Role of Ultra Sonography in Cervical Lymphadenopathy and Its Correlation with Cytopathological and/or Histopathological Features

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Original Research Article

Abstract: Cervical lymph nodes are common sites of involvement in tuberculosis, distant metastasis and lymphoma. Lymphomatous nodes are difficult to differentiate from metastatic nodes in clinical examinations, the treatment of lymphoma and metastasis is different and diagnosis of these two conditions is important. Imaging techniques plays pivotal role in diagnosing head and neck pathologies especially those involving deeper soft tissues. To evaluate the role of ultrasonogrphy for differentiating cervical lymphadenopathy. This conducted in study kamineni hospitals, l.b. Nagar, hyderabad over a period of August 2013 to May 2015 in 64 patients. Diagnosing malignant lymph nodes with USG the as compared to pathological diagnosis the Sensitivity is 82.61% and Specificity is 95.12%. Diagnosing infective /inflammatory lymph nodes with USG the as compared to pathological diagnosis the Sensitivity is 79.41% and Specificity is 83.33%. USG is useful modality for differentiating reactive and pathological lymph nodes.
Keywords: Cervical lymphadenopathy, ultrasonography, pathological   diagnosis.

INTRODUCTION

Cervical lymph nodes plays important role in a number of disease conditions. The most commonly seen causes of cervical lymphadenopathy are tuberculosis, distant metastasis and lymphoma. Lymphadenopathy is one such condition where critical evaluation becomes mandatory not only to diagnosis and assesses the severity of the disease and proper treatment [1]. Especially in head and neck malignancies presence of metastatic nodes on one side of the neck reduces 5-year survival rate to 50% whereas bilateral involvement of neck further reduces survival rate to 25%.

Henceforth cervical lymphadenopathy assessment is vital as it aids in selection of treatment modalities and predicting prognosis [2, 3].

Clinical examination of cervical lymph nodes diagnosis is difficult due to their diverse location and multiple numbers. Ultrasound has higher sensitivity (96.8%) than palpation (73.3%) for detection of cervical lymph nodes [4]. Ultrasonography using stringent criteria of nodal metastasis, which are easy to identify and reliable, is superior to palpation for early detection of regional lymph node metastases of melanoma [5]. CT and MRI can be used for evaluation of lymph nodes (<5mm), but they are less sensitive than ultrasound in detecting nodes <2 mm in diameter [6, 7]. Ultrasonography has gained recent popularity in maxillofacial imaging as it is non-ionizing, non-invasive, and cost effective [8-10]. Ultrasound guided fine needle aspiration cytology technique showed improved diagnostic sensitivity accuracy with 97.9% and 100% specificity more than conventional fine needle aspiration cytology [11,12].

Hence the study was designed to evaluate the reliability of grey scale ultrasound in differentiating the pathologies of cervical lymph nodes and to emphasize its sensitivity and specificity. Ultrasound is a useful imaging modality in evaluation of cervical lymphadenopathy because of its high sensitivity (98%) and specificity (95%) when combined with fine needle aspiration cytology (FNAC) [13].

AIMS AND OBJECTIVES

AIM: To evaluate the role of ultrasonogrphy for differentiating cervical lymphadenopathy due to various causes like tuberculosis, metastasis and lymphoma.

OBJECTIVE
- To differentiate cervical lymphnodes on the basis of sonographic features.
- To compare USG findings with pathological diagnosis.

MATERIALS AND METHODS
This conducted in study kamineni hospitals, l.b. Nagar, hyderabad during the period of August 2013 to May 2015 in 64 patients.

Inclusion criteria
- All patients (both sex groups) referred for USG with clinical suspicion of cervical lymphadenopathy
- Incidentally detected cervical lymph nodes on USG neck.

Exclusion criteria: Age < 5years

Methods
Clinical history of the patients with enlarged cervical nodes on USG neck details was recorded. These patients will then undergo FNAC of the most representative lymph node (The ultrsonographic findings will not be revealed to the pathologist who will be performing FNAC). Finally correlate the reports of ultrasonographic findings with pathology.

Method of ultrasonography
- Ultrasonography of neck region was done using a 10MHz linear transducer.

Lymph node parameters evaluated
- Short axis: maximum transverse dimension of the lymph node, ≥ 10 mm was taken as significant.
- Shape: The shape of the lymph node will be assessed by the L/S (long axis/short axis) ratio. An S/L ratio > 0.6 will indicate a round node whereas an S/L ratio < 0.6 will indicate an oval or elongated node.

Echogenicity: Was classified as hypoechoic / hyperechoic / heterogeneous. The internal echo of lymph nodes was assessed by the presence of hyperechoic echogenicity. Strong echoes will be considered when there is single or multiple coarse high-echo spots located focally either in the central or peripheral area of the node.
Fatty hilum: Presence or absence of echogenic hilum
Discrete / matted (fusion tendency): Fusion of lymph nodes will be considered when there is partial or complete disappearance of a borderline echo between them ; otherwise the lymph node is called discrete.
Matrix: Presence or absence of necrosis /calcification.

Vascularity
- Hilar - flow signals branching radially from the hilus and the signals are not along the periphery of the nodes
- Peripheral - flow signals along the periphery of the lymph nodes, with branches perforating the periphery of the node and not arising from the hilar vessels
- Mixed flow - presence of hilar and peripheral flow signals
- Apparently avascular - absence of vascular signals within the lymph nodes. .

On the basis of these ultrasound parameters the lymph nodes were provisionally divided into normal, infective and malignant.

Fine needle aspiration cytology (FNAC) Method
Fine needle aspiration cytology (FNAC) is widely accepted as the accurate, sensitive, specific and cost-effective procedure in the diagnosis of lymphadenopathy [14].

Lymphnode Biopsy: Insufficient diagnoses of FNAC; the biopsy of lymph node was done by using H&E staining.

Ultrasound and FNAC / HPE correlation
The pathological impression was divided into reactive, infective and malignant corresponding to USG diagnosis normal, infective and malignant, the correlation was done with USG findings and pathological diagnosis. Lymphoma included under malignant lymphadenopathy and tuberculosis under infective.

Statistics
The morphological parameters of the lymph nodes were described as percentage positive out of the total number of lymph nodes examined. Sensitivity, Specificity, Positive Predictive value and Negative Predictive value of sonography in diagnosing infective and malignant lymph node was calculated.

RESULTS
- In this study 64 patients were included as per the inclusion criteria, the nodes were evaluated with USG of neck for cervical lymph nodes followed by FNAC /HPE from the lymph node.For 5 patients HPE was done; remaining 59 patients were diagnosed on the basis of FNAC.
- Study population included 34 males and 30 females, mean age is 44.9 years. Pathologically examination identified as malignant patients were 23 (35.93 %), reactive were 7 (10.93 %) and 34 (53.12 %) as inflammatory /infective.In 23 malignant patients, 14 male (61%) and 9females (39%), the mean age is 56.56 years.in 34 infective/

inflammatory patients, 14 female and 20 male, the mean age is 37 years.

Differentiating cervical lymph nodes on the basis of sonographic features

TAable-1: Using 9 mm as cut off for normal and abnormal lymph nodes gave following results

	Pathologically diagnosed as abnormal (+ve)	Pathologically diagnosed as reactive (-ve)	Total
USG diagnosis as abnormal (+ Ve)	50	3	53
USG diagnosis as normal (- Ve)	7	4	11
Total	57	7	64
Sensitivity			87.72%
Specificity			57.14%
Positive predictive value			94.34%
Negative predictive value			36.36%

Table-2: Tabulation of USG findings (for pathologically diagnosed lymphadenopathy)

	Reactive	Infective	Malignant
Mean short axis	10.14 mm	13.11 mm	19.1 mm
Shape (round)	28.5%	14.7%	82.60%
Fatty hilum (absent)	42.85%	76.47 %	100%
Echogenecity (heterogeneous)	14.28%	29.41 %	52.17%
Fusion tendancy	0%	20.58 %	21.73%
Necrosis	0%	29%	17.39%
Calcification	0%	2.9%	21.73%
Vascularity Peripheral Mixed	28.57% 0%	38.23% 2.9%	39.13% 21.73%

**Table-3: USG findings for diagnosing malignant lymph node as compared to pathological diagnosis**

|	Pathologically diagnosed as malignant (+ve)	Pathologically diagnosed as non-malignant (-ve)	Total
USG diagnosis as malignant (+ve)	19	2	21
USG diagnosis as non-malignant (-ve)	4	39	43
Total	23	41	64
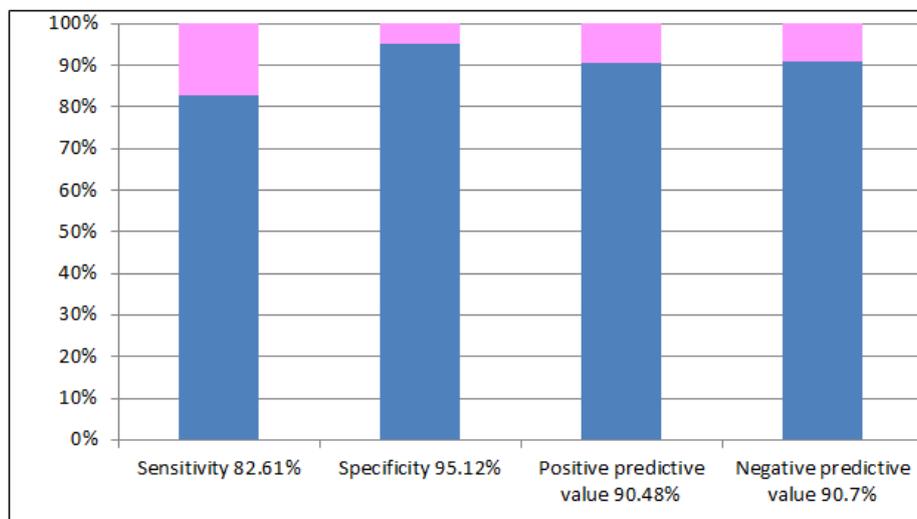
Fig-1: Sensitivity, specificity, positive predictive value and negative predictive value of USG for diagnosing malignant lymph nodes

Table-4: USG findings for diagnosing infective /inflammatory lymph nodes were compared to pathological diagnosis

	Pathologically diagnosed as infective / inflammatory (+ ve)	Pathologically diagnosed as non-infective / non inflammatory (- ve)	Total
USG diagnosis as infective (+ ve)	27	5	32
USG diagnosis as non-infective (-ve)	7	25	32
Total	34	30	64
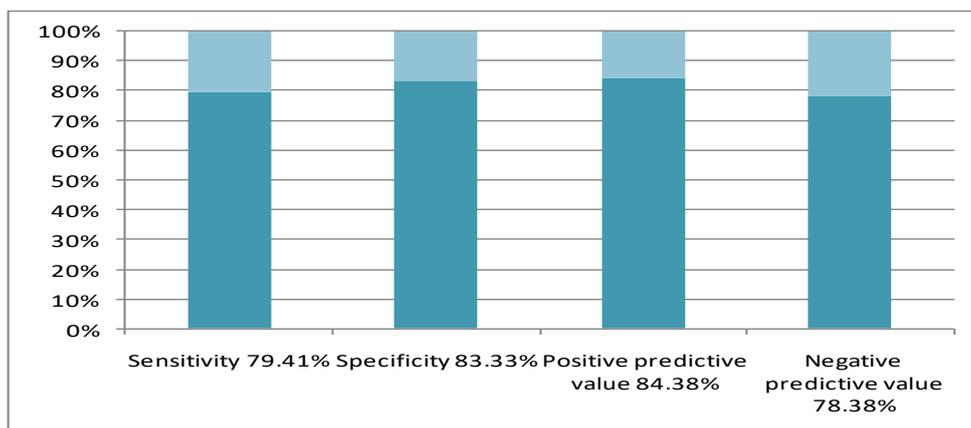
Fig-2: Sensitivity, specificity, positive predictive value and negative predictive value of USG for diagnosing infective / inflammatory lymph nodes
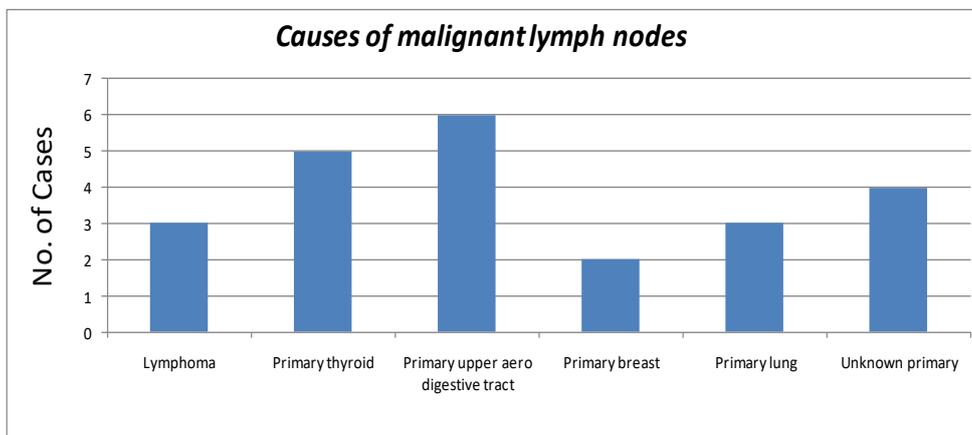
Fig- 3: No of cases distributed as per the cause of malignant cervical lymph nodes. Metastasis from primary in upper aero digestive tract was the most common cause

Table-5: Sensitivity and specificity for individual usg parameters for diagnosing malignant lymph nodes

	Sensitivity	Specificity	PPV	NPV
Round shape	82.61 %	82.93 %	73.08%	89.47%
Fatty hilum	100%	29.27%	44.23%	100%
Matting	21.74%	82.93%	41.67%	65.38%
Necrosis	17.39%	75.61%	28.57%	62%
Calcification	21.74%	97.56%	83.33%	68.97%
Heterogeneous echotexture	52.17%	73.17%	52.17%	65.63%
Vascularity peripheral	80.96%	60.98%	55.56%	89.29%

DISCUSSION

The clinical evaluation of cervical lymph nodes will be a difficult task as there are about 300 cervical lymph nodes in the neck varying in size from 3 to 25mm which were embedded within soft tissues of the neck. Henceforth cervical lymphadenopathy

assessment is vital as it aids in selection of treatment modalities predicting prognosis [14]. Metastatic cervical lymph nodes are site-specific. In patients with a known primary tumour, the distribution of metastatic nodes assists in tumour staging; however, if the primary tumour is not identified, the distribution of proven metastatic nodes may give a clue to identify the primary tumour. Different sonographic criteria have been established by which normal lymph nodes can be distinguished from abnormal nodes[15-17].

Reasons for performing FNAC in the lymph nodes which appear normal on USG

For cases which were diagnosed as normal on USG, FNAC was performed because of the clinical indications – known case of malignancy / long duration of pyrexia of unknown origin or in some cases long standing cervical region swelling.

Distribution and number

Distribution of cervical lymph nodes is particularly helpful in case of malignancy. Lymph nodes in drainage area can point towards primary malignancy.

Level II lymph nodes were most common location in current study – detected in 17 cases among 23 malignant lymphadenopathy. Metastatic lymph nodes from upper aero digestive tract, carcinoma thyroid was commonly found along level II and III. This is in accordance with study done by Ying and Ahuja [18].Multiple lymph nodes is common feature seen nearly all the studies regardless of study population.

Lymph node size

Although size is traditionally used to distinguish between benign and malignant lymph nodes, its inaccurate sole criteria cut off value for short axis measurement for differentiating normal and abnormal lymph node is controversial.

Study	Cut off value for short axis measurement for abnormal lymph node
Mizanur Rahman *et al*. [19]	10 mm
M W van den Brekel *et al*.[20]	10 mm (for metastatic lymph node)
Toriyabe Y *et al*. [21]	10 mm

Char Character	Study done by Chintamaneni Raja Lakshmi *et al*. [22]	Current study
Reactive lymph node	8 mm	10.14 mm
Infective lymph node	12.4 mm	13.11
Malignant lymph node	22.9 mm	19.1 mm

Mean short axis measurement of > 10 mm in current study can be attributed to effect of extreme values.

Shape

Most investigators have suggested short axis/long axis ratio as the most reliable indicator for metastatic nodes [23, 24].In current study 20 (86.95 %) of the 23 malignant lymph nodes showed round shape.

Character	Study done by Chintamaneni Raja Lakshmi *et al*. [22] *(Percentage of round lymph nodes)*	Current study *(Percentage of round lymph nodes)*
Normal lymph node	33.3 %	28.57 %
Inflammatory/ infective lymph node	26.7 %	20.58 %
Malignant lymph node	86.7 %	86.95 %

Echogenecity

Normal and reactive nodes were predominantly hypoechoic when compared with the adjacent muscles. Metastatic nodes can be hypoechoic, mixed echoic or hyperechoic. Therefore, hyperechogenicity is a useful sign to identify metastatic nodes. Toriyabe Y, Nishimura T *et al*. [21] observed heterogeneous and anechoic patterns in metastatic nodes. In our study 13 (56.52 %) out of 23 malignant lymph nodes revealed heterogeneous echopattern. While benign lymph nodes were predominantly hypoechoic.

Fatty hilum

Ying *et al*. Found as, echogenic hilus to be a normal sonographic feature of normal cervical lymph nodes in 96% of cases; they stated that although metastatic nodes lack this feature, hilum may be present in the early stage of involvement in which medullary sinuses have not been sufficiently disrupted to eradicate it. The feature is also shown by tubercular lymph nodes.Present study, loss of fatty hilum is seen in 43% cases these findings attributed to the fact that all the malignant cases were in advanced stage.

Matrix

A. Intranodal Necrosis: Out of 4 malignant lymph nodes 3 showed cystic necrosis (2 malignant squamous cell carcinoma and 1 malignant papillary cell carcinoma). B.Calcification: Intranodal calcification is exceptional finding incervical lymph nodes. Ahuja and Ying found that 50 – 60% metastatic lymph nodes from papillary carcinoma of thyroid show punctuate irregular calcification. However other causes are tuberculosis [25] and sarcoidosis [26].

Rosario *et al.* [27] study reported as 578 nodes in known cases of thyroid cancer - 12 of 17 nodes with calcifications were metastases, and the remaining 5 were detected in postoperative scar tissue. No calcification was seen in reactive lymph nodes. In current study 83 % (n=5) were malignant and remaining were tubercular lymph node.

Fusion tendency (discrete / matted)

Ying and Ahuja [28] *et al.* showed that matting is common features in malignant and tuberculous nodes compared to normal or reactive lymph node. Present study showed the matting observed in 12 cases, which 6 were diagnosed as tubercular lymph node, 1as infective MRSA culture positive and 5as malignant lymphadenopathy.

Vascularity

Ying and Ahuja showed that normal and reactive lymph nodes tend to have hilar vascularity or appear apparently avascular, whereas metastatic nodes usually show peripheral or mixed vascularity, and lymphomatous nodes predominantly demonstrate mixed vascularity [29]. The study was showed consistent with 87% of malignant lymph nodes showing peripheral or mixed vascularity.

Sonographic features of nodes with corresponding pathological diagnosis

Recent studies revealed sonological features of the lymphadenopathy and its conclusions are mentioned below:

	Rahul Khanna *et al.*			Present study		
	Reactive	Infective	Malignant	Reactive	Infective	Malignant
Absent hilus	9 %	26 %	83 %	42.85 %	76.47%	100 %
Matting	No	81 %	66%	No	20.58 %	21.73 %
Common Shape	Oval	Oval	Round	Oval	Oval	Round

CONCLUSION

USG is useful modality for differentiating reactive and pathological lymph nodes. No single USG parameter is accurate sole criteria for evaluation of cervical lymph nodes but combination of parameters is quite useful.

Short axis enlargement, loss of fatty hilum, heterogeneous echotexture, fusion tendency, necrosis, and calcification are features of abnormal lymph nodes.

Abnormal lymph nodes with round shape and peripheral / mixed vascularity are commonly malignant. While tubercular lymph nodes are oval and showed variable vascularity patterns.

Lymphomatous lymph nodes show similar USG features as that of malignant lymph nodes with involvement of lymph nodes at multiple levels.

LIMITATIONS OF THE STUDY
- Inter observer variability of USG cervical lymph nodes was not assessed.
- Long term follow up of cases was not obtained.

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