Evaluation of sonographic and strain elastographic findings in tubercular cervical lymphadenopathy.Evaluation of sonographic and strain elastographic findings in tubercular cervical lymphadenopathy.

RENU YADAV (DOC.RENU0803@GMAIL.COM)
Vardhman Mahavir Medical College and Safdarjung Hospital https://orcid.org/0000-0003-4559-0596
AMITA MALIK
Vardhman Mahavir Medical College and Safdarjung Hospital
RAJNI PRASAD
Vardhman Mahavir Medical College and Safdarjung Hospital

Research Article

Keywords: Sonography, Sonoelastography, Tubercular lymphadenitis, Strain ratio, Color coded elastogram

Posted Date: February 25th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1127425/v1

Abstract

Purpose– Tuberculous cervical lymphdaenopathy is the most common manifestation of extrapulmonary tuberculosis and frequently present imaging diagnostic dilemma with metastatic lymphadenopathy. Ours is observational study done to evaluate the role of sonography including Doppler and strain elastography in tubercular cervical lymphadenopathy.

Methods-100 fine needle aspiration cytology/histopathological examination(FNAC/HPE) proven tubercular lymph nodes were evaluated with sonography and strain elastography Features evaluated with sonography are location, size, short/long axis diameter(S/L) ratio, presence or absence of echogenic hilum ,intra-nodal necrosis, intra-nodal calcification associated soft tissue features like periadenitis or collection and pattern of vascularity. With strain elastography(USE) color coded elastograms and strain ratio were evaluated.

Results-On evaluation tubercular nodes are large size, S/L ratio >0.5, show intra-nodal necrosis and peripheral vascular pattern. 91% tuberculous lymph nodes had color coded elastograms>2 pattern which is similar to malignant lymph nodes and 99% of tuberculous lymph nodes show strain ratio< 1.99.

Conclusion - Grey scale and Doppler assessment of tubercular lymph nodes reveals findings similar to that encountered in metastatic nodes, hence differentiation difficult .While strain ratio being semi-quantitative is more objective criteria of assessment compared to color coded elastograms. Hence adding semi-quantitative elastographic evaluation with US will help in further characterization of tuberculous nodes.

Introduction

Cervical lymphadenopathy is a common clinical entity with varied causes ranging from benign to malignant. Amongst benign causes, tuberculous lymphadenopathy is the most common etiology in endemic areas.[1] Its incidence also increasing in developed countries with the increasing prevalence of acquired immunodeficiency syndrome (AIDS). Tuberculous lymphadenitis is the most common form of extrapulmonary tuberculosis.[2] It is frequently bilateral with predilection for the posterior triangle of the neck. The involvement of lower cervical group of lymph nodes concomitantly increases the incidence of pulmonary involvement.[3] There are three patterns of lymph node involvement. Imaging findings depends upon the stage of the disease at the time of examination. In the acute stage of tubercular granuloma, the lymph nodes are enlarged with homogeneous appearance. As the diseases progresses, the second pattern or the most common pattern of a suppurative node with central necrosis is seen. The third pattern is of a fibrocalcified node, frequently seen in chronic phase or treated patients.[3,4,5] Proper diagnosis is required before initiating treatment due to prolonged and cumbersome drug regime. Radiological evaluation is performed in patients lacking the typical associated clinical features, nodes not amenable to clinical examination and patients not responding to treatment.

FNAC/ biopsy remains the gold standard for final diagnosis of cervical lymphadenopathy. On histopathological examinatione majority of these nodes turn out to be benign, as malignancy accounts for less 1% of all cases of lymphadenopathy,[6] hence an effective non-invasive imaging assessment can help preclude the need for invasive diagnostic procedures for obtaining a definite diagnosis.

Imaging modalities available for assessment of lymph nodes are Ultrasound (US), including color Doppler and sonoelastography, Computed Tomography(CT) and Magnetic Resonance Imaging(MRI).

Ultrasound is commonly used for evaluation of cervical lymphadenopathy as the nodes are superficial, easily accessible, non-invasive and free from risk of radiation. On US, a node is assessed for its location, size, shape, echogenecity, presence of intranodal necrosis, calcification and ancillary features, such as, matting and soft tissue edema. On Color Doppler, the pattern of vascularity was assessed.

CT and MRI helps to further characterize the sonographic abnormalities, confirm lymph nodes situated in deeper locations, with superior anatomical localization. However CT is associated with risk of radiation and MR studies are time consuming and require sedation in pediatric population.[7]

Ultrasound elastography (USE) has principle similar to the clinical method palpation and is a more objective method of assessment. The principle underlying strain elastography is that tissue compression produces a strain (displacement). This strain is seen to be lower in stiff tissues than in the softer tissues.[8] Strain elastography is a very promising imaging modality for characterization of lymph nodes, especially the cervical lymph nodes which are easily accessible and effective compression can be applied using the transducer, against the underlying structures to obtain the color coded elastogram and strain ratio.

The current study aims to assess the utility of strain elastography in tuberculous nodes, which account for significant proportion of benign cervical lymphadenopathy.

Material And Methods

100 consecutive patients with tuberculous lymphadenitis confirmed on FNAC or histopathology with age >5years were enrolled in the study after obtaining a written, informed consent. A lymph node with >50% cystic area, presence of macro-calcifications or inadequate reference muscle tissue surrounding region of interest (ROI) were excluded from the study. In case of patient with multiple LNs, after ruling out exclusion criteria representative LN with adequate surrounding reference tissue was taken up. History regarding onset, duration, progression, associated symptoms like fever, weight loss, change in voice was taken followed by general physical examination and local examination of enlarged lymph nodes. Local examination included assessment for distribution, size, consistency, fixity to overlying and underlying structures.

1. *Sonography* – Neck US was performed in both the transverse and longitudinal planes, with patients in supine position with the neck hyper-extended by placing a pillow under the patient's shoulders and lower neck for support. The scans were performed using Philips iU22 US scanner, equipped with

linear array transducer of frequencies 5-17MHz and 3-9MHz. Nodes were evaluated for their **distribution, size, shape, nodal margins, presence or absence of echogenic hilum, echogenecity, presence of intranodal calcifications, intranodal reticulations and intranodal necrosis. Ancillary features such as matting and adjacent soft tissue edema were also assessed.**

2. On *color Doppler* sonography vascular patterns were categorized as – **Hilar**, **Avascular**, **Peripheral**, **Spotted**, and **Mixed.**
3. *Ultrasound elastography* - was performed using Philips iU22 scanner equipped with linear array transducer of frequency 5-17MHz with strain compression elastographic capability. The elasticity image of the lymph node was evaluated qualitatively using color coded elastograms and semi-quantitatively using strain ratio. Five patterns as described by Alam et al, were used for evaluation of color coded elastograms. The following patterns are described, with hard area displayed as red, soft as blue and tissues with intermediate strain as green:

Pattern 1 -absent or a very small hard area (red).

Pattern 2 - hard area (red) < 45% of the lymph node

Pattern 3 - hard area (red)≥ 45%

Pattern 4 -peripheral hard and central soft area

Pattern 5 - hard area (red) occupying entire lymph node with or without a soft rim.

The Strain ratio was calculated by the machine as ratio of strain of adjacent muscle to the strain of the lymph node.

Strain ratio>1.99 was calculated from receiver operating characteristics (ROC) curves plotted to differentiate benign from malignant lymph nodes (LNs) was used.

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Results

Demographic distribution -

Age of the patients included in the study ranged from 7 -36yrs with mean age of 23.6yrs.

Sonographic parameters -

B-mode sonography-

LN Size >8mm was observed in all the patients. S/L ratio > 0.5, intra-nodal calcification and loss of echogenic hilum was observed in 3/4th of the population with intranodal necrosis was present in more than half of the studied LNs.(Table-1)

Matting and soft tissue edema was seen in 30% of tubercular nodes.

Color Doppler-

70% of the tubercular nodes showed peripheral vascular pattern.

Sono-elastographic parameters –

Color coded elastogram-

Color coded elastogram ≤ 3 was observed in more than 91% of the LNs with approximately 3/4th of the LNs show color coded elastogram pattern 3 while 9% showed pattern > 3. (Table-2)

Strain ratio ≤ 1.99 was observed in 96% of the LNs while only 4% showed >1.99.(Table-3)

Discussion

Tuberculous lymphadenitis is the most common form of extrapulmonary tuberculosis.[2] It is versatile masquerader as it can resemble infection or neoplasm and poses a diagnostic challenge to the clinicians [9] and on ultrasound and elastography.[10]

B-mode sonography-

Tubercular lymph nodes are large, S/L ratio>0.5, shows absence of echogenic hilum, intranodal necrosis, calcification. Similar observations were made by Park J H et al.[11] Ying et al[12] in their study including 315 tuberculous nodes, reported that 79% had increased S/L ratio >0.5 however the percentage was less than that in metastatic nodes 95%. Absent hilus was reported in approx 76-86% of tuberculous nodes . Nodal calcification is late feature in tubercular lymphadenitis may help in diagnosis, however metastasis from papillary carcinoma thyroid may present with nodal calcification. Due to edema and periadenitis acoustic interface is blurred between nodes and surrounding tissues. Similar findings are also seen post radiotherapy. However in the absence of history these findings are highly suggestive of tubercular.[13]

Color Doppler findings-

Vascular pattern on color doppler imaging depends upon the degree of intranodal necrosis and stages of the disease. Cystic necrosis destroys the blood vessels of the lymph nodes resulting in avascular pattern, seen in 6-41% of tuberculous nodes .[14, 15,] Avascularity may also be seen in later stages of the disease, when fibrosis and hyalinization cause compression or obliteration of intranodal vessels.[16]

Grey scale and Doppler assessment of tubercular lymph nodes reveals findings similar to that encountered in metastatic nodes, hence differentiation difficult. Further tuberculosis and metastasis are two major contributors to cervical lymphadenopathy .

Strain elastography-

Most of the tubercular nodes had color coded pattern of ≤3except 8% similar to metastatic LNs. Balasubrmaniam S et al[17]. in their study considered ≤ 2 benign pattern while >2malignant pattern. 83% tuberculous LNs show ≤ 2 pattern while 91% show ≤ 3. They stated that tuberculous LNs cannot be diagnosed on elastography due to overlapping features with both benign and malignant nodes. Tuberculous lymphadenitis with scarring calcification and necrosis may demonstrate stiffer areas. Similar findings were also observed by Ying L et al[18]. , Teng D K et al.[19] and . Hasan D I et al. [20]

Strain ratio ≤ 1.99 was observed in 99% of LNs except one. Hence strain ratio being semiquantitative assessment helps in differentiation of tuberculous lymph nodes from metastatic LNs which demonstrate SR >1.99. Available literature on strain elastography in cervical lymphadenopathy shows strain ratio between 1.5 to 2.39 to differentiate benign from malignant lymphadenitis with no specific data on tubercular lymph nodes which are considered part of benign spectrum.[21] Cut-off calculated from ROCs in our study to differentiate benign from malignant is within the available literature. 82.6% of tubercular lymph nodes show strain ratio <1.5, this increases to 95% with strain ratio ≤ 1.99. Representative cases from our study are described in Fig 1,2 and 3.

Limitation- Strain elastography is free hand compression technique, with degree of compression can alter tissue stiffness, hence operator dependent. Ours was a retrospective study with inherent observer bias.

Conclusion

Strain ratio is a more objective criteria of assessment compared to color coded elastograms. Hence adding semi-quantitative strain elastographic evaluation with US may help in further characterization of lymph nodes above sonographic assessment.

Abbreviations

AIDS- Acquired immunodeficiency syndrome

CT- Computed Tomography

FNAC/HPE- fine needle aspiration cytology/histopathological examination

LNs- Lymph nodes

MRI- Magnetic Resonance Imaging

ROC -Receiver operating characteristics

ROI- Region of interest

SAD- Short axis diameter

S/L -short/long axis diameter

US- Ultrasound

USE-Ultrasound elastography

Declarations

Ethics approval and consent to participate –

The study was approved by the ethical committee of Vardhman Mahavir Medical College & Safdarjung Hospital, New Delhi. India 110029 with approval number IEC/VMMC/SJH/Thesis/November -2014/411 Written informed consent was obtained from all study subjects before enrolling into study.

Consent for publication- Not applicable.

Availablility of data and materials- Analyzed data is included in the article. Dataset used for the current study is available with the corresponding author and available on request.

Competing interests- None.

Conflict of interest- None

Funding – None

Authors' contribution-

Each author contributed substantially to the design of work. **RY and AM** collected, analyzed and interpreted the patient data generated from sonographic and sonoelastographic examination in cervical lymphadenopathy. **RP** performed the histopathological examination of FNAC/biopsy slides. **RY and AM** were major contributor in manuscript writing. All authors have read and approval the final manuscript and take full accountability of work and data given.

Acknowledgements - None

Consent to participate – Informed consent was obtained from all study participants.

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Tables

Table-1: Showing percentages of different sonographic parameters in studied tuberculous LNs.

Variables	Present (%)
Size >8mm	100
S/L ratio >0.5	74
Echogenic hilum	74
Intranodal necrosis	60
Intranodal calcification	70

Table-2: Showing color coded elastogram pattern in tuberculous LNs.

Color coded elastogram	Tuberculous LNs(%)
2	13
3	78
≥4	8.6

Table -3: Showing strain elastogram pattern in tuberculous LNs.

Strain ratio	Tuberculous LNs(%)
< 1	57
1-2	39
>2	4

Figures

Figure 1

Grey-scale1(A) and color Doppler 1(B) images of a 18 years old male patient shows enlarged node with SAD 14mm , S/L ratio 0.67, heterogeneous echotexture with necrotic areas within and show displaced vascularity. Elastographic images1(C) of LN with color coded elastograms pattern 5 and strain ratio 1.02.

Figure 2

Grey-scale2(A) and color Doppler2(B) images of 26 years old female patient shows LN is well defined, has SAD 1.2cm, S/L ratio 0.62 and multiple punctate hyperchoic calcific foci. On color Doppler LN shows peripheral vascularity. USE 2(C) image shows color coded elastogram shows pattern 3 and SR =1.8.

Figure 3

Grey-scale3(A) and Color Doppler 3(B) images of 8 year old boy shows the node is round with SAD= 9.8mm , S/L ratio 0.8 and avascular pattern on color Doppler imaging. Elastographic images3(C) shows color coded elastograms pattern 4 and strain ratio 1.96.

Supplementary Files

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