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Original article

Sonographic Evaluation of Cervical Lymphadenopathy in Differentiation of Benign From Malignant Neck Nodes

Annitha Elavarasi Jayamohan[1*], Suresh V Reddy[2], Ajit Kumar Reddy[3], Prakash Manikka Lakshmanan[4], Krishnappa Nasappa[5], Sanjay Sanabe Chikkananjaiah[6], Harini Bopaiah[7], Antony Jean[8]

[1&3] Senior Residents, [2&6]Associate Professors, [4]Professor, [5]Professor & HOD,[7]Assistant Professor, Department of Radiology, Kempegowda Institute Of Medical Sciences, Bangalore.
[8]Consultant, Medall Diagnostics.

ABSTRACT

Background: Nodes are the common site for Inflammatory, Infective (Viral, Bacterial, and Protozoan) and neoplastic involvement. Cervical lymph nodes, which have the advantage of being located superficially, can be studied with even better spatial resolution using ultrasound. The purpose of the study was to differentiate between benign and malignant cervical lymph nodes by means of ultrasound with colour doppler. To correlate between the Ultrasound findings and histopathological findings of cervical lymph nodes. **Material and Methods:** Patients with clinical evidence of cervical lymphadenopathy sent for ultrasound guided FNAC or biopsy are included in the study. Various parameters were assessed and level staged according AJCC based nodal classification. Nodes were categorized as benign, malignant and indeterminate based on select criteria. Subsequently FNAC or biopsy was done and results correlated. **Results:** There was strong association of hilar echo with histology where benign nodes showed preservation of central fatty hilum and all malignant nodes were found to be devoid of central hilar echo pattern(P=0.040*). Peripheral and mixed vascular patterns were seen in malignancy and central vascularity & lack of vascularity in benign and indeterminate nodes (P<0.001**). The study showed a Sensitivity of 81.82 and a Specificity of 95 with a PPV of 90 and a NPV of 90.32 and found to have strong significance between Sonographic and Histological findings. **Conclusion:** The study showed good correlation between colour doppler ultrasound and histopathology finding in differentiation benign and malignant cervical lymph nodes especially based on hilar echogenicity, echopattern of the node and distribution of vascularity.

KEYWORDS: Sonographic evaluation, Cervical, Lymphadenopathy.

INTRODUCTION

The lymph nodes are situated in groups or chains such that the afferent lymphatic vessels leading to these lymph nodes drain discrete anatomic regions. Most lymph nodes have an oval or bean shape with a slight depression on the hilar side. The hilum contains rterioles, venules, and efferent lymphatic vessels. There are usually only 2 or 3 efferent vessels at the hilum, but about 6 and 25 afferent lymphatic vessels that enter the nodal periphery away from the hilum[1]. Of the 800 lymph nodes in the human body there are about 300 lymph nodes in the neck [2]. The American joint Committee on Cancer (AJCC) classification divides palpable cervical lymph nodes into seven levels which are based on the extent and level of cervical nodal involvement by metastatic tumour and has been widely used by surgeons and oncologists [3].

Lymph nodes are the common site for Inflammatory, Infective (Viral, Bacterial, and Protozoan) and Neoplastic involvement. The diagnosis of malignant lymphadenopathy helps in staging of primary malignant lesions of head and neck and its therapeutic planning. There will be morphological and angio-architectural difference among various cervical nodal diseases which aid in differentiating benign from malignant lymph nodes [4,5]. The histologic changes seen within the node in nodal diseases have been used to explain morphologic changes in lymph nodes depicted by gray-scale sonography [6].

The normal blood vessel morphology in metastatic nodes is destroyed by neoplastic infiltration, whereas in inflammatory nodal disease there will be dilatation of

intranodal vessels due to local humoral agents.The development of ultrasound with advancement in color doppler imaging helps to characterize the node. Cervical lymph nodes, which have the advantage of being located superficially, can be studied with even better spatial resolution [4,7]. High-resolution ultrasound is a useful imaging tool for the assessment of cervical lymph nodes because of its high imaging resolution, its high sensitivity (98%) and specificity (95%) when combined with fine-needle aspiration cytology (FNAC) [8-10]. Moreover, ultrasound is non-invasive and easily available; therefore, it is suitable for monitoring disease, progression and follow-up assessment after treatment.

Cervical lymph nodes can also be evaluated with CT, but CT holds risk of radiation and is less sensitive in the detection of small nodes. MRI can be used to assess cervical lymph nodes, but it is time consuming, costly and has its inherent contraindication [11]. The use of fine needle aspiration cytology (FNAC) in the investigation of lymphadenopathy has become an acceptable technique. However it remains invasive even if minimal.

We therefore performed the study to differentiate between benign and malignant lymph nodes by means of ultrasound and Doppler. Likewise to correlate between the Sonographic findings and histopathological findings of cervical lymph nodes. Thus to determine the value of Ultrasound including colour Doppler so as to minimize the need for invasive methods or even surgery.

MATERIALS AND METHODS

Patients with clinical evidence of cervical lymphadenopathy resulting from a variety of diseases diagnosed on the basis of history and clinical examination, who were sent for ultrasound guided FNAC or biopsy, are included in the study. The study was a observational prospective type involving a single group of patients. Patients of all age groups and both sexes referred for sonographic evaluation – image guided FNAC for cervical lymphadenopathy were included in the study. Patients not willing to give consent and those with preexisting bleeding disorders were excluded.

Ultrasound of the neck was performed by using a GE Voluson 730 Pro ultrasound systems with a linear transducer (7-12 MHz). Thyroid gland evaluation was done for all cases, first to rule out primary lesions, followed by cervical lymphadenopathy evaluation in all levels according to AJCC nodal classification. Ultrasound with colour Doppler parameters were noted down and classified as benign , malignant or indeterminate. Image guided FNAC / Biopsy was done and the histopathological report was correlated with the ultrasound sonographic classification.

All records of the 31 patients under study were maintained confidentially. All relevant data including patient name, age, sex, hospital number, patients complains, clinical finding, Lab investigation and other radiological investigation was collected and entered into performa along with the Ultrasound and pathological finding.

This was a prospective observational study, which was conducted at the Mahatma Gandhi Medical College and Research Institute Hospital, a rural tertiary care hospital with an annual volume of above 100,000 patients over one year period.The Institutional Medical Ethics Committee approved this study. From January 2010 until April 2011 we examined patients of all age group who were referred with clinical reference as cervical lymphadenopathy. Written informed consent was obtained from the patients after which Sonographic examination was done. We excluded all patients not willing to give consent as well as those with pre-existing bleeding disorders.

Statistical Methods

All data was entered into a Performa Sheet which was then entered into Excel [MS Excel 2011]. The Sheet had a visual map for marking and divided into indications for both genders. Other biographical details were also collected including date of birth, weight and height.

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD [Min-Max] and results on categorical measurements are presented in Number [%]. Significance is assessed at 5 % level of significance. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Diagnostic statistics viz. Sensitivity, Specificity, PPV, NPV and Accuracy have been computed to find the correlation USG and Biochemical findings. Statistical softwares (viz. SPSS 15.0), were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS

A prospective evaluation study with 31 patients was undertaken to study the differentiation between benign and malignant cervical lymph nodes by means of Colour Doppler ultrasound. Multiple lymph nodes were found to be more common in comparison to solitary lymph nodes. There is no significant correlation between histopathology finding and age, gender. However significant association was found between histological findings and co existing pathology like thyroid, mediastinal or abdominal masses.

Shape, multiplicity and margin were seen to be statistically of poor significance (Table 1). There was strong association of hilar echo with histology where benign nodes showed preservation of central fatty hilum and all malignant nodes were found to be devoid of central hilar echo pattern(P=0.040*). Isoechoic pattern was found in both malignant and indeterminate but never in benign lymph nodes; Heterogeneous echo pattern were common to both benign and malignant but not indeterminate (Table 1).

Presence of vascularity showed no significant association, with histopathology as seen in all cases of malignancy and a greater portion of benign nodes (P=0.040*). However, absence of vascularity showed strong association with benign nodes (Table 1). Distribution pattern of vascularity showed statically significant correlation with Histopathology; peripheral and mixed patterns in malignancy and central vascularity & lack of vascularity in benign and indeterminate nodes (P<0.001**). Avascular lymph node were histologically proven to be of tuberculous etiology (Table 1). It was noted that nine patients were found to have malignant nodes both sonographically and histologically. One patient was found to be sonographically

indeterminate and histologically benign (*false positive*). Two patients were found to be sonographically benign and histologically indeterminate (*false negative*). Nineteen patients were found to be benign both sonographically and histologically (Table 2 & 3).

The study showed a Sensitivity of 81.82 and a Specificity of 95 with a Positive Predictive value of 90 and a Negative Predictive value of 90.32 and found to have strong significance between Sonographic and Histological findings.

Table 1: Comparison of Characteristics of cervical lymph node with Histopathology findings

USG	Histopathology				
	Characteristics	**Benign(n=20)**	**Malignant(n=9)**	**Indeterminate(n=2)**	**P value**
Shape	Oval	14(7.0%)	4(44.4%)	2(100%)	0.229
	Round	2(10%)	4(44.4%)	0(0%)	
	Matted	4(20%)	1(11.1%)	0(0%)	
Multiplicity	Single	1(5%)	1(11.1%)	0(0%)	0.591
	Multiple	19(95%)	8(88.9%)	2(200%)	
Hilum	Absent	12(60%)	9(100%)	1(50%)	0.040*
	Present	8(40%)	0(0%)	1(50%)	
Echo	Hypoechoic	6(30%)	1(11.1%)	0(0%)	0.010*
	Isoechoic	0(0%)	3(33.3%)	1(50%)	
	Heterogeneous	6(30%)	3(33.3%)	0(0%)	
	Calcific	1(5%)	2(22.2%)	0(0%)	
	Central fatty	7(35%)	0(0%)	1(50%)	
Margins	Well defined	16(80%)	6(66.7%)	2(200%)	0.788
	Irregular	4(20%)	3(33.3%)	0(0%)	
Vascularity	Absent	8(40%)	0(0%)	1(50%)	0.040*
	Present	12(60%)	9(100%)	1(50%)	
Distribution	No vascularity	8(40%)	0(0%)	1(50%)	<0.001**
	Central	8(40%)	0(0%)	1(50%)	
	Peripheral	0(0%)	5(55.6%)	0(0%)	
	Mixed	4(20%)	4(44.4)	0(0%)	

Table 2: Correlation of USG diagnosis and Histopathology (n=31)

USG diagnosis	Histopathology					
	Benign		**Malignant**		**Indeterminate**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Benign	19	61-3	0	0.0	2	6.5
Malignant	0	0.0	9	29.1	0	0.0
Indeterminate	1	3.2	0	0.0	0	0.0
Total	20	64.5	9	29.1	2	6.5
USG diagnosis is significantly associated with Histology with P<0.001**(by 3x3 Fisher Exact test)						

Table 3: Correlation of USG diagnosis with Histology findings: An observation

USG	Histopathology		
	Benign	**Malignant**	**Indeterminate**
Benign	19	-	2
Malignant	-	9	-
Indeterminate	1	-	-
(**P value** - <0.001**)			

DISCUSSION

It has been reported that ultrasound is superior to clinical examination in the detection of cervical lymphadenopathy with sensitivity of 96.8% and 73.3% respectively [12]. Our study was conducted with 31 patients where the youngest was 18 years old and the oldest patient was 70 years.

On the basis of size alone, about 80% of enlarged nodes are truly malignant and 20% are enlarged from benign hyperplasia. Nodal size alone, however, has been shown to be an unreliable criterion for differentiating reactive from malignant lymph nodes [13]. In our study, there was no significant difference in shape and size between malignant

and benign lymph nodes contrary to finding of Gary et al [14].

Only two cases had calcification in lymph nodes, so was not included as criteria for characterization. One patient had micro calcification in histological proven case of Tuberculosis and second patient had cluster of calcification in lymph node in case of metastasis. Ishii et al mentioned that presence of calcifications can also be useful in predicting the benign or malignant nature of lymph nodes. Most authors have reported calcifications only in malignant nodes [11]. We did not observe any calcifications in reactively enlarged benign lymph nodes [10].

H J steinkamp et al evaluated short- and long-axis diameters of 730 enlarged cervical lymph nodes with ultrasonography to determine valid diagnostic parameter in the differentiation between benign and malignant nodal disease. 95% of enlarged cervical nodes shown on ultrasound to have a L/S ratio of more than 2 were correctly diagnosed as benign. Nodes presenting with a more circular shape and a L/S ratio of less than 2 were diagnosed correctly as metastases with 95% accuracy. This is in contrast to our study , stated that the L/S ratio of lymph nodes provides an excellent criterion for differentiation between benign and malignant enlargement in cervical lymphadenopathy [15].

In our study, Shape, multiplicity and margin were seen to be statistically of poor significance. Considering the characteristics Oval shape was found to be dominant while round and matted were more or less the same. P value for shape was 0.229, multiplicity was 0.591 and margin was 0.788. In a study conducted by Choi MY et al benign lymphadenopathies represented 89% and 83% of avascular and central hilar vascularity, respectively. However, malignant lymphadenopathies dominated in nodes that were of spotted (72%), peripheral (60%), and mixed type (80%).

Likewise vascularity showed significant association with histologically proved cases of malignancy (100%). Distribution patterns of vascularity being of strong significance showed peripheral (55.6%) & mixed patterns (44.4%) in malignancy. Central vascularity and lack of vascularity were seen in both benign and intermediate nodes.

Similar to our study, Dangore et al evaluated 143 cervical lymph nodes and stated that Correlation of patterns of colour Doppler flow signals with pathological diagnosis showed that central flow for benign nodes and peripheral flow for malignant nodes were highly significant parameters (P , 0.01). CDUS has a higher specificity than clinical evaluation, being 94.28% and 58.76%, respectively. Accuracy of the CDUS examination was also definitely higher than clinical evaluation at 92.85% and 63.67%, respectively. Nodal vascularity can be used to differentiate benign from malignant lymphadenopathy [16].

In our study the presence of vascularity showed no significant association, with histopathology as seen in all cases of malignancy and a greater portion of benign nodes (P=0.040*). However, absence of vascularity showed strong association with benign nodes. Arborizing pattern of vascularity was consistent with lymphoma histopathologically. Distribution pattern of vascularity showed statically significant correlation with histopathology; peripheral and mixed patterns in malignancy and central vascularity & lack of vascularity in benign and indeterminate nodes (P<0.001**).

Controversial to our study, Sanja et al concluded that Ultrasonography itself cannot exactly distinguish benign from malignant lesions, but an echo graphic appearance can suggest malignancy and help in the selection of the correct nodes to aspirate with sonographically guided FNAB, which is crucial for a final diagnosis. In sampling, nodes with a rounded appearance should be chosen primarily; a round shape with an L/T ratio of less than 2 in hypoechoic nodes without a hyperechoic hilum indicates the presence of metastases.

In this study, the absence of an echogenic hilum and the presence of cystic portions and calcifications were significantly greater in malignancies than in benign lesions. The decision to use ultrasonographically guided FNAC as well as the choice of nodes to be punctured should be in concordance with these morphologic criteria of size, shape, location, and internal architecture [17].

There was strong association of hilar echo with histology in our study, where benign nodes showed preservation of central fatty hilum and all malignant nodes were found to be devoid of central hilar echo pattern(P=0.040*). Hefeda, et al consider abnormal hilar echoes as the most sensitive and specific parameter. In our study Isoechoic pattern was seen with both malignant and indeterminate but never benign lymph nodes; Heterogeneous echo pattern were common to both benign and malignant but not indeterminate; only two cases had calcification, so was not included as criteria for characterization.

There was significant correlation between histopathology finding and thyroid pathology in our study. Only one metastatic case from thyroid was included in our study. There was no evidence of cystic portion in lymph nodes. Sanja et al stated that detection of cystic portions in 21.3% of metastatic nodes, and all of them were metastases of papillary carcinoma. There was no cystic degeneration among benign lymph nodes in their study [17]. Paul et al stated that US proved highly efficacious as an adjunctive procedure to the other imaging modalities, specifically CT, in the preoperative evaluation of patients with malignant head and neck diseases [18].

Our study shows good correlation between colour doppler ultrasound and histopathology finding in differentiation benign and malignant cervical lymph nodes especially, based on hilar echogenicity, echo pattern of the node and distribution of vascularity. Both USG and histology were accurately able to identify malignant nodes in nine patients. Twenty one patients were diagnosed to be benign sonographically while twenty were found to be benign histologically. Out of Twenty Histological benign cases, Nine were Tuberculosis, Eight were Reactive lymphadenopathy, One was Hamartomatous lesion, Two were Inflammatory and three were Granulomatous lymphadenopathy. Out of nine Histologically Malignant cases, Eight were Metastatic lymph nodes and one was Lymphoma.

Histologically one patient did not provide a definitive diagnosis hence was allocated into indeterminate. Likewise another lymph node was given a differential of Tuberculosis and Lymphoma hence was allocated as the second patient in

indeterminate category. One patient did not fall into either category sonographically as the nodes showed loss of hilum but showed hilar vascularity.

A study conducted by Couto et al Diagnostic value of ultrasound and color Doppler in Identifying axillary lymph node metastases in patients with breast cancer showed a sensitivity of 71.4%, a specificity of 71.4%, a negative predictive value of 80.6% and a positive predictive value of 60.0%22. Another study conducted by Ariji et al Power Doppler Sonography of Cervical Lymph Nodes in Patients with Head and Neck Cancer showed high levels of sensitivity (83%) and specificity (98%) in depicting metastatic lymph nodes [19].

Ultrasonography of cervical lymph nodes by Michael et al mention a high sensitivity (98%) and specificity (95%) when combined with fine-needle aspiration cytology (FNAC) [20].This study showed a Sensitivity of 81.82% and a Specificity of 95% with a Positive Predictive value of 90% and a Negative Predictive value of 90.32% and found to have strong significance between Sonographic and Histological findings.

Limitations

Study included a small group. A larger group of patients are required for confirmatory findings and arrive at definitive criteria.

CONCLUSION

The study shows good correlation between colour doppler ultrasound and histopathology finding in differentiation benign and malignant cervical lymph nodes especially based on hilar echogenicity, echo pattern of the node and distribution of vascularity.

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*Corresponding author: Annitha Elavarasi Jayamohan
E-Mail: anithaela@gmail.com