Research Article

The role of gray scale and color Doppler ultrasound imaging in cervical lymphadenopathy evaluation and differentiation

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ABSTRACT

Background: Cervical lymph nodes are also common sites of involvement of lymphoma; tuberculous (TB) lymphadenitis; and other benign and malignant lymphadenitis. It is essential to evaluate the cervical lymph nodes in various head and neck diseases. The role of gray scale sonography of neck lymph nodes is well established and it is widely utilizes for the evaluation of the number, size, site, shape, borders, matting, adjacent soft-tissue edema, and internal architectures of cervical lymph nodes. The advance research in power Doppler sonography (PDS) has further increased the utilization of ultrasonographic (USG) evaluation of cervical lymph nodes for diagnostic purpose. **Objectives:** The aim of this study is to evaluate the importance of gray scale, Doppler and spectral waveform study in differentiation of benign and malignant neck lymphadenopathy and to find out sensitivity and specificity of gray scale, Doppler and spectral waveform study in differentiation of benign and malignant neck lymphadenopathy. **Materials and Methods:** Patients were chosen from the outpatient department and from admissions in wards of otorhynolaryngology and surgery department. Patients with neck swelling are screened with USG. If USG shows the enlarged lymphnode, then detailed study was performed by gray scale, color, power Doppler, and by spectral waveform analysis. For differentiation from metastatic lymph nodes criteria given by Ahuja was utilized. **Results:** A total of 100 enlarged neck lymph nodes studied in 75 patients with neck lymphadenopathy. Metastatic lymph node enlargement was 38.67%, lymphoma 6.67%, TB 28%, and reactive 26.66%. Moreover male: female ratio was 2.6:1. The percentage of L/S ratio <2 for metastatic, lymphoma, and TB are 68%, 78%, and 72%, respectively While 60% of reactive nodes shows L/S ratio 2 or >2. 76% metastatic, 56% lymphoma, 72% of TB lymphadenopathy had the loss of echogenic hilum, whereas 76% reactive nodes preserved echogenic hilum. The mean resistive index (RI) and pulsatality index (PI) value of metastatic nodes 0.81, 1.87, lymphomatous nodes 0.8, 1.36; TB nodes 0.67, 1.17 and for reactive nodes 0.61, 1.05, respectively. Sensitivity of RI for malignant lymph nodes is 39%, specificity is 84%. While the sensitivity of PI for malignant lymph nodes is 44%, specificity is 87%. **Conclusion:** Gray scale and PDS helps in differentiation of metastatic, lymphomatous, and TB nodes from reactive nodes. The sonographic criteria most predictive of metastatic cervical lymph nodes were absent hilar echoes, increases in short axis length, necrosis, peripheral, or mixed vascularity. However, there is similarity in appearance to some extent between TB nodes, benign reactive neck nodes, and metastatic nodes. And thus, histological analysis is still utilized for a definitive diagnosis.

KEY WORDS: Gray Scale Sonography; Power Doppler Sonography; Cervical Lymphadenopthy

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INTRODUCTION

Cervical lymph nodes are also common sites of involvement of lymphoma; tuberculous (TB) lymphadenitis; and other benign and malignant lymphadenitis.[1,2] Metastatic cervical lymph nodes are common in patients with head and neck[3] and non-head and neck[4] cancers. They are also the major indicator

of survival rate in patients of the head and neck cancers. As the metastatic cervical nodes in patients with squamous cell carcinoma in the head and neck reduces the 5-year survival rate to 50%, further reduces the 5-year survival rate to 25% if another metastatic node found on the contralateral side.[5] Along with assessment of prognosis evaluation of cervical lymph nodes helps in planning treatment. Differentiation of lymphomatous and metastatic lymphnodes is difficult by just clinical examinations. And the treatment for lymphoma and metastases is different. For that accurate diagnosis is indeed necessary.

TB lymphadenitis is very much in common in country like India and other developing countries of South East Asian region. The incidence of TB lymphadenitis increased with increased prevalence of acquired immune deficiency syndrome. Furthermore, an accurate diagnosis of TB lymphadenitis is essential.[6]

There are many studies which clearly explain the role of gray scale sonography as an initial investigation of choice for evaluation of neck lymph nodes.[4] The Gray-scale sonography is widely used in cervical lymph nodes evaluation accurately in number, site, size, borders, shape, matting, adjacent soft-tissue edema, and internal architectures of cervical lymph nodes. When combined with fine-needle aspiration cytology, sonography is more accurate than is clinical examination because of its high sensitivity and specificity.[7]

Recent studies on power Doppler sonography (PDS) of cervical lymphnodes have further increased the amount of information that helps in accurate diagnosis of cervical lymphadenopathy. With PDS, presence and distribution of intranodal vascularity and intravascular resistance can be evaluated. Furthermore, the data from some studies suggest that the distribution of intranodal vascularity and intranodal resistance helps in differentiation of benign from malignant nodes with a high degree of accuracy.[7,8] However, very few studies with Doppler sonography evaluation of cervical lymphnodes have been found.

Hence, the objective of the present study was to evaluate the importance of gray scale, Doppler and spectral waveform study in differentiation of benign and malignant neck lymphadenopathy and to find out sensitivity and specificity of gray scale, Doppler and spectral waveform study in differentiation of benign and malignant neck lymphadenopathy.

MATERIALS AND METHODS

This was a prospective observational study. The study was carried out in the Department of Radiodiagnosis, Medical College and SSG Hospital, Vadodara, over 2½ years starting from 2012 to 2014. The study was conducted mainly with the help of department of ENT. Prior permission from the Institutional Ethics Committee permission for the study was taken.

The study was conducted on 75 patients. Patients were chosen from the outpatient department and from admissions in wards of Otorhynolaryngology and Surgery Department. Written informed consent was obtained from each participant before enrolment into the study. Patients with neck swelling are screened with ultrasonography (USG). If USG shows the enlarged lymphnode, then detailed study was carried out by gray scale, color, power Doppler, and by spectral waveform analysis.

Method of Study

Equipment

All patients were examined on Esaote AU5 color Doppler machine with 7-10 MHz linear transducer and with Gray scale, color, and spectral Doppler. A 3.5-7 MHz convex transducer is sometimes useful to assess deep lesions. Cervical lymph nodes were scanned from various regions such as submental area (Region 1) then submandibular, parotid, upper, middle and lower cervical, supraclavicular fossa and posterior triangle (Region 2-8).

Common ultrasound scan planes used in the examination of cervical nodes in different regions of the neck were as follows.[6]

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

When PDS was used, the Doppler setting is optimized for detecting small vessels were at high sensitivity, low wall filter, pulsed repetition frequency at 700 Hz, medium persistence, and the color gain was initially increased to a level which shows color noise, and then decreased to the level where the noise just disappears.

With the use PDS, the vascular pattern and displacement of vascularity of the lymph nodes were assessed. The vascular pattern of the lymph nodes was classified into four categories:

1. Hilar - Flow signals branching radially from the hilus and the signals are not along the periphery of the nodes
2. 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.
3. Mixed - Presence of hilar and peripheral flow signals.
4. Apparently avascular – The absence of vascular signals within the lymph nodes.

The displacement of vascularity was also assessed. As the common cause of displacement are cystic necrotic lesion or metastatic or local tumor infiltration.

The vascular resistance, that is, resistive index (RI) and pulsatality index of the lymph nodes were evaluated with the help of Spectral Doppler. Prominent vessels were chosen for the measurement of PI and RI and measurements were obtained from three consecutive waveforms. For the measurement of blood flow velocity like peak systolic velocity and end diastolic velocity angle correction was made at an angle of 60 or less.

For gray-scale sonography - Ahuja and Ying.[9]

Lymph nodes were considered to be metastatic if they demonstrated intranodal necrosis or if they met at least three of the following criteria:
S: L ratio >/= 0.5 (this criterion is not applicable to submandibular nodes because normal submandibular nodes are also round) (Ying et al. 1996).[4]
Hypoechoic
Absence of echogenic hilus
Lymph nodes in the drainage site of the primar.
Lymph nodes were considered to be nonmetastatic if they demonstrated at least two of the following features:
S: L ratio <0.5 (this criterion is not applicable to submandibular nodes)
Presence of echogenic hilus
Lymph nodes in the submandibular, parotid, upper cervical regions and posterior triangle, where normal lymph nodes are commonly seen in Oriental populations (Ying et al., 1996; 2000)
And for PDS, Lymph nodes were considered metastatic if they demonstrated at least one of the following criteria:
Presence of peripheral or mixed vascularity
R I ≥0.8, and 3, PI ≥1.6
Lymph nodes were considered to be nonmetastatic if they demonstrated at least one of the following criteria:
Presence of central vascularity, absence of peripheral vascularity or apparent a vascularity
RI <0.8
PI <1.6

S: L: Short axis to long axis, RI: Resistive index, PI: Pulsatality index, PDS: Power Doppler sonography

Above all measurements were taken in analysis. Moreover, statistical analysis was performed using Excel sheet.

RESULTS

Over 2½ years total 100 enlarged neck lymph nodes studied in 75 patients with neck lymphadenopathy.

Age-wise distribution of the cases shows that 82.67% of all cases were from age group of 21-60 years with the highest age group was 51-60 years of age with 22.67%. Gender-wise distribution shows that 49 (65.33%) out of 75 were male and only 26 (34.67%) were female. The male: female ratio was 1.9:1 (Table 1). The type-wise distribution of lymphadenopathy is also seen in the Table 1. It shows the most common type of lymphadenopathy is metastatic, that is, 38.67%. Other types were lymphoma (6.67%), TB (28%), and reactive (26.66%). The metastatic lymphadenopathy was seen after 30 years of age. Moreover, it was common in male than female with ratio of 2.6:1. While 3 out of 5 cases of lymphoma was seen below 30 years. The cases of TB were distributed to all age group with commonest between 21 and 30 years of age. Furthermore, male: female ratio was 1.6:1 for TB lymphadenitis. While the ratio for reactive lymphadenitis was 1.5:1. Table 2 shows the common presenting complaints of patients at the time of presentation.

Table 3 shows the USG findings of 100 lymphnode of 75 cases. It shows the mean L/S axis length of metastatic nodes 24 × 15, lymphomatous nodes 26 × 17, TB nodes 20 × 12 and reactive nodes are 21 mm × 10 mm. While 19 (76%) out of 25 reactive nodes showed preserved echogenic hilum in reactive lymphadenopathy. This table shows 1 (3%) metastatic nodes, 3 (10%) TB nodes and 1 (4%) reactive nodes shows calcification. The metastatic node which shows calcification was post radiotherapy patient. Out of 100 nodes 33 (89%) metastatic, 5 (56%) lymphoma, 27 (93%) TB, 10 (40%) reactive nodes shows intranodal necrosis. As the table depict that out of 100 nodes 16 (43%) metastatic, 20 (69%) TB and 7 (28%) reactive nodes show ill-defined border. While all lymphomatous nodes having well-defined border. 21 (72%) of TB lymph nodes shows adjacent soft tissue edema and 20 nodes (69%) are matted as compared to metastatic nodes 6 (16%) and 12 (32%), respectively. Only 1 (11%) lymphomatous and 7 (28%) reactive nodes show adjacent soft tissue edema.

The spectral flow analysis of 79 nodes shows 19 (58%) metastatic, 6 (66%) lymphomatous, 14 (74%) tubercular and 18 (95%) reactive nodes are having RI value <0.8. 13 (41%) metastatic and 3 (34%) lymphomatous nodes have RI value >0.8 (Table 3). The PI value of 14 (44%) metastatic, 4 (44%) lymphomatous, 4 (21%) tubercular, and 1 (5%) reactive nodes are having PI value >1.5 (Table 4). Sensitivity of RI for malignant lymph nodes is 39%, specificity is 84%. While the sensitivity of PI for malignant lymph nodes is 44%, specificity is 87%. As shown in Table 5, out of 25 reactive nodes 11 (44%) shows central, 7 (28%) mixed, 5 (20%) were avascular. Majority of reactive nodes showing mixed or peripheral vascularity are showing perinodal hypoechoic areas suggestive of parilyphadenitis and having tenderness. 13 (45%) TB nodes showing mixed vascularity, other 7 (24%) peripheral, 3 (10%) central, and 6 (21%) are avascular. Out of 37 metastatic nodes 14 (38%) peripheral, 16 (43%) showing

Table 1: Age and gender wise distribution of various types of lymphadenopathy in all patients

Age (years)	Metastatic		Lymphoma		TB		Reactive		Total (%)
	Male	Female	Male	Female	Male	Female	Male	Female	
0-10	0	0	0	0	0	2	2	0	4 (5.33)
11-20	0	0	1	0	2	1	1	1	6 (8)
21-30	0	0	1	1	4	3	3	2	14 (18.67)
31-40	4	3	1	0	3	0	3	1	15 (20)
41-50	8	2	0	0	2	1	2	1	16 (21.33)
51-60	8	2	0	0	2	1	1	3	17 (22.67)
61-70	1	1	0	1	0	0	0	0	3 (4)
Total	21	8	3	2	13	8	12	8	75 (100)
	29 (38.67%)		5 (6.67%)		21 (28%)		20 (26.66%)		
Male: Female ratio	2.6:1		1.2:1		1.6:1		1.5:1		1.9:1

TB: Tuberculous

Table 2: Symptomatology

Symptoms	Pain over swelling	Fever	Weight loss	Lab finding (ESR)
Metastatic (29)	8	2	5	1
TB (21)	6	15	13	7
Lymphoma (5)	3	0	2	0
Reactive (20)	9	5	1	2

ESR: Erythrocyte sedimentation rate, TB: Tuberculous

mixed vascular pattern. 8 (89%) of lymphomatous nodes revealed mixed vascularity.

For gray-scale sonography Ahuja and Ying[9] criteria used as discussed in methodology. As shown in Table 6, for gray scale sonography, sensitivity 81.1%; specificity 72%; positive predictive value 78%; negative predictive value 72%. Moreover for gray-scale and PDS sensitivity 87%; specificity 84%; positive predictive value 89%; negative predictive value 81%.

DISCUSSION

The present study consisted of 75 patients, with the highest number of patients 12 (30%) in from the age group of 21-30 years in the cases of benign lymphadenopathy, in rest of age group incidence remains the same.

In the present study, the mean L/S axis length of metastatic nodes 24 × 15, lymphomatous nodes 26 × 17, TB nodes 20 × 12 and reactive nodes are 21 cm × 10 cm. Tschammler et al.[10] demonstrated the mean longest diameter of 48 reactive lymph nodes (longest diameter, 13.5 mm ± 6.0), 56 metastases nodes (longest diameter, 19.2 mm ± 8.8), 12 malignant lymphomas (longest diameter, 23.2 mm ± 10.5). While in this study, the percentage of <2 L/S ratio are nearly similar in metastatic, lymphoma, and TB; 68%, 78%, and 72%, respectively and 14 (60%) out of 25 reactive nodes shows L/S ratio 2 or >2. Ying et al.[11] gray-scale sonography, normal and Reactive nodes tend to be hypoechoic compared with adjacent muscles and oval (short axis-to-long axis ratio [S/L]: <0.5) except for submandibular and parotid nodes, which are usually round (S/L: 0.5), and to have an echogenic hilus. Similar findings were seen with study by Papakonstantinou et al.[12] It shows L/S <2 in lymphoma (78%), and bacterial lymphadenitis (73%) while L/S >2 in 91% of reactive nodes. In the present study 28 (76%) metastatic, 5 (56%) lymphoma, 21 (72%) of TB lymphadenopathy shows loss of echogenic hilum. 19 (76%) out of 25 reactive nodes shows preserved echogenic hilum. While study done by Ahuja and Ying[9] shows metastatic, lymphomatous, and TB nodes had L/S <2 (63-94%) and without echogenic hilus (57-91%). Furthermore, borders were sharp and well define in metastatic and lymphomatous nodes (56-100%), but uncommon in TB (49%). A statistically significant relationship was found between hilarechogeneity and diagnosis in present study. Ying et al.[13] echogenic hilus is a normal sonographic feature of most of the normal cervical lymph nodes (86%), and it is commonly seen in larger nodes. On ultrasound, echogenic hilus is appeared to be continuous with the adjacent soft tissues. However, during early stage of involvement in metastatic, TB or lymphamatous lymphnodes have medullary sinus are without much necrosis or disruption. And so there may be presence of echogenic hilus.[14] Therefore, the presence or absence of echogenic hilus should not be the only criteria in the diagnosis. A cytological diagnosis, preferably by an ultrasound-guided fine needle aspiration, should always be sought. The present study shows 1 (3%) metastatic nodes, 3 (10%) TB nodes and 1 (4%) reactive nodes shows calcification. The metastatic node which shows calcification was post radiotherapy patient. Also study by Ying and Ahuja[6] shows that intranodal calcification is common in lymphomatous and TB nodes after treatment but the calcification is usually dense and shows acoustic shadowing. From this finding, it can be said that nodal calcification is not a reliable predicator of either benign or malignant disease. However, it can differentiate limited number of lesions such as TB, treated lymphoma, and metastatic thyroid carcinoma, adenocarcinoma, or squamous carcinoma. Intranodal necrosis

Table 3: USG findings

USG findings	Metastatic	Lymphoma	TB	Reactive	Total
Mean length (mm)					
Long axis	24	26	20	21	
Short axis	15	17	12	10	
L/S ratio (%)					
2 or >2	12 (32)	2 (22)	8 (28)	15 (60)	36
<2	25 (68)	7 (78)	21 (72)	10 (40)	64
Total	37	9	29	25	100
Echogenic hilum (%)					
Preserved	4 (11)	0	6 (21)	19 (76)	29
Distorted	5 (13)	4 (44)	2 (7)	0	11
Absent	28 (76)	5 (56)	21 (72)	6 (24)	60
Total	37	9	29	25	100
Calcification (%)					
Present	1 (3)	0	3 (10)	1 (4)	5
Absent	36 (97)	9 (100)	26 (90)	24 (96)	95
Total	37	9	29	25	100
Intra nodal necrosis (%)					
Present	33 (89)	5 (56)	27 (93)	10 (40)	75
Absent	4 (11)	4 (44)	2 (7)	15 (60)	25
Total	37	9	29	25	100
Nodal border (%)					
Well defined	21 (57)	9 (100)	9 (31)	18 (72)	57
Ill redefined	16 (43)	0	20 (69)	7 (28)	43
Ancillary features (%)					
Adjacent soft tissue edema					
Present	6 (16)	1 (11)	21 (72)	7 (28)	35
Absent	31 (84)	8 (89)	8 (28)	18 (72)	65
Matting					
Present	12 (32)	4 (44)	20 (69)	6 (24)	42
Absent	25 (68)	5 (56)	9 (31)	19 (76)	58
Both present	5 (14)	1 (11)	20 (69)	6 (24)	32
Both absent	24 (65)	5 (56)	7 (24)	18 (72)	54

USG: Ultrasonographic

Table 4: The spectral flow analysis

Arterial blood flow indexes	Metastatic (%)	Lymphoma (%)	TB (%)	Reactive (%)
RI (<0.8)	19 (59)	6 (66)	14 (74)	18 (95)
RI (>0.8)	13 (41)	3 (34)	5 (26)	1 (5)
PI (<1.5)	18 (56)	5 (56)	15 (79)	18 (95)
PI (>1.5)	14 (44)	4 (44)	4 (21)	1 (5)
Total	32	9	19	19
Mean				
RI	0.81	0.8	0.67	0.61
PI	1.87	1.36	1.17	1.05

RI: Resistive index, TB: Tuberculous, PI: Pulsatality index

is very much high in the present study. According to study done by Ahuja et al.[15] the differentiating ultrasound findings between NHL and metastases are the distribution of the nodes, distal enhancement and lack of intranodal necrosis. Other US features of abnormal nodes helped identify abnormality but did not help in differentiation. Ahuja and Ying[16] metastatic,

Table 5: Vascularity

Vascularity	Metastatic (%)	Lymphoma (%)	TB (%)	Reactive (%)	Total
Central	3 (8)	0	3 (10)	11 (44)	
Peripheral	14 (38)	1 (11)	7 (24)	2 (8)	
Mixed	16 (43)	8 (89)	13 (45)	7 (28)	
Avascular	4 (11)	0	6 (21)	5 (20)	
Total	37	9	29	25	100

TB: Tuberculous

Table 6: Performance of grey-scale sonography and combining grey-scale and PDS in classifying metastatic and non-metastatic lymph nodes

Sonography	Malignant	Benign (reactive)
Grey scale		
Test +ve	30	7
Test –ve	7	18
Total	37	25
Grey + Doppler		
Test +ve	32	4
Test –ve	5	21
Total	37	25

PDS: Power Doppler sonography

lymphomatous, and TB nodes were round (63-94%) and without echogenic hilus (57-91%). Also, 56-100% of lymphomatous and metastatic lymphnodes had sharp border, whereas in TB lymphdenitis only 49% had sharp borders. Other features like perinodal edema was seen in the present study 21 (72%) of TB lymph nodes shows adjacent soft tissue edema and 20 nodes (69%) are matted as compared to metastatic nodes 6 (16%) and 12 (32%), respectively. Only 1 (11%) lymphomatous and 7 (28%) reactive nodes show adjacent soft tissue edema. Intranodal cystic necroses, displaced hilar vascularity, adjacent soft tissue edema and matting and are common features in TB.[16]

In the present study, the sensitivity of RI for malignant lymph nodes is 39%, specificity is 84%, and sensitivity of PI for malignant lymph nodes is 44%, specificity is 87%. Na et al.[17] found in their study that cut-off values of 0.8 for the RI and 1.5 for the PI were 100% specific for malignancy. While, the sensitivities at these values were 47% and 55%, respectively. On comparison with histological examination it was found that most of the flow signals in lymph nodes with malignant disease which were representing arterioles or veins in the septa between tumors or near the capsule. And Tschammler et al.[18] found that a PI >1.8, or a resistance >0.9 indicate lymph node metastases with positive prediction of 93% and specificity of 97%.While Ahuja et al.[19] found that intranodal vascularity, RI and PI were significantly reduced after radiation therapy to the nodes. In study Choi et al.[20] the mean resistive index for metastatic lymphnodes and benign lymphnodes were 0.92 ± 0.23 and 0.59 ± 0.11, respectively. Similarly, the mean PI were 2.66 ± 1.59 and 0.90 ± 0.23, respectively in lymph nodes involved with metastases and affected by benign processes.

The present study shows the vascular pattern, out of 25 reactive nodes 11 (44%) shows central, 7 (28%) mixed, 5(20%) were avascular. Majority of reactive nodes showing mixed or peripheral vascularity are showing perinodal hypoechoic areas suggestive of parilyphadenitis and having tenderness. 13 (45%) TB nodes showing mixed vascularity, other 7 (24%) peripheral, 3 (10%) central and 6 (21%) are avascular. Out of 37 metastatic nodes 14 (38%) peripheral, 16 (43%) showing mixed vascular pattern. 8 (89%) of lymphomatous nodes revealed mixed vascularity. Study done by Steinkamp et al.[21] shows that reactive lymph nodes had intense hilar perfusion (82.1%) and nodal metastases had peripheral perfusion (84.7%). Lymph nodes involved in malignant lymphoma were highly perfused with 90.9% of nodal center as well as periphery were involved. Ahuja et al.[22] study showed that most of the metastatic nodes have capsular vascularity (capsular - 16%; capsular and hilar - 78%), whereas the most of the reactive nodes had hilar vascularity (98%). The difference was significant.

In the present study, the sensitivity, specificity, positive predictive value and negative predictive value of grayscale sonography for diagnosis was 81.1%, 72%, 78%, and 72%, respectively. While the sensitivity, specificity, positive predictive value and negative predictive value 87%, 84%, 89%, and 81%, respectively in differentiation of benign and malignant in combined study by grey scale and color Doppler. Ahuja and Ying[9] high sensitivity (95%) and specificity (83%) in classifying metastatic and nonmetastatic nodes with the help of gray-scale sonography.

CONCLUSION

Gray scale and PDS helps in differentiation of metastatic, lymphomatous, and TB nodes from reactive nodes. The sonographic criteria most predictive of metastatic cervical lymph nodes were absent hilar echoes, increases in short axis length, necrosis, peripheral, or mixed vascularity. Cut off RI >0.8 and PI >1.5 have high specificity but less sensitive. However, there is similarity in appearance to some extent between TB nodes, benign reactive neck nodes, and metastatic nodes. And thus, histological analysis is still utilized for a definitive diagnosis.

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