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Original Research Article

UTILITY OF ULTRASONOGRAPHY DIAGNOSIS FOR CERVICAL LYMPHADENOPATHY IN CENTRAL INDIAN POPULATION- A HOSPITAL BASED OBSERVATIONAL STUDY

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Abstract:

Background: Cervical lymph nodes are frequently involved in a number of disease conditions. The most commonly seen causes of cervical lymphadenopathy are tuberculosis, distant metastasis and lymphoma.

Objective: To assess the usefulness of ultrasonography in the differential diagnosis of cervical lymphadenopathy. *Methods:* ultrasonography of cervical lymph nodes was performed with a real-time linear scanner using a 7.5- or 11-MHz probe. Ultrasonography findings were retrospectively reviewed in 432 lymphnodes of 120 patients. USG findings were reevaluated by FNAC, CECT neck, MRI and core needle biopsy wherever required.

Results: out of 432 lymphnodes; 108 tuberculous lymphadenitis, 46 metastatic, 59 lymphoma, 114 inflammatory and 105 normal lymph nodes were observed. Ultrasonography features were found to be stronger in tubercular, metastatic and lymphomatous lymphnodes. Hypoechoic center was prominently observed in tubercular and metastatic form. In most of the patients, FNAC result was equivocal and a subsequent excision biopsy of the lymph node was carried out to confirm the diagnosis. Lymphadenitis was diagnosed with a sensitivity of 100% and a specificity of 100%.

Conclusion: This study concluded that cervical group of lymph nodes with ultrasonography features such as round shape, absence of hilar echo, sharp nodal borders, Hypoechoic internal echogenicity and presence of intranodal necrosis were highly suggestive of metastatic cervical lymph nodes. Ultrasonography along with other radiological and histopathological parameters can be very effective in early diagnosis of high risk diseases.

Keywords: Ultrasonography; Tuberculous Lymphadenitis; Malignant Lymphoma; Metastatic Node.

Introduction

The body has approximately 600 lymph nodes, but only those in the submandibular, axillary or inguinal regions may normally be palpable in healthy people. Lymphadenopathy refers to nodes that are abnormal in side, consistency or number. There are various classifications of lymphadenopathy, but a simple and clinically useful system is to classify lymphadenopathy as "generalized" if lymph nodes are enlarged in two or more noncontiguous areas or "localized" if only one area is involved. Distinguishing between localized and generalized lymphadenopathy

is important in formulating a differential diagnosis. In primary care patients with unexplained lymphadenopathy, approximately three fourths of patients will present with localized lymphadenopathy and one fourth with generalized lymphadenopathy. 1,2

Cervical lymphadenopathy refers to lymphadenopathy of the cervical lymph nodes (the glands in the neck). The term lymphadenopathy strictly speaking refers to disease of the lymph nodes,6 though it is often used to describe the enlargement of the lymph nodes.1-4 Similarly, the term lymphadenitis refers to inflammation of a lymph

node, but often it is used as a synonym of lymphadenopathy.^{5,7}

Cervical lymphadenopathy is a sign or a symptom, not a diagnosis. The causes are varied, and may be inflammatory, degenerative, or neoplastic. In adults, healthy lymph nodes can be palpable, in the axilla, neck and groin. In children up to the age of 12 cervical nodes up to 1 cm in size may be palpable and this may not signify any disease. If nodes heal by resolution or scarring after being inflamed, they may remain palpable thereafter. In children, most palpable cervical lymphadenopathy is reactive or infective. In individuals over the age of 50, metastatic enlargement from cancers of head and neck region and aerodigestive tract should be considered. The symptom of the sign of the symptom of the sign of the symptom of the symptom

Causes of lymphadenitis are Infections like Pericoronitis, Staphylococcal lymphadenitis, Mycobacterial lymphadenitis, Rubella, Cat scratch Infectious mononucleosis, Streptococcal fever, pharyngitis, Viral respiratory infection, Toxoplasmosis, Tuberculosis, Brucellosis, Primary herpes simplex infection, Syphilis, Cytomegalovirus, HIV, Histoplasmosis, Chicken pox. 1-8

Ultrasound may be used to confirm the presence of an abnormal lymph node and characterize its size, shape, borders, internal architecture, vascularity, and perinodal soft tissues [3]. Benefits of ultrasound include the lack of ionizing radiation and the ability to characterize the nature of lymph nodes as either cystic or solid. Both contrast-enhanced CT and MRI may be used to further characterize the extent of pathology.

On ultrasound, B-mode imaging depicts lymph node morphology, whilst power Doppler can assess the vascular pattern11 B-mode imaging features that can distinguish metastasis and lymphoma include size, shape, calcification, loss of hilar architecture, as well as intranodal necrosis.11,13 Soft tissue edema and nodal matting on B-mode imaging suggests Tuberculous cervical lymphadenitis or previous radiation therapy. ¹⁶⁻¹⁸ Serial monitoring of nodal size and vascularity are useful in assessing treatment response. ¹⁹⁻²¹

The ultrasonography characteristics of lymphomatous swelling include multiple round Hypoechoic masses with posterior echo enhancement. However, Tuberculous lymphadenitis also has some of these features, and discriminating between the two by using color Doppler sonography is difficult.10

Difficulty in ultrasonography differentiation between Tuberculous lymphadenitis and metastatic lymph nodes also has been reported.^{23,24} Hence,

Differentiating tuberculous lymphadenitis from malignant lymphoma and metastatic lymph nodes is difficult in each case.

Although the finding of lymphadenopathy sometimes raises fears about serious illness, it is, in patients seen in primary care settings, usually a result of benign infectious causes. Most patients can be diagnosed on the basis of a careful history and physical examination. Localized Adenopathy should prompt a search for an adjacent precipitating lesion and an examination of other nodal areas to rule out generalized lymphadenopathy. In general, lymph nodes greater than 1 cm in diameter are considered to be abnormal. Supraclavicular nodes are the most worrisome for malignancy. A three- to four-week period of observation is prudent in patients with localized nodes and a benign clinical picture. Generalized Adenopathy should always prompt further clinical investigation. When a node biopsy is indicated, excisional biopsy of the most abnormal node will best enable the pathologist to determine a diagnosis.

The cause of lymphadenopathy is often obvious: for example, the child who presents with a sore throat, tender cervical nodes and a positive rapid strep test, or the patient who presents with an infection of the hand and axillary lymphadenopathy. In other cases, the diagnosis is less clear. Lymphadenopathy may be the only clinical finding or one of several nonspecific findings, and the discovery of swollen lymph nodes will often raise the specter of serious illness such as lymphoma, acquired immunodeficiency syndrome or metastatic cancer. The physician's task is to efficiently differentiate the few patients with serious illness from the many with self-limited disease.

The purpose of our study was to assess the usefulness of ultrasonography with a high-frequency transducer in the differentiation of cervical tuberculous lymphadenitis from malignant lymphoma and metastatic lymph nodes. This article reviews the evaluation of patients with a central clinical finding of lymphadenopathy, emphasizing the identification of patients with serious illness.

MATERIAL AND METHODS

This was an observational retrospective study performed on patients referred for cervical swelling

in the Department of radiology for ultrasonography. The study was performed in two year period from October 2016 to October 2018. The age range of patients was 20-70 years. Approval from Institutional ethical committee was taken before initiation of the study.

A pre designed Performa was used to record relevant information like patient data, history, clinical findings and investigation report from individual cases. Detail local intra and extraoral examination of neck for organ-specific drainage, neck node was done for its site, size, number and its apparent relation to surrounding structure. Cases of cervical lymphadenopathy, with or without previous history of any medical or surgical treatment for the same and cases which were regular for post treatment follow-up were included in the study.

The Ultrasonography scanning was performed using a 7.5- or 11-MHz linear transducer. Patient lay in the supine position, with the neck of the patient hyper extended with a pad or pillow under the shoulders to provide optimum exposure of the neck. Scans were obtained with the transducer placed transversely and longitudinally and measurements made in the plane that showed a maximum cross sectional area. For color Doppler assessment of the cervical nodes, scanning was done using the slow frame rate, low pulse repetition frequency, narrow gate, low wall filter setting, and high Doppler gain in order to maximize the Doppler sensitivity so as to detect even small flow in the enlarged nodes. The parameters which were considered in this study and their definition are as follows:

- Site: lymph nodes were classified according to the cervical nodal chain into different groups.
- Multiple lymph nodes were defined as involvement of more than 2 nodes.
- Fusion of lymph nodes was defined as partial or complete disappearance of a borderline echo between them.
- Ultrasonography characteristics were described as delineation of multiple lymph nodes, a tendency towards fusion, an internal echo, an irregular margin, the presence of strong echoes and posterior enhancement.
- The internal echo of lymph nodes was assessed by the presence of hyper echoic echogenicity.

- Strong echoes were defined as single or multiple coarse high-echo spots located focally either in the central or peripheral area of the node.
- The shape of the lymph node was assessed by the L/S (long axis/short axis) ratio means L/S ratio <2 indicates a round node whereas an L/S ratio >2 indicates an oval or elongated node.
- Echo texture and homogeneity: lymph nodes were divided as Hypoechoic, isoechoic, or hyper echoic to surrounding muscles and with homogenous or heterogeneous echo pattern.
- Margins: based on the margins, lymph nodes were divided into 2 groups, those with well-defined/ sharp margins and those with ill-defined/unsharp margins.
- Ancillary features: presence or absence of calcification, intranodal necrosis, posterior enhancement, and matting.
- Status of the surrounding tissue as normal or abnormal.
- Vascular pattern: assessed by color flow mapping and was classified as hilar, peripheral, or mixed.

All images were analyzed retrospectively by the same two experienced radiologists mentioned earlier. They analyzed the images in consensus in a blinded fashion. The interval between imaging acquisition and retrospective imaging analysis was at least 3 months. The readers were instructed to capture the target lymph node with an annotation on the representative US images. After 6 months, each reader independently reinterpreted the imaging features of the target lymph node.

Statistical analysis was performed by using MS Excel-2010 and SPSS software trial version 21.0

RESULTS

Among the 120 patients a total of 432 lymph nodes were evaluated ultrasonographically. The various parameters studied were L/S ratio (long axis to short axis ratio) of lymph nodes, margins, Hypoechoic center, fusion tendency, peripheral halo, absent hilus and strong internal echoes. Following ultrasonography, FNAC of the most prominent node was carried out.

Table 1: Demographic variables (n=120)

Demographic variables	Group Number of patients		%
Gender	Male	72	60
	Female	48	40
Age group (years)	20-35	30	25.0
	36-50	29	24.16
	51-70	61	50.83
Social status	Low economy	46	38.33
	Middle class	23	19.16
	Higher middle class	51	42.07

According to demographic findings by Table 1, male predominance was observed in cervical lymphadenopathy. Patients were evaluated in three age groups i.e. 20-35 years, 36-50 years and 51 onwards. The highest prevalence of lymphadenopathy observed in third group i.e. 61 patients in 51-70 years age group (50.83%). There was higher incidence observed in low economy and higher middle class.

Table 2: Ultrasonography findings correlated with tissue diagnosis in 432 cervical lymph nodes of 120 patients.

The 'p values' compare the significance of difference between all lymphadenopathy.

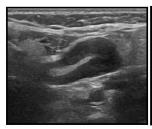
Characteristics	Tubercular	Metastatic	Hodgkin's Lymphoma	Inflammatory	Normal	p-value
L/S Ratio	1.7 ± 0.7	1.3 ± 0.3	1.5 ± 0.5	2.3 ± 1.0	2.3±1.9	<0.01
Irregular margins	63 (59%)	24 (52.17%)	13 (22.03%)	9(7.89%)	Nil	>0.01
Hypoechoic center	78 (72.22%)	29 (63.04%)	11 (18.64%)	10(8.77%)	Nil	>0.01
Fused	57 (52.77%)	32 (69.56%)	8 (13.56%)	Nil	Nil	>0.01
Peripheral halo	72 (66.66%)	26 (56.52%)	4 (6.77%)	Nil	Nil	<0.01
Internal echo	52 (48.14%)	5(10.87%)	Nil	Nil	Nil	<0.001
Absent hilus	16 (14.81%)	37 (80.43%)	15(25.42%)	11 (9.65%)	Nil	<0.01
Total nodes(432)	108 (25.0)	46 (10.65)	59 (13.65)	114 (26.38)	105(24.30%)	

Table 2 denoted comparison of all characteristics of lymph node pathology mostly tubercular, metastatic, lymphoma, inflammatory with normal lymph node. Long axis to short axis ratio was highest in normal lymphnode as length of normal lymph node is greater than width. Normal shape of lymphnode found to be elongated or oval. Lowest L/S ratio observed in metastasis and Hodgkin's lymphoma, as the shape of lymphnode found to be round or irregular. Margins were found to be very irregular in tubercular lymph nodes. Inflammatory lymph nodes have smooth margins because of higher fluid content. Hypo echoic

center was seen mostly in tubercular lymph nodes as they present with liquefaction foci and least prevalence in inflammatory lymphnodes. 57 (52.77%) fused tubercular lymph nodes were found to be more commonly. Peripheral halo 72 (66.66%) and internal echo found to be most prevalently in tubercular lymphnodes. Fusion, Peripheral halo, Internal echo were absent in inflammatory and normal lymphnodes. Hilus found to be absent in normal lymphnode.

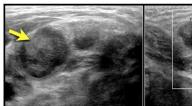
Differential diagnosis of lymphadenitis is shown in the atlas at the end of this manuscript. Image (a) normal lymphnode. Image (b) inflammatory lymphnode, Image (c) lymphomatous lymphnode, Image (d) malignant lymphoma, Image (e) metastatic lymphnode, Image (f) reactive lymphnode and Image (g) shows tubercular lymphadenitis.

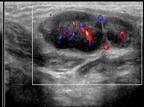
In most of the patients, FNAC result was equivocal and a subsequent excision biopsy of the lymph node was carried out to confirm the diagnosis. Core needle biopsy was not attempted as it is difficult to do on lymphnodes less than 1.5 cm in size and there is a risk of injury to underlying vascular structures. Some lymphnode pathology was confirmed by CECT neck and MRI scanning.



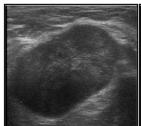


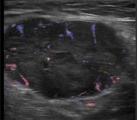
a. Normal lymph node



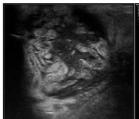


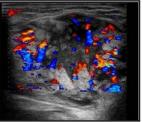
b. Infective lymph node



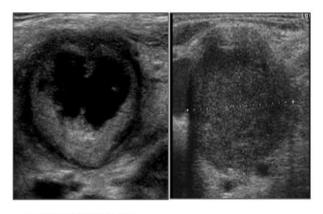


c. Lymphoma





d. Malignant lymphoma

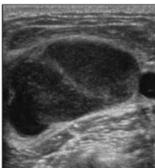


e. Metastatic lymph node





f. Reactive lymph node





g. Tuburcular lymph node

DISCUSSION

Differentiation between tubercular, metastatic, lymphomatous, reactive and inflammatory cervical lymph nodes is extremely important for further treatment. It is also important to make the correct diagnosis as early as possible to control or treat prior upstaging of the metastasis which can lead to make a curable lesion incurable. Clinicians have traditionally relied on FNAC to achieve a tissue diagnosis in cervical lymphadenopathy. However the FNAC report is frequently equivocal. Tubercular lymph nodes may granulomatous labeled as reactive or lymphadenitis, similarly in metastatic lymph nodes, sampling errors might occur because the lymph node chosen for FNAC may be reactive while the secondary

deposit is harbored by other lymph nodes. Also FNAC is unreliable in differentiating between a metastatic and lymphomatous lymph node. Core needle biopsy is difficult to obtain because of their small size, typically less than 1.5 cm.

Among the 120 patients a total of 432 lymph nodes were evaluated ultrasonographically. The various parameters studied were L/S ratio (long axis to short axis ratio) of lymph nodes, margins, Hypoechoic center, fusion tendency, peripheral halo, absent hilus and strong internal echoes. Following ultrasonography, FNAC of the most prominent node was carried out.

The highest prevalence of lymphadenopathy observed in third group i.e. 61 patients in 51-70 years age group (50.83%). There was higher incidence observed in low economy and higher middle class. This observation was also observed in the study conducted by Na DG et al,²Ahuja AT et al⁴ and Lenghel LM et al.¹⁰

Normal and reactive nodes were predominantly hypoechoic when compared with the adjacent muscles. Metastatic nodes were usually hyper echoic. Therefore, hyperechogenicity is a useful sign to identify metastatic nodes as stated by Ying and Hyu J et al. we also observed same feature in recent study conducted by Lenghel LM et al. 10

Metastatic nodes are ultrasonographically characterized by a smaller long axis to short axis ratio (L/S ratio), absence of hilus and a Hypoechoic center. Long axis to short axis ratio was highest in normal lymphnode as length of normal lymph node is greater than width. Normal shape of lymphnode found to be elongated or oval. Lowest L/S ratio observed in metastasis and Hodgkin's lymphoma, as the shape of lymphnode found to be round or irregular. This was because metastatic nodes tend to assume a more spherical shape. These findings were also observed in the previous studies conducted by Liao LJ et al, 13 Dude SM et al, 14 and Gupta A et al. 16

An absent hilus was found in normal lymphnode and metastatic nodes while tubercular and lymphomatous nodes had absent hilus. This was because metastatic nodes tend to assume a more spherical shape. Steinkamp HJ et al report that 95% of metastatic nodes had L/S ratio of less than 2 [4]. We also found a Hypoechoic center in 78 (72.22%) of tubercular lymph nodes which could reflect central necrosis. Fusion tendency was found in Tubercular,

Metastatic and Hodgkin's Lymphoma which could denote extra nodal spread and should be considered as a prognostic sign and also the need for post surgery adjuvant radiotherapy. Kim HC et al report the usefulness of 3 D ultrasonography for measuring volume of cervical lymph nodes. They found that a cut off volume of 0.7 cm3 had a 80% sensitivity and 90% specificity for differentiating metastatic from lymphadenopathy. 5,7,9 ultrasonography can evaluate the vascular pattern, displacement of vascularity, vascular resistance and pulsatility index. These features have been reported to have a sensitivity of 88% for the diagnosis of metastatic nodes and 67% for lymphoma with a specificity of 100%. 11,14 The limiting feature of Doppler and power ultrasound studies is their inability to distinguish between inflammatory and neoplastic nodes reliably on the basis of their flow pattern. Both metastatic and inflammatory nodes have associated vascularisation, which could appear similar on Doppler scan.

The main distinguishing feature of lymph nodes in lymphoma was a homogeneous pattern. This could be attributed to the fleshy nature of these nodes and absence of either calcification or necrosis within them.8 Ultrasonography is increasingly being recognized as a noninvasive tool for the evaluation of cervical lymph nodes. The sonographic appearance of normal nodes differs from those of abnormal nodes. Sonographic features, which help to identify abnormal nodes, are shape, absent hilus, intranodal necrosis, calcification, matting, peripheral halo and a prominent vascularity. A normal node should be discoid, with a hilus, sharp margins, absence of matting, calcification, necrosis or soft tissue edema. The sonographic features of matting are a tendency towards fusion, of calcification is a strong internal echo, of necrosis is an Hypoechoic center and of soft tissue edema is a peripheral halo. Distinction between normal and abnormal cervical lymph nodes is fairly straightforward. However distinguishing tubercular from metastatic or lymphomatous lymph nodes is not very precise because of over lapping of characteristics. The most significant many distinguishing feature in our study was strong echoes within the node, which reflects intranodal calcification, caseation and granuloma formation. It is difficult to assign a cut off value separating the 3 categories because of overlap of cases, but this feature can be taken into consideration with other findings while arriving at a diagnosis. 57 (52.77%)

fused tubercular lymph nodes were found to be more commonly. Peripheral halo 72 (66.66%) and internal echo found to be most prevalently in tubercular lymphnodes. Fusion, Peripheral halo, Internal echo in inflammatory and were absent normal lymphnodes. Hilus found to be absent in normal lymphnode. Other characteristics like irregular margin, Hypoechoic center, fusion tendency and peripheral halo can be used to distinguish normal from abnormal nodes but are not of value in distinguishing between the 3 important causes of cervical lymphadenopathy.

CONCLUSION

Cervical lymphadenopathy can be radiologically evaluated by various modalities like CT, MRI, PET, and radionuclide imaging. As all these are expensive and not easily available. The present study was one such attempt to prove the efficacy of ultrasound which is affordable, nonionizing, noninvasive, and easily available.

This study concluded that cervical group of lymph nodes with ultrasonography features such as round shape, absence of hilar echo, sharp nodal borders, Hypoechoic internal echogenicity and presence of intranodal necrosis were highly suggestive of metastatic cervical lymph nodes; however nodal borders and echogenicity hilus criteria revealed high sensitivity and specificity of 100%. Ultrasonography along with other radiological and histopathological parameters can be very effective in early diagnosis of high risk diseases.

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