

Diagnostic Accuracy of High Resolution Ultrasound to Differentiate Neoplastic and Non Neoplastic Causes of Cervical Lymphadenopathy

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ABSTRACT

Introduction: Lymph nodes are normal structures distributed throughout the human body and are enlarged in various disease entities. Identifying the relevant lymph nodes is important in treating these patients. High resolution sonography (HRSG) and fine needle aspiration cytology (FNAC) play crucial role in planning the treatment.

Objective: To assess the diagnostic accuracy of HRSG differentiate neoplastic and non neoplastic causes of enlarged cervical lymph nodes.

Materials and Methods: HRSG evaluation of enlarged cervical lymph nodes were performed to differentiate neoplastic from non neoplastic lymph nodes followed by FNAC correlation and the accuracy of HRSG was studied.

Results: One hundred and fourteen lymph nodes of 106 patients were analysed to accomplish the study objective. In our study, HRSG had 96% sensitivity and 90.6% specificity for differentiating between neoplastic and non-neoplastic cervical lymphadenopathy. Similarly positive and negative predictive values were 88.9% and 96.7% respectively. Overall accuracy of HRSG was 93%.

Conclusion: Owing to high sensitivity and negative predictive value, HRSG with Doppler is an excellent first line investigating tool for enlarged lymph nodes and avoids invasive procedures like FNAC in cases of reactive/ inflammatory (non-neoplastic) lymph nodes. However, neoplastic diagnosis of HRSG needs further confirmation by FNAC.

Keywords: Cervical lymphadenopathy, High resolution ultrasound, Neoplastic

INTRODUCTION

Lymph nodes are normal structures distributed throughout the human body. Enlarged cervical lymph node/s is one of the common presenting symptoms or clinical signs in diverse groups of diseases [1]. Incidental cervical lymph nodes are seen commonly in asymptomatic patients and in patients with known malignancy [2]. Hence, identifying the relevant lymph nodes is important in treating these patients. Differentiating malignant from non malignant causes of cervical lymphadenopathy is crucial in deciding the next course of action. Because of the superficial location and availability of high resolution sonography (HRSG), evaluation of cervical lymph node by ultrasound has become the first line of investigation followed by ultrasound guided fine needle aspiration cytology (FNAC) in suspected cases of enlarged cervical lymph nodes [3-7]. If a fairly accurate diagnosis is given by HRSG then many of the invasive FNACs could be avoided. In pursuit of the following objectives, this study was planned.

OBJECTIVE

To assess the diagnostic accuracy of HRSG with colour Doppler imaging to differentiate neoplastic and non neoplastic causes of enlarged cervical lymph nodes when compared to pathological diagnosis.

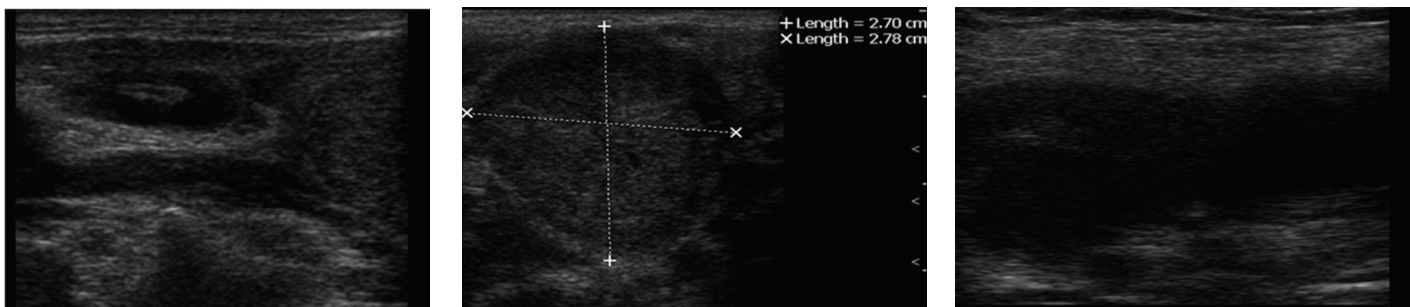
MATERIALS AND METHODS

The present study was conducted at Yenepoya Medical College Hospital, Deralakatte, Mangalore, India. All the patients with clinically enlarged cervical lymph node/s referred for ultrasound study in our hospital were the participants. The study was conducted over a period of four months with an average of one case per working day. Patients with prior biopsy proven diagnosis and those who were not willing for FNAC were excluded from the study.

HRSG evaluation of cervical lymphnode was performed by keeping the patient in supine position with extended neck using a pillow below the shoulder. HRSG of neck was performed using Philips EnVisor C HD multi frequency linear transducer (7.5 to 10 MHz) with Colour, Power and spectral Doppler facility.

The cervical lymph nodes were identified based on their location (level I to VI) and side (right or left) [2]. Level VII nodes were not included as they are not visualized satisfactorily with ultrasound. For each of the lymph node the location, size, shape and ratio of length to breadth of lymph node (long axis and short axis measurements) were documented [2,8]. In addition, presence or absence of central fatty hilum [Table/Fig-1], echo texture [Table/Fig-2], necrosis [Table/Fig-3] and calcification [Table/Fig-4] within the CLN were noted. In case of patients with multiple lymph nodes, the lymph nodes were categorized as discrete or conglomerate [2]. Using Colour Doppler imaging, intra nodal vascularity was looked for. If there was demonstrable vascularity, angle corrected spectral Doppler tracings were obtained and intra nodal resistive index [Table/Fig-5] was measured using the formula: $RI = \frac{\text{Peak Systolic Velocity} - \text{End Diastolic Velocity}}{\text{Peak Systolic Velocity}}$ [9]. Based on all the aforesaid key sonographic features, the enlarged cervical lymph nodes were broadly categorized into neoplastic and non-neoplastic [8-11] [Table/Fig-6].

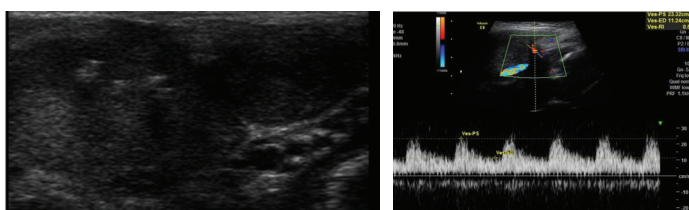
After HRSG evaluation, USG guided FNAC of all the enlarged cervical lymph nodes was performed under aseptic precaution using 21 gauge needles and sent for cytological study to the Department of Pathology, Yenepoya Medical College, Deralakatte. The FNAC reports of all the 116 lymph nodes of 108 patients were documented. The pathologist was not informed about the sonographic diagnosis. Whenever the cytologist gave an inconclusive diagnosis, repeat FNAC was done and a second opinion was obtained to arrive at a diagnosis. In the end, sonographic and pathological diagnoses were



[Table/Fig-1]: Non neoplastic benign oval lymph node with preserved central fatty hilum.

[Table/Fig-2]: Cervical lymph node showing loss of central fatty hilum and round shape – suggestive of neoplastic involvement (FNAC – metastatic adenocarcinoma)

[Table/Fig-3]: HRSG of lymph node showing loss of central fatty hilum with necrosis, round in shape (FNAC – metastatic squamous cell carcinoma)



[Table/Fig-4]: HRSG of Cervical lymph node showing calcification in a round lymph node with loss of central fatty hilum (FNAC – metastatic osteosarcoma)

[Table/Fig-5]: HRSG of neoplastic cervical lymph node with spectral Doppler showing low resistance spectral pattern with RI of 0.52

Sonographic features	Non-neoplastic	Neoplastic
Size	Small	Comparatively large
Long to short axis ratio (shape)	Long axis > short axis (oval)	Long axis $\approx$ short axis (round)
Central Fatty hilum	Preserved	Absent
Echo texture	Hypoechoic	Predominantly Hyperechoic or mixed
Doppler resistive index	High resistance	Low resistance
Necrosis	$\pm$ (more so in tuberculosis)	$\pm$ (commonly seen in metastatic squamous cell carcinoma)
Calcification	$\pm$	$\pm$

[Table/Fig-6]: Sonological features of neoplastic and non-neoplastic lymph nodes

compared. Sensitivity, specificity, positive and negative predictive values of HRSG was calculated keeping pathological diagnosis as gold standard.

The study protocol was approved by the institutional review board and ethical clearance was obtained from the university ethics committee before the inception of data collection. Informed consent from the patient (or guardian in case of minor) was obtained before enrolling them in this study.

RESULTS

Our study population consisted of 108 patients among which 66 (61.1%) were males and 50 (48.9%) were females. Mean age of the study participants was 45.73 ± 18.5 y (range of 13-81y). A total of 116 cervical lymph nodes in 108 patients were evaluated by HRSG and USG guided FNAC. Out of 108 patients, one had neuroma and another had lipoma of the neck which was considered as cervical lymphnodes by the clinician. Therefore, they were excluded and remaining 114 lymph nodes of 106 patients were analyzed to accomplish the study objective.

USG diagnosis	Echo texture			Contour		Central fatty hilum		Necrosis		Calcification		Conglomeration		Total
	Hypo	Hyper	Mixed	Round	Oval	+	-	+	-	+	-	+	-	
Neoplasm	21	0	33	48	6	2	52	36	18	4	50	6	48	54
Inflammatory	45	0	15	12	48	46	14	10	50	3	57	0	60	60

[Table/Fig-7]: Ultrasonographic findings of clinically enlarged cervical lymph nodes and diagnosis

After detailed evaluation of cervical lymph nodes using various HRSG key parameters, we reported 47.4% (n=54) as neoplastic deposits and the rest of them were inflammatory (n=60). [Table/Fig-7].

FNAC reports of all the cervical lymph nodes were analysed, in which, more than half (56.1%, n=64) of the enlarged cervical lymph nodes of our study were diagnosed as non-neoplastic. Among them inflammatory/reactive (26.3%) and tubercular (26.3%) were the predominant causes. Among neoplastic (43.9%) causes squamous cell (21.1%) and adenocarcinomas (14%) were predominant and others were lymphoma (7%), metastatic melanoma (0.9%), metastatic osteosarcoma (0.9%) [Table/Fig-8].

Both pathological and sonographic diagnoses were compared to determine the diagnostic accuracy of HRSG to differentiate neoplastic and non neoplastic causes of enlarged cervical lymphadenopathy. In our study, HRSG had 96% sensitivity and 90.6% specificity for the same. Similarly positive and negative predictive values were 88.9% and 96.7% respectively. The overall accuracy of HRSG to differentiate neoplastic and non neoplastic causes of enlarged cervical lymphadenopathy was 93% [Table/Fig-9].

DISCUSSION

HRSG is being commonly used for enlarged cervical lymph nodes as a non invasive diagnostic tool without the risk of radiation. Its accuracy to differentiate neoplastic and non neoplastic causes would be crucial for the clinician to decide management protocol [3-7]. It would also avoid invasive FNACs by differentiating non neoplastic from neoplastic lymph nodes. Many studies are undertaken in this regard by various authors considering a few HRSG key features to differentiate neoplastic and non neoplastic cervical lymphadenopathy. This study attempted to test the differentiating accuracy of HRSG by considering all the possible key sonographic features and Doppler resistive index to assess the nature of enlarged cervical lymph nodes.

As described by Michiel WM et al., [1] the inflammatory lymph nodes are smaller in size compared to the neoplastic lymph nodes, however the size of the lymph node alone is not a useful finding in assessing the benignity of the node. Ahuja AT et al., [2] have found that preserved fatty hilum is a feature of benignity of the lymph node [2,8]. On Doppler resistive index assessment, inflammatory lymph nodes reveal high RI and low RI is seen in neoplastic lymph nodes [8,11-14].

Ahuja AT et al., [2] have found that the sonographic appearances of normal nodes differ from those of abnormal nodes and concluded that HRSG features of lymph nodes like shape, fatty hilum, necrosis, calcification, matting and intranodal vascularity are helpful

Pathological diagnosis		Frequency	%
Non-neoplastic	Inflammatory/Reactive	30	26.3
	TB	30	26.3
	Kikuchi's disease	3	2.6
	Fibrotic lymph node	1	0.9
Neoplastic	Squamous cell carcinoma	24	21.1
	Adenocarcinoma	16	14.0
	Lymphoma	8	7.0
	Osteosarcoma	1	0.9
	Melanoma	1	0.9
Total		114	100

[Table/Fig-8]: Pathological diagnosis of clinically enlarged cervical lymph nodes

USG diagnosis	Pathological diagnosis		Total
	Neoplastic	Non neoplastic	
Neoplastic	48 (96)	6 (9.4)	54 (47.4)
Non neoplastic	2 (4)	58 (90.6)	60 (52.6)
Total	50 (100)	64 (100)	114 (100)

[Table/Fig-9]: Comparison between ultrasonographic and pathological diagnoses of clinically enlarged cervical lymph nodes

*figures in parenthesis are percentages

in differentiating the same. The same authors have confirmed the usefulness of Doppler ultrasound in differentiating benign from malignant lymph nodes [8,9].

The present study we considered multiple HRSG features to differentiate neoplastic and non neoplastic cervical lymph nodes revealed high sensitivity (96%) and high negative predictive value (96.7%) of HRSG to differentiate neoplastic and non neoplastic causes. Specificity (90.6%) and positive predictive value (88.9%) were also fairly good. Owing to high sensitivity and negative predictive value, the radiologist can predict with reasonable accuracy the non neoplastic nature of the enlarged lymph node by HRSG. However, neoplastic causes of enlarged cervical lymph nodes diagnosed by HRSG require further confirmation by FNAC.

CONCLUSION

Owing to high sensitivity and negative predictive value, HRSG with Doppler is an excellent first line investigating tool for enlarged Lymph nodes and avoids invasive procedures like FNAC in cases of reactive / inflammatory (non-neoplastic) Lymph nodes. However, neoplastic diagnosis of HRSG needs further confirmation by FNAC.

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