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Original Article

Ultrasonographic Evaluation of Cervical Lymphadenopathy with Cytological Correlation

Suresh Kumar[1], Sonjjay Pande[2], Gourav Shrivastava[3]

[1]Assistant Professor, Department of Radio Diagnosis, NSCB Medical College Jabalpur, Madhya Pradesh, India, [2]Professor, Department of Radiodiagnosis, NSCB Medical College Jabalpur, Madhya Pradesh, India, [3]Post-graduate Student, Department of Radio Diagnosis Diagnosis, NSCB Medical College Jabalpur, Madhya Pradesh, India

Abstract

Introduction: Cervical lymphadenopathy is one of the most common causes of mass in head and neck region; there are various causes of CL common among them are reactive, tuberculosis, metastasis, and lymphoma.

Aims and Objectives: The aims and objectives of this study were to study and differentiate between neoplastic (malignant) and nonneoplastic (reactive and tubercular) cervical lymph nodes by high-resolution ultrasonography. To correlate between ultrasound and fine needle aspiration cytology (FNAC) in cervical lymphadenopathy.

Material and Methods: Data were collected from a total of 80 cases referred for an ultrasound of neck to the Department of Radiodiagnosis, NSCB Medical College, Jabalpur, from December 2015 to December 2016, with 5-10 MH linear transducer using SIEMENS ultrasound machine. Lymph nodes were assessed using gray scale and color Doppler parameters such as nodal level and site, size, shape, L/S ratio, border, hilum, echotexture, necrosis, matting, and angioarchitecture. A provisional diagnosis was suggested after the ultrasound examination, and these findings were correlated with FNAC/histopathological findings.

Results: In our study, out of 45 non-neoplastic nodes (reactive and tubercular), only 40 nodes were identified as non-neoplastic (reactive/tubercular) on ultrasound prior to FNAC/histopathology. Out of 35 possible neoplastic (malignant nodes) detected on ultrasound, only 29 lymph nodes turned out to be neoplastic on FNAC/histopathology. Lymph node with oval shape (L/S ratio >2) echogenic hilum, homogenous echotexture, and hilar vascularity was considered as significant parameters in detecting non-neoplastic (reactive) lymph nodes, which showed matting with soft tissue edema. Nodes which were round shape (L/S ratio <2), absent hilum, heterogeneous echotexture, hilar, capsular vessels, and mixed vascularity were considered as significant parameters in detecting neoplastic (malignant) lymph nodes. Correlation of sonographic findings with FNAC/histopathological findings was performed. Sensitivity and specificity of ultrasound in differentiating neoplastic from non-neoplastic cervical lymphadenopathy was found to be 90% and 74%, respectively.

Conclusions: This study concludes that ultrasonographic examination proved as a valuable primary investigation to identify lymph nodes and differentiate non-neoplastic and neoplastic lymphadenopathy.

Key words: Cervical lymphadenopathy, Ultrasonography, Malignant

INTRODUCTION

Cervical lymphadenopathy is one of the most common causes of mass in head and neck region; there are various causes of CL common among them are reactive, tuberculosis, metastasis, and lymphoma.

Ultrasonographic criteria for distinguishing neoplastic and non-neoplastic lymph nodes have been studied under site, shape, size, echogenicity, hilum, matting, nodal border, long/short axis ratio, intranodal necrosis, and angioarchitecture.[1]

Ultrasonographic features that help to identify abnormal nodes as well as giving clues to neoplastic nodes are heterogeneous echogenicity, absent hilus, invasion, and

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Corresponding Author: Dr. Suresh Kumar, F-54, Doctors Colony Medical College Campus Jabalpur, Madhya Pradesh, India.
Phone: +91-7354085808. E-mail: suresh6932@gmail.com

intranodal necrosis. The shape is the best method to attempt the differentiation between neoplastic and non-neoplastic lymph nodes. The long/short diameter ratio of lymph node provides excellent criteria for differentiation between neoplastic and non-neoplastic cervical lymphadenopathy.[2]

By using color/power Doppler sonography can further characterize lymph nodes as non-neoplastic (reactive, tubercular) and neoplastic. The non-neoplastic (reactive) nodes show increased central hilar vascularity, with radial symmetry whereas, neoplastic (malignant) nodes show absent hilar vascularity and increased peripheral vascularity.[1]

MATERIALS AND METHODS

In this study, 80 patients age between 12 and 60 years with cervical lymphadenopathy referred for ultrasonography of neck to the Department of Radiodiagnosis, NSCB Medical College, over a period of December 2015 - December 2016 are included in this study. All scans carried out on 5-10 MHz linear transducer using SIEMENS ultrasound-guided (USG), Philips machine.

Inclusion Criteria

1. All patients coming for ultrasound neck.
2. Patients more than 12 years of age of either sex.

Exclusion Criteria

1. Moribund patients.
2. No fine needle aspiration cytology (FNAC) available.
3. Patient with no evidence of cervical lymphadenopathy on ultrasound.

Common ultrasound scan planes used in the examination of cervical nodes in different regions of the neck.

Regions	Scan plane(s)
Submental	Transverse
Submandibular	Transverse
Parotid	Transverse and longitudinal
Upper cervical	Transverse
Middle cervical	Transverse
Lower cervical	Transverse
Supraclavicular fossa	Transverse
Posterior triangle	Transverse and longitudinal

The criteria that are followed in this study to differentiate between reactive, tubercular, and neoplastic (malignant) lymph nodes (Table 5):

1. Distribution includes levels and side;
2. Number;
3. Size;
4. Shape includes L/S ratio;
5. Echogenic hilum - wide, narrow, and absent;
6. Border - sharp and unsharp;
7. Homogenecity and heterogenecity;
8. Central necrosis and cystic necrosis;
9. Matting;
10. Vascularity and angioarchitecture: Hilar vessels, peripheral vessels, mixed vessels, focal absence of perfusion and absence of perfusion.

Non-neoplastic lymph nodes include reactive and tubercular. Lymph node oval shape, echogenic hilum, homogenous echotexture, matting, L/S ratio >2, and hilar vascularity were considered as reactive lymphadenopathy. Nodes hypoechoic, round without echogenic hilus, intranodal cystic necrosis, nodal matting, and adjacent soft tissue edema were considered tubercular lymphadenitis.

Round shape, absent hilum, heterogenous echotexture, sharp borders, L/S ratio <2, capsular vessels (peripheral), mixed vascularity, displacement of vessels, and focal absence of perfusion were considered in detecting neoplastic lymph nodes. Since there was no difference between primary malignancy and metastasis sonologically, results of the examination were grouped as malignant under neoplastic category.

USG Guided FNAC

The most promising contribution of ultrasound is in the guidance of FNAC in non-palpable lymph nodes. Under aseptic precaution and ultrasound guidance, 21/22 gauge needle with syringe is introduced into enlarged abnormal lymph nodes, and sample is sent for analysis.

RESULTS

In our study most common no. of cases seen in age group (13-20) as shown in Table 1, out of 45 non-neoplastic nodes (reactive and tubercular), only 40 nodes were identified as non-neoplastic (reactive/tubercular) on ultrasound before FNAC/histopathology. Out of 35 possible neoplastic (malignant nodes) detected on ultrasound, only 29 lymph nodes turned out to be neoplastic on FNAC/histopathology. Lymph node with oval shape (L/S ratio >2) echogenic hilum, homogenous echotexture, and hilar vascularity were considered as significant parameters in detecting non-neoplastic (reactive) lymph nodes, which showed matting with soft tissue edema. Nodes which were round shape (L/S ratio <2), absent hilum, heterogeneous echotexture, hilar, capsular vessels, and mixed vascularity were considered as significant parameters in detecting neoplastic (malignant) lymph nodes. Correlation of sonographic findings with FNAC/histopathological findings was performed. Sensitivity and specificity of ultrasound in differentiating neoplastic from

non-neoplastic cervical lymphadenopathy was found to be 90% and 74%, respectively.

Our study had a high sensitivity of 91.3%, specificity of 75.93%, positive predictive value of 91.11%, and also a negative predictive value of 76.36% in differentiating neoplastic from non-neoplastic lymphadenopathy (Table 4).

Table 10 shows most of benign, reactive, tubercular and malignant lymph nodes showing lymph node perfusion, which is not significant and nonspecific criteria.

On USG at level I an oval lymph node with maintained Hilum and hilar vascularity suggestive of reactive lymph node confirmed on FNAC (Figure 1).

Table 1: Age distribution

Age groups (in years)	Number of cases
13-20	17
21-30	11
31-40	13
41-50	15
51-60	7
61-70	9
>70	8

Table 2: Diagnosis of cervical lymphadenopathy on USG

Diagnosis on USG	Number of lymph nodes
Malignant	35
Tubercular	21
Reactive	24
Total	80

USG: Ultrasound-guided

Table 3: Diagnosis of cervical lymphadenopathy on FNAC/histopathology

Diagnosis on USG	Number of lymph nodes
Malignant	29
Tubercular	21
Reactive	30
Total	80

USG: Ultrasound-guided, FNAC: Fine needle aspiration cytology

Table 4: Comparison of USG diagnosis with FNAC diagnosis

USG diagnosis	FNAC diagnosis			
	Malignant	Tubercular	Reactive	Total
Malignant	20	10	3	35
Tubercular	5	8	8	21
Reactive	4	3	17	24
Total	29	21	30	80

χ^2=110.2, *P*<0.001, USG: Ultrasound-guided, FNAC: Fine needle aspiration cytology

On USG oval lymph node with maintained Hilum and hilar vascularity suggestive of reactive lymph node but on FNAC it was proved to be malign CM ant (Figure 2).

DISCUSSION

Ultrasound is preferred over computed tomography (CT) and magnetic resonance imaging (MRI) in evaluation cervical lymphadenopathy.

1. In differentiating benign and malignant lymph nodes, the size cannot be considered as sole criteria.
2. The presence of central nodal necrosis is thought to be one of the most specific signs of metastatic involvement with a specificity of 95-100%. In CT, the nodal necrosis is observed as central low attenuation. Infection and other causes can also appear as a central nodal necrosis on CT.[3]
3. Finally, CT and MRI are expensive and not readily accessible for repeated use during follow-up of the patients.

Ultrasonography is cost-effective, easily available, radiation free, non-invasive, safe and is primary investigation to

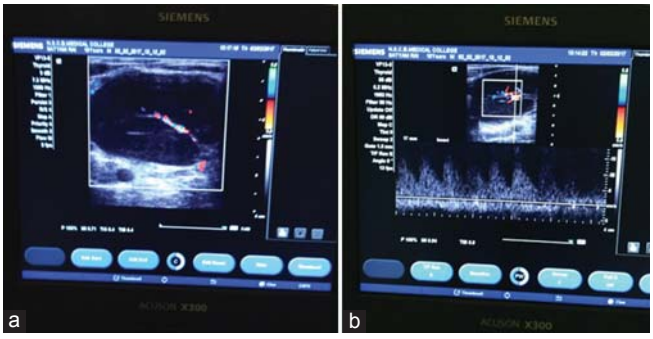

Figure 1: (a and b) 15-year-old male presented with swelling in neck

Figure 2: 65-year-old male presented with swelling in neck

Table 5: Distribution of L/S ratio on USG to FNAC/ histopathology diagnosis

Category	L/S<2	L/S>2	Total
Malignant (%)	22 (75)	7 (24)	29
Tubercular (%)	9 (44)	12 (57)	21
Reactive (%)	12 (40)	18 (60)	30
Total (%)	43 (53)	37 (47)	80

χ^2=23.26, *P*<0.001, USG: Ultrasound-guided, FNAC: Fine needle aspiration cytology

Table 6: Distribution of border according to USG in comparison with FNAC/histopathology diagnosis

Category	Sharp border (%)	Unshrap border (%)	Total
Malignant	19 (65)	10 (34)	29
Tubercular	8 (38)	13 (61)	21
Reactive	12 (40)	18 (60)	30
Total	39 (48.8)	41 (51.2)	80

χ^2=4.4, *P*=0.11, USG: Ultrasound-guided, FNAC: Fine needle aspiration cytology

Table 7: Distribution of lymphnode echotexture according to USG in comparison with FNAC/ histopathology diagnosis

Category	Homogenous (%)	Heterogeneous (%)	Total
Malignant	10 (34)	19 (65)	29
Tubercular	15 (71)	6 (28)	21
Reactive	23 (76)	7 (23)	30
Total	48 (60)	32 (40)	80

χ^2=16.38, *P*<0.001, USG: Ultrasound-guided, FNAC: Fine needle aspiration cytology

Table 8: Hilar vascularity on USG diagnosis with hilar vascularity on FNAC/histopathology diagnosis

Category	Present (%)	Absent (%)	Total
Malignant	7 (24)	22 (75)	29
Tubercular	3 (14)	18 (85)	21
Reactive	22 (73)	8 (26)	30
Total	32 (40)	48 (60)	80

χ^2=42.68, *P*<0.001, USG: Ultrasound-guided, FNAC: Fine needle aspiration cytology

Table 9: Capsular vascularity on USG diagnosis with hilar vascularity on FNAC/histopathology diagnosis

Category	Present (%)	Absent (%)	Total
Malignant	3 (10)	26 (89)	29
Tubercular	1 (4.7)	20 (95)	21
Reactive	3 (10)	27 (90)	30
Total	7 (8.7)	73 (91.2)	80

P=0.04, USG: Ultrasound-guided, FNAC: Fine needle aspiration cytology

differentiate malignant, tubercular, and reactive cervical lymphadenopathy.[3] Ultrasound examination of the lymph nodes can be done in all planes so that exact nodal size and shape can be evaluated.[4]

Figure 3: Tubercular lymph node with absent hilum showing capsular and hilar vascularity (mixed) on Doppler evaluation

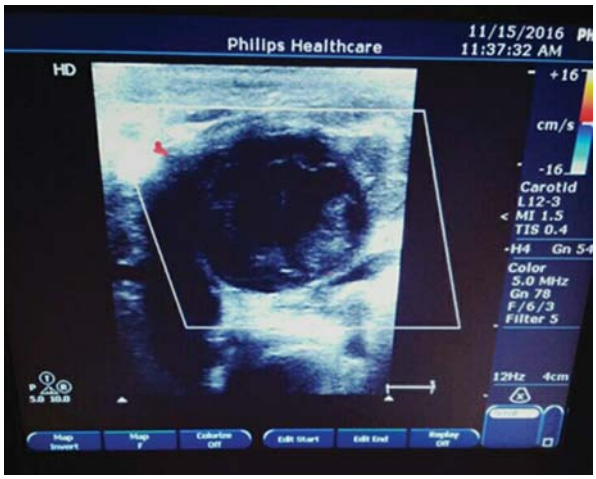

Figure 4: 19-year-old male, known case of lymphoma on ultrasound-guided there is enlarged level II round lymph node with absent hilum, sharp borders and heterogeneous echo texture proved on fine needle aspiration cytology

Ultrasound Correlation with FNAC/Histopathology

In a study done by Danninger *et al*.,[5] ultrasonography sensitivity and specificity for detecting malignant nodes was 96% and 69%, respectively.

Ahuja and Ying.[6] concluded that ultrasound was 95% sensitive and 83% specific for classifying metastatic/non-metastatic lymph nodes (Table 2).

In our study on USG out of 80 lymph nodes, 35 were malignant, 21 were tubercular and 24 were reactive lymph nodes. On FNAC/histopathology out of 80 lymph nodes, 29 lymph nodes were malignant, 21 were tubercular, and 30 were reactive lymph nodes (Table 3).

In our study, the ultrasonography sensitivity, specificity, positive and negative predictive values are 90%, 74%, 77%

Table 10: No perfusion on USG diagnosis with no perfusion on FNAC

Category	Present (%)	Absent (%)	Total
Malignant	2 (6.8)	27 (93.10)	29
Tubercular	3 (14)	18 (85.70)	21
Reactive	4 (13)	26 (86)	30
Total	9 (11.2)	71 (88.7)	80

USG: Ultrasound-guided, FNAC: Fine needle aspiration cytology

and 92%, respectively, for differentiating neoplastic from non-neoplastic cervical lymphadenopathy.

Thus, our study confirmed the reliability of ultrasound sensitivity and specificity in evaluating cervical lymph nodes on ultrasound as reported in literature.

Lymph Node Border

Sharp and unsharp Border: Sharp borders in malignancy are due to the infiltrating tumor cells which replace normal lymphoid tissues and it causes an increasing acoustic impedance difference between lymph nodes and surrounding tissues whereas unsharp borders in malignant nodes indicate invasion into adjacent structures. But in benign because of edema or active inflammation of the surrounding tissues, they will have unsharp borders. In a study by Ahuja and Ying,[1] they concluded that border sharpness is not helpful in diagnosis.

In our study, out of 29 malignant nodes, 19 shows sharp border, out of 30 reactive 18 shows unsharp border, out of 21 tubercular 13 shows unsharp border. In this study, the *P* value for the border was 0.09, which showed the association to be not significant (Table 6).

Lymph Node Hilum

Widened, narrow and absent: In malignancy/metastases infiltration of the malignant tissue result in early distortion of internal nodal architecture with invasion of hilum, resulting in narrowing or absence of hilum (Figure 3). In case of reactive nodes, pathogen reaches nodal cortex in early stages induces lymphocyte proliferation and if inflammatory stimulus still persists, causes formation of new germinal center resulting in widening of hilum.

In one study done by Vasallo *et al*.,[4] 26 of benign nodes 58% showed a wide central hilum, 35% showed a narrow hilum and 8% no hilum. Of 68 malignant nodes, only 6% of nodal metastasis exhibited a wide central hilum, 48% exhibited no hilum, and 46% showed narrow hilum.

In our study, 83% of malignant nodes showed absent hilum, 13% of malignant nodes showed narrow hilum. 65% of tubercular nodes showed absent hilum and 23% with narrow hilum. 46% of reactive nodes showed wide hilum. The $P < 0.01$ shows significant association.

Echotexture of the Lymph Nodes

Homogeneous and heterogeneous: In one study done by Toriyabe *et al*.,[7] 17 of 19 nodes which showed heterogeneous echotexture were proved as malignant and 30 out of 33 lymph nodes which are homogenous echotexture were proved benign/reactive by histopathology study.

Our study shows 23 of reactive lymph nodes are homogeneous and 19 of the malignant lymph nodes are heterogeneous correlating with the previous study (Table 7).

The *P* value for this criterion was 0.0015, which showed the association to be significant.

Matting

Ahuja and Ying.[1] stated that matting is the important criteria to diagnose tubercular lymph nodes. Because of the soft tissue edema surrounding the affected lymph nodes results in matting of the lymph nodes.

Ahuja *et al*.[8] stated that matting and adjacent soft tissue edema is common in tuberculous nodes; however, they are rarely seen in malignancy.

In our study, out of 80 nodes, 28 showed matting all of which are tubercular (100%). Reactive and malignant lymph nodes show no matting.

Vascular Pattern

Hilar vascular pattern

Benign/reactive nodes tend to have a prominent hilar vascularity due to increase in the vessel diameter and blood flow as the infection progresses (Figure 4).

In a study done by Na *et al*.,[9] 97% of benign/reactive and 18% of malignant lymph nodes showed hilar vessels.

In our study of 80 lymph nodes: Malignant 7, tubercular 3, and reactive 21 showed hilar vessels. The *P* value for this criterion was <0.01, which showed the association to be very significant (Table 8).

Capsular (Peripheral) Flow

In a study done by Na *et al*.,[9] there is peripheral vascularity with the loss of central nodal vascularity is tubercular nodes 24 and metastatic.[8]

Our study shows tubercular 7 and malignant 3 lymph nodes showed only capsular vascularity which was statistically not significant (Table 9).

Mixed vascular pattern

In our study of 100 lymph nodes: Malignant 80%, reactive 10%, and tubercular 62% showed mixed vascularity. The *P* value for this criterion was <0.001 showed the association to be statically significant.

In a study done Na *et al*.,[9] 85% of malignant and 76% of tubercular nodes showed mixed vascular pattern.

This mixed vascularity flow is seen in tubercular, however, more commonly in malignant nodes.

Limitations of Doppler

According to Na *et al*.,[9] it is very difficult to detect superficially located, slow flow signals, It is difficult to obtain Doppler spectral wave forms in non-cooperative patients.

CONCLUSION

This Study Concludes that

1. High resolution sonographic and color Doppler examination proved as a valuable primary investigation to identify lymph nodes and helps to differentiate neoplastic (malignant) from non-neoplastic (reactive and tubercular) lymph nodes.
2. Ultrasound evaluation is very sensitive in differentiating between cystic/necrotic foci and solid swellings.
3. Ultrasound helps in identifying abnormal nodes and useful for guided FNAC.
4. Finally, all ultrasound diagnosis must be correlated with FNAC/histopathology study not only to determine whether the nodes are malignant, reactive, tubercular, nodes but also to determine the histology of the neoplasm.

At the End of Our Study, We Present Evaluation Criteria that Help in Differentiating Non-neoplastic from Neoplastic Cervical Lymph Nodes

1. Gray scale findings of size, shape, long axis/short axis ratio, nodal echogenic hilum, lymph node echogenicity, matting, and nodal necrosis.
2. Color Doppler findings of focal absence of perfusion, capsular vessels, hilar vascularity and mixed vascularity.

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