diagnosis    | 18        | 5          | 2                  |
Chart 1: Receiver operating characteristic (ROC) curve of the ADC value for discrimination between benign and malignant (metastatic and lymphoma) lymph nodes.

Receiver operating characteristic (ROC) curve was used to evaluate the diagnostic capability of the ADC value in differentiating benign from malignant (metastasis and lymphoma) lymph nodes (Fig 21). The area under the curve (AUC) was 0.93 with CI (0.81–1.00), std error = 0.063 and p < 0.001. The ADC value of $1.04 \times 10^{-3}$ mm$^2$/s was used as a cutoff value for differentiation benign from malignant lymph nodes with sensitivity and specificity, 85.7% and 100%, respectively.

| Area   | Std. Error$^a$ | Asymptotic Sig.$^b$ | Asymptotic 95% Confidence Interval |
|--------|----------------|---------------------|-----------------------------------|
| .937   | .063           | .001                | Lower Bound Upper Bound           |

The test result variable(s): ADC Value has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

Discussion

Diffusion-weighted magnetic resonance imaging (DW-MRI) is an imaging technique showing molecular diffusion. Cell size, density and integrity influence the signal intensity seen on diffusion-weighted images. This technique is a helpful complementary tool to distinguish tumoral from non-tumoral tissue, and has several interesting applications in the evaluation of head and neck cancer especially in head and neck lymphadenopathy.$^1$ Differentiation of treatment-induced tissue changes, especially after chemo and/or radiotherapy is another area in which DWI may be very helpful.
The aim of the study was to calculate the ADC values in MRI of the enlarged cervical lymph nodes and there correlation with histopathological findings and to evaluate the potential role of MRI with DWI sequence in characterization of enlarged cervical lymph nodes. In the study of 25 patients, lymph nodes in 19 (76%) patients showed diffusion restriction on DWI and in 6 (24%) patients did not show any restriction on DW imaging, as in 19 patient lymph nodes were hypointense on ADC map and in 6 patient lymph nodes were hyperintense on ADC map. Noha Abd Elshafy Elsaid et al\(^6\) showed in their study that all malignant nodes (n = 24) show restricted diffusion evidenced by increased signal on DWI and low signal on ADC maps. In 5/8 cases with inflammatory diseases, lymph nodes showed reduction of signal intensity on DWI and intermediate signal intensity on ADC maps reflecting facilitated diffusion. 3/8 cases of benign lymphadenopathy, diagnosed as reactive lymphoid hyperplasia and chronic granulomatous infection show increased signal on DWI. Varun Goel et al\(^3\) showed that 21 out of 47 benign lymph nodes showed low signal intensity on DWI, whereas it presented high signal on the ADC maps. However malignant disease appeared hyperintense on DWI and showed low signal intensity on ADC maps. In our study, the ADC values of the benign neck lymph nodes were significantly higher than those of metastatic nodes and nodal lymphoma. Furthermore, the ADC values of the metastatic lymph nodes were significantly higher than those of nodal lymphoma. This was in agreement with Yaser G. Abish et al\(^4\) who concluded that the mean ADC values of the benign lymph nodes (1.48±0.32 × 10\(^{-3}\)) which was significantly higher than Metastatic lymph nodes (0.91±0.73 × 10\(^{-3}\)) and lymphomatous group (0.75±0.04 × 10\(^{-3}\) mm \(^2\)/s).

In our study of 25 patients, on comparing MRI diagnosis with cytological diagnosis, out of 19 cases, which were malignant on MRI, 18 were malignant on cytology. In one patient MRI and DWI were suggestive of malignant etiology but on FNAC it was proved as Tubercular. 4 patients were tubercular on MRI and 5 patients were tubercular on cytological diagnosis and 2 patients showed infective etiology on MRI and cytology. Rujuta Narendra Rege et al\(^5\) when compared MRI diagnosis with cytological diagnosis showed that in their total patients (n=46), 19 patients showed lymph nodes which were neoplastic on MRI and 18 on cytological diagnosis, 27 were tubercular on MRI and cytological diagnosis and 1 patient showed infective etiology on cytological diagnosis and not any node showed infective etiology on MRI. In our study of 25 patients, the difference between the mean ADC values of benign and malignant lesions was statistically significant with p value less than 0.05. Noha Abd Elshafy Elsaid et al\(^6\) also concluded that the p value was statistically significant with p value <0.001 which was in accordance with our study. Perronea A et al\(^7\) reported that the ADC value of benign lymph nodes were significantly higher than those of malignant lymph nodes with a p value <0.01. Rujuta Narendra Rege et al\(^5\) also showed that ADC value is highly significant in the differentiation of benign and malignant lymph nodes with p value of <0.001.

**Conclusion**

MR diffusion imaging is an important supportive tool in differentiation between benign and malignant lymph nodes, can to a lesser extent differentiate between the types of malignant lymphadenopathy and can be used as an indicator for treatment response post chemo and radiotherapy and detection of residual/recurrent pathology. DWI, due to its ability to probe the tumoural microstructure, its short acquisition time, its high repeatability could be assumed to be the most noninvasive tool to differentiate between benign and metastatic lymph nodes in patients with cervical lymphadenopathy.
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