ORIGINAL ARTICLE

Evaluation of Cervical Lymphadenopathy by Ultrasonography Using Color and Power Doppler and Comparison with Histopathology

Diptiman Baliarsingh[1], Vikas Agrawal[2], Ashutosh Hota[3], Rajlaxmi Panigrahi[4]

Abstract

To evaluate and determine the efficacy of ultrasound and Doppler for differentiating among various benign and malignant causes of cervical lymphadenopathy. Out of 88 cases, the final tissue diagnosis on the basis of histopathology was found to be tubercular in 35 (40%), reactive/inflammatory in 30 (34%), metastatic in 16 (18%), and lymphoma in seven (8%) cases with cervical lymphadenopathy. In our study, metastatic nodes were present in all neck lymph node levels but most commonly being the involvement of levels I, II, III, and V with most common primary site being oral cavity. Ninety percent of tubercular nodes were less than 3 cm in size, whereas majority of metastatic nodes were more than 3 cm in size with 40% of cases having size greater than 6 cm. Reactive nodes had L/S ratio of 2.1 ± 0.8, tubercular nodes had 1.7 ± 0.5, lymphomatous nodes had 1.6 ± 0.4, and metastatic nodes had 1.1 ± 0.4. Sixty-two percent of tubercular nodes and 44% of metastatic nodes had sharp border. Eighty-seven percent of metastatic nodes and 71% of lymphomatous nodes had absent hilus, while only 28% of tubercular nodes had absent hilus and 90% of reactive nodes had widened hilus. Fourteen percent of tubercular and 6% of metastatic nodes showed intranodal calcification. Seventy-one percent of tubercular and 68% of metastatic nodes had intranodal necrosis with cystic necrosis being commoner, and only 13% of reactive nodes showed intranodal cystic necrosis. Eighty-two percent of tubercular and 75% of metastatic nodes had matting. Twelve percent of metastatic nodes and 28% of tubercular nodes showed peripheral vascularity, whereas 87% of metastatic nodes and 71% of tubercular nodes showed mixed vascularity, and 60% of reactive nodes showed hilar vascularity. In our study of differentiating non-neoplastic from neoplastic lymphadenopathy on the basis of ultrasonography and Doppler with final histopathology, a sensitivity of 92.3%, specificity of 86.9%, PPV of 95.2%, and NPV 80.0% was found.

Keywords: Cervical lymphadenopathy, Color Doppler, Power Doppler, Ultrasonography.

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Introduction

Imaging in head and neck pathologies plays a vital role during diagnosis. Involvement of deeper soft tissues, i.e., muscles, vessels, and lymph nodes, has to be evaluated critically to assess the severity of a disease and its prognosis as well as treatment planning. The cervical group of lymph nodes are involved in many disease conditions of head and neck, namely tuberculosis, lymphoma, and metastasis from different sites. The diseases of head and neck manifest as cervical lymphadenopathy in their course of natural history. Ultrasound has higher sensitivity (96.8%) than that of palpation (73.3%) for detection of cervical lymphadenopathies.[1] This study is done to show the efficacy of ultrasound and Doppler in differentiating reactive, tubercular, and malignant cervical lymph nodes. Computed tomography (CT) and magnetic resonance imaging (MRI) can be used for evaluation of cervical lymph nodes but they seem to be less sensitive for nodes with diameter <5 mm.[2] Ultrasound can detect nodes with diameter <2 mm.[3] Ultrasound is preferred over CT and MRI for evaluation of cervical neck nodes because of nonionizing, noninvasive, cost factor, availability, and determination of characteristics of cervical nodes in greater detail than CT and MRI by using high-resolution transducers, i.e., shape, margins, ecotexture, intranodal necrosis, matting, and vascular pattern.

Tubercular lymphadenopathy is commonly seen in India and South East part of Asia. With the increasing incidence of HIV-AIDS, accurate diagnosis of tubercular lymphadenitis remains an essential part of management of such patients suffering from immunodeficiency diseases. Cervical lymph nodes are also commonly involved in lymphoma. It is important to diagnose lymphoma by radiological and pathological examination and, clinically, the associated presence or absence of B-symptoms. Metastasis from cancers from various sites of head and neck, namely, oral cavity, pharynx, larynx, and paranasal sinuses, can present as cervical lymphadenopathy. A mere presence of

[1]Department of Otolaryngology and Head and Neck Surgery, Hi-Tech Medical College and Hospital, Bhubaneswar, Odisha, India

[2]Department of Radiodiagnosis, Hi-Tech Medical College and Hospital, Bhubaneswar, Odisha, India

[3]Department of ENT and Head and Neck Surgery, All India Institute of Medical Sciences, New Delhi, India

[4]Department of Otolaryngology and Head and Neck Surgery, Hi-Tech Medical College and Hospital, Bhubaneswar, Odisha, India

Corresponding Author: Diptiman Baliarsingh, Department of Otolaryngology and Head and Neck Surgery, Hi-Tech Medical College and Hospital, Bhubaneswar, Odisha, India, e-mail: diptimanbaliarsingh@gmail.com

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a metastatic neck node has a 5-year survival rate of 50%, and with bilateral involvement of neck, it reduces further to 25%.[2] As the treatment of tubercular, lymphomatous and metastatic lymphadenopathy is different, and accurate diagnosis is important for further therapeutic intervention.

Ultrasound has a sensitivity of 98% and specificity of 95% when used as an imaging modality in combination with fine needle aspiration cytology (FNAC) in evaluation of cervical lymphadenopathy.[4] By the help of Doppler sonography, the vascularity of the lymph nodes can be determined which acts as an adjunct to the sonographic findings in the evaluation of cervical neck nodes.

Materials and Methods

This study was carried out in our institution with patients presenting to the Department of Otolaryngology and Head and Neck Surgery with a cervical lymphadenopathy, and after thorough clinical examination and history taking, they were sent to the Department of Radiodiagnosis where ultrasonography was conducted. The patients were evaluated with FNAC and planned for biopsy. A total of 107 patients were evaluated from July 2015 to June 2016. Out of 107 patients, 88 had undergone biopsy for histopathological diagnosis were only included in this study. Patients who were excluded mostly had reactive nodes on FNAC and were subsequently cured with medical management. Ultrasonography with Doppler imaging of the neck nodes was carried out in 107 patients using a 10 MHz linear transducer and 3.5–5 MHz curvilinear transducer using SEIMENS Acuson X300 and GE Voluson E6 ultrasound equipments. The lymph nodes were assessed using gray scale and color Doppler and power Doppler with parameters, such as level and site of nodal involvement, size, shape and L/S ratio, echotexture, margins, hilum, intranodal necrosis, calcification, and matting. Doppler was used to determine the angio-architecture, i.e., vascular pattern, and displacement of vascularity, resistance index, and pulsatility index. The findings of ultrasonography were correlated with the final histopathology report of cervical lymph nodes in these patients.

Results

A total of 88 patients with cervical lymphadenopathy were assessed with ultrasonography with Doppler imaging and were correlated with final histopathology reports. The various parameters studied in ultrasonography were level and site of nodal involvement, size, shape and L/S ratio, echotexture, margins, hilum, intranodal necrosis, calcification, and matting (Table 1). Doppler was used to determine the angio-architecture, i.e., vascular pattern, and displacement of vascularity, resistive index, and pulsatility index. Out of 88 cases, the final tissue diagnosis on the basis of histopathology was found to be tubercular in 35 (40%), reactive/inflammatory in 30 (34%), metastatic in 16 (18%), and lymphoma in 7 (8%) cases with cervical lymphadenopathy. In our study, metastatic nodes were present in all neck lymph node levels but most commonly being the involvement of levels I, II, III, and V with most common primary site being oral cavity. Ninety percent of tubercular nodes were less than 3 cm in size, whereas majority of metastatic nodes were more than 3 cm in size with 40% of cases having size greater than 6 cm. Reactive nodes had long axis/short axis ratio (L/S ratio) of 2.1 ± 0.8, tubercular nodes had 1.7 ± 0.5, lymphomatous nodes had 1.6 ± 0.4, and metastatic nodes had 1.1 ± 0.4. Sixty-two percent of tubercular nodes and 44% of metastatic nodes had sharp border. Eighty-seven percent of metastatic nodes and 71% of lymphomatous nodes had absent hilus, while only 28% of tubercular nodes had absent hilus and 90% of reactive nodes had widened hilus. Fourteen percent of tubercular and 6% of metastatic nodes showed intranodal calcification. Seventy-one percent of tubercular and 68% of metastatic nodes had intranodal necrosis with cystic necrosis being commoner, and only 13% of reactive nodes showed intranodal cystic necrosis. Eighty-two percent of tubercular and 75% of metastatic nodes had matting. Twelve percent of metastatic nodes and 28% of tubercular nodes showed peripheral vascularity, whereas 87% of metastatic nodes and 71% of tubercular nodes showed mixed vascularity, and 60% of reactive nodes showed hilar vascularity. In our study of differentiating non-neoplastic from neoplastic lymphadenopathy on the basis of ultrasonography and Doppler with final histopathology, a sensitivity of 92.3%, specificity of 86.9%, positive predictive value of 95.2%, and negative predictive value 80.0% was found.

Discussion

In the neck, the cervical lymph nodes are a collection of lymphoid tissue and lymphatic vessels. There are approximately 300 lymph nodes in the neck. They are usually embedded in the soft tissues of the neck.[5,6] Each node in the neck is surrounded by fibrous tissue forming a capsule and is divided into cortex and medulla. The cortex is mainly composed of lymphoid follicles, which are aggregates of densely packed lymphocytes. The medulla usually contains medullary trabecullae, cords, and sinuses. The afferent vessels vary in number and enter into the lymph node through the capsule of the lymph node. The medullary sinuses are usually filled with lymph from which the lymph drains into efferent lymphatic vessel. There is also presence of blood vessels in lymph nodes. The efferent vessel of lymph node along with blood vessels enters and/or exit through the hilum of lymph node. The paracortex is an area of transition between cortex and medulla where the lymphocytes from blood usually return to the lymphatic system.[5,6]

Table 1: Ultrasound correlation with histopathology

Characteristics of node	*Reactive (n = 30)*	*Tubercular (n = 35)*	*Lymphoma (n = 7)*	*Metastatic (n = 16)*
L/S ratio	2.1 ± 0.8	1.7 ± 0.5	1.6 ± 0.4	1.1 ± 0.4
Border (unsharp)	3 (10%)	22 (62%)	1 (14%)	9 (56%)
Hilus (absent)	3 (10%)	10 (28%)	5 (71%)	14 (87%)
Echotexture (hyperechoic)	—	5 (14%)	—	1 (6%)
Intranodal necrosis	4 (13%)	25 (71%)	1 (14%)	11 (68%)
Matting	—	29 (82%)	1 (14%)	12 (75%)
Peripheral halo	—	30 (86%)	—	10 (62%)

The classification system used by surgeons and oncologists is given by American Joint Committee on Cancer (AJCC) is level I–VII (Fig. 1), i.e., level IA—submental, level IB—submandibular, level II—upper internal jugular, level III—middle internal jugular, level IV—lower internal jugular, level V—posterior triangle, level VI—anterior compartment, and level VII—superior mediastinal. Yet, Hajek et al.[7] established another classification system for ultrasonographic examination (Fig. 2), in which the cervical neck nodes are classified into eight regions as per their location in neck. In this system, the lymph node levels and the scan plane(s) differ, mentioned in bracket, i.e., region I—submental (transverse); region II—submandibular (transverse); region III—parotid (transverse and longitudinal); region IV—upper cervical (transverse); region V—middle cervical (transverse); region VI—lower cervical (transverse); region VII—supraclavicular fossa (transverse); and region VIII—posterior triangle (transverse and longitudinal). The examination is done with the patient supine with first scanning of submental area (region I) and turning the patient's head to opposite side and scanning in a sequence from submandibular (region II) to posterior triangle (region VIII).

With the use of Doppler sonography, the pattern of vascularity and its displacement in the lymph nodes are assessed. It is classified into four categories. Category I—Hilar; category II—peripheral; category III—mixed; and category VI—apparently avascular. The vascularity is also assessed for displacement, if present is usually due to infiltration by tumor and intranodal cystic necrosis.

Ultrasound and Doppler correlation with FNAC or histopathology was compared with various studies. Ahuja and Ying[8] reported a sensitivity of 95% and specificity of 83% for classifying metastatic and nonmetastatic lymph nodes in the neck by ultrasonography. In a study done by Komma et al.[9] a sonographic sensitivity of 90% and specificity of 74% was found. In our study of 88 cases (Fig. 3), ultrasonography showed 30 lymph nodes were tubercular, 25 were malignant (metastatic and lymphoma), and 33 were reactive. On final histopathology, 35 lymph nodes were found to be tubercular, 23 were malignant (metastatic and lymphoma), and 30 were reactive. The sensitivity, specificity, positive predictive value, and negative predictive value of ultrasound and Doppler based on final histopathological diagnosis were 77.1, 94.3, 90.0, and 86.2%, respectively, in tubercular lymphadenopathy; 86.9, 92.3, 80.0, and 95.2%, respectively, in malignant lymphadenopathy, and 86.7, 87.9, 78.8, and 92.7%, respectively, in reactive lymphadenopathy. In determining non-neoplastic from neoplastic lymphadenopathy, there was a sensitivity of 92.3%, specificity of 86.9%, positive predictive value of 95.2%, and negative predictive value 80.0%.

The sonographic features for diagnosis of cervical lymphadenopathy are as follows:

- Level and site—In our study, reactive lymphadenopathy was most commonly seen in level II >V; tubercular lymphadenopathy was seen commonly in level V >II; lymphoma was seen in level II and III. In lymphomas, level V lymph nodes were predominantly involved. When the primary site of tumor is identifiable, the known tumor spread pattern helps in tumor staging and management. If there is a metastatic node and the primary site is not identifiable, then the proven pattern of spread of metastasis gives a clue to identify the site of primary. Metastasis from oropharyngeal, hypopharyngeal, and laryngeal carcinomas commonly involve levels II, III, and IV; metastasis from oral cavity cancer involves levels I and II and may involve III and occasionally IV; metastasis from nasopharyngeal carcinoma involves levels II and V; metastasis from thyroid carcinomas usually involve

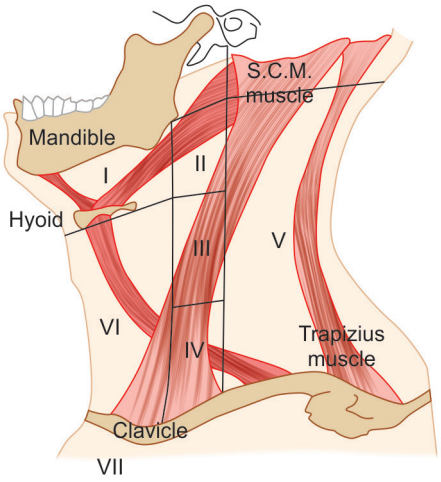


Fig. 1: AJCC classification of cervical lymph nodes

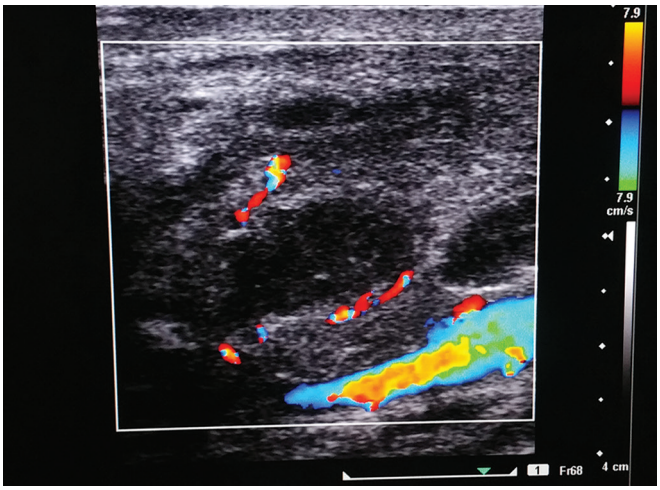


Fig. 2: Hajek classification system of neck regions for ultrasonography

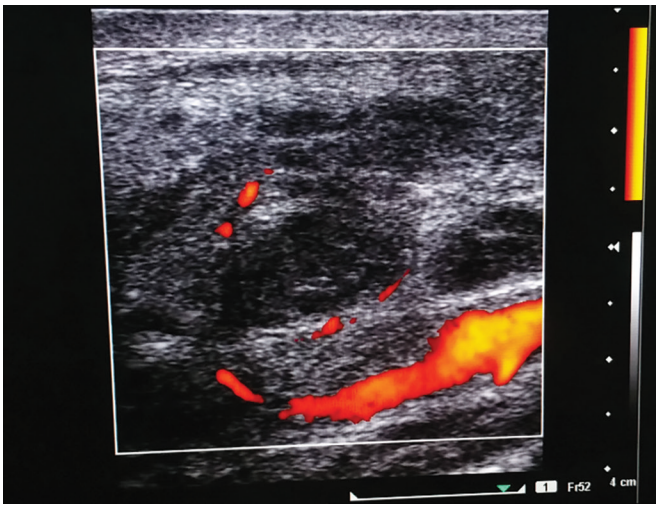
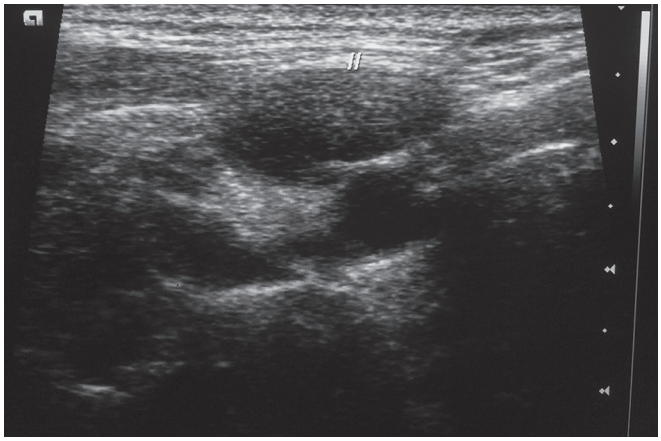


Fig. 3: Photographs showing cervical lymphadenopathy in patients of different age and sex groups

levels II, III, and IV. In our study, metastatic nodes were present in all neck lymph node levels but most commonly being the involvement of levels III >V >II, with most common primary site being buccal mucosa of oral cavity.

- Size—Malignant nodes are usually large, and larger the node, greater the staging, worse the prognosis, although metastatic deposits can be found in small nodes. Reactive or inflammatory nodes may reach the dimensions like that of large malignant nodes.[10] In our study, majority of tubercular nodes (90%) were less than 3 cm in size, whereas majority of metastatic nodes were more than 3 cm in size with 40% of cases having greater than 6 cm in size (Fig. 4).
- Shape and L/S ratio—The round shape or long axis to short axis ratio (L/S ratio) <2 is seen in metastatic and tubercular nodes. Normal and reactive nodes have oval shape with L/S ratio >2. Metastatic nodes in the early stage of involvement can be oval in shape. A study by Komma et al.[9] showed L/S ratio <2 in 79% of malignant nodes, L/S ratio >2 in 80% reactive nodes, and L/S ratio <2 in 60% 0f tubercular nodes. Another study done by Na et al.[11] showed malignant nodes showed L/S ratio <2 in 85% and L/S ratio >2 in 15% cases. In our study, reactive nodes had L/S ratio of 2.1 ± 0.8, tubercular nodes had 1.7 ± 0.5,



Q2 **Fig. 4:** Gray scale ultrasonography shows oval-shaped enlarged lymph node with fatty hilum

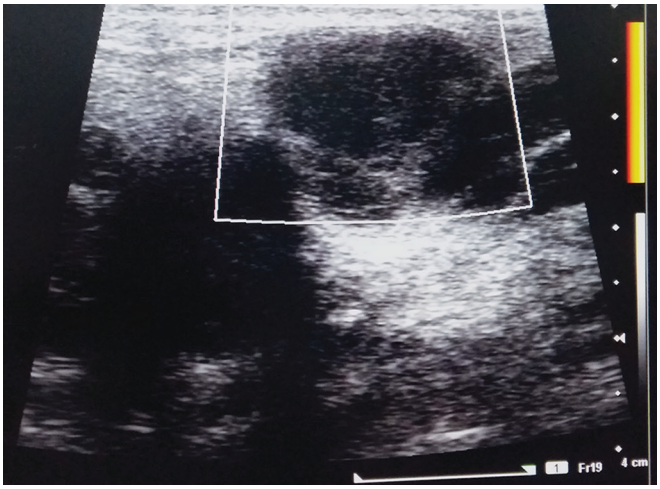


Fig. 5: Gray scale ultrasonography showing multiple enlarged and heterogeneous lymph nodes with loss of nodal architecture

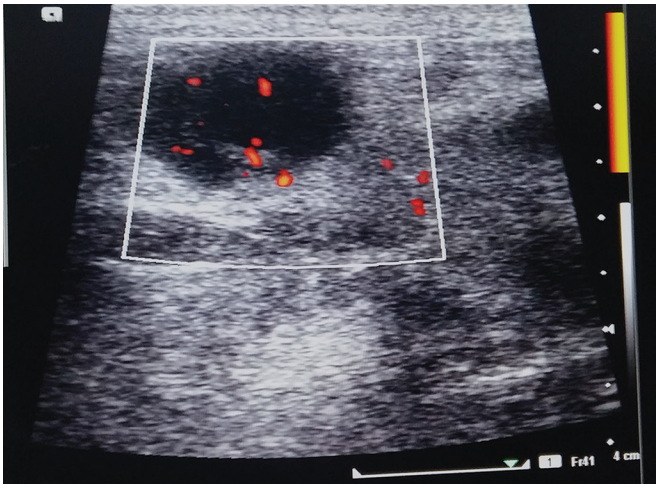


Fig. 6: Gray scale ultrasonography showing enlarged and heterogeneous lymph node with loss of nodal architecture and absent hilum Q3

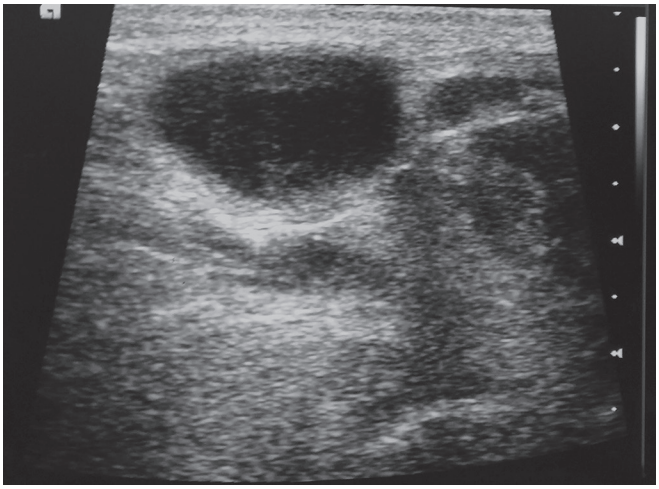


Fig. 7: Gray scale ultrasonography showing enlarged and heterogeneous lymph node with loss of nodal architecture and absent hilum

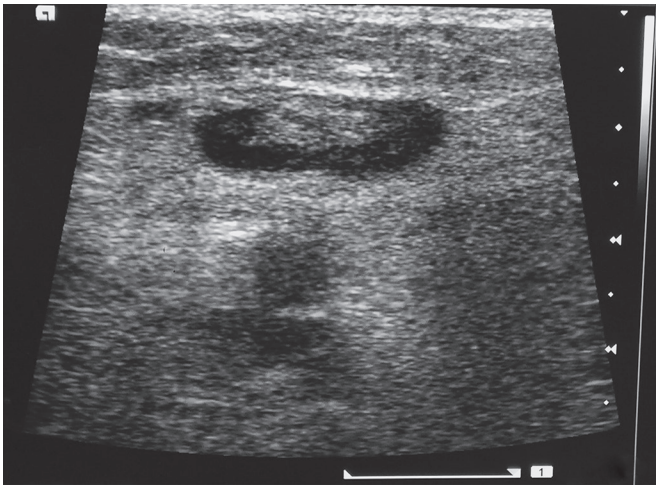


Fig. 8: Gray scale ultrasonography shows oval-shaped enlarged lymph node with fatty hilum

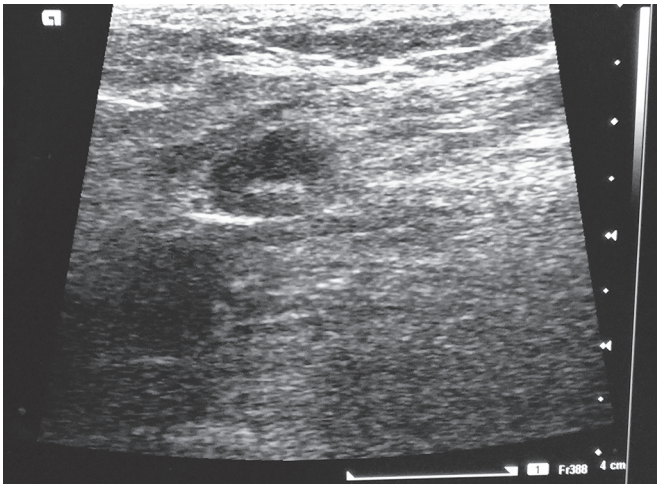


Fig. 9: Gray scale ultrasonography showing small normal-sized lymph node with normal nodal architecture and central hilum

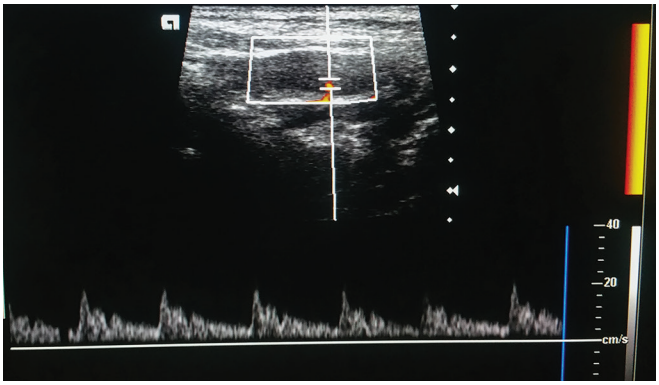


Fig. 10: Doppler study with spectral of hilum of lymph node showing normal hilar arterial flow

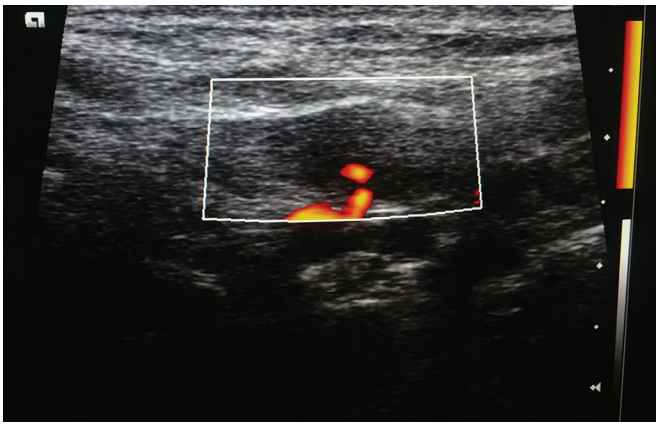


Fig. 11: Power Doppler ultrasonography study showing normal single vascular pole at hilum of lymph node

lymphomatous nodes had 1.6 ± 0.4, and metastatic nodes had 1.1 ± 0.4 (Figs 4 to 9).

- Border—Reactive or inflammatory, tubercular, and normal nodes usually have irregular or unsharp border mostly due to edema or active inflammation of surrounding tissues.[12] Metastatic and lymphomatoid nodes have regular or sharp margins because of infiltration of normal lymphoid tissue by tumor cells. The presence of an unsharp border in a proven metastatic node indicated extracapsular spread. A study done by Komma et al.[9] showed 52% of malignant nodes showed sharp border, and 68% of reactive nodes and 69% of tubercular nodes showed unsharp border. In our study, 62% of tubercular nodes and 44% of metastatic nodes had sharp border (Figs 4 to 6).
- Hilus—Narrowing or absence of hilum is seen in malignancy or metastatic involvement of lymph nodes because of infiltration malignant tissue results in early distortion of the nodal architecture with invasion of hilum. Reactive or inflammatory nodes usually have lymphocyte proliferation in nodal cortex causing widening of hilum. A study done by Komma et al.[9] showed 83% of malignant nodes showed absent hilus, 64% of tubercular nodes showed absent hilus, and 48% of reactive nodes showed widened hilus. In another study done by Vasallo et al.,[12] 58% of benign nodes showed widened hilus, whereas malignant nodes showed absent hilus in 48% and 46% showed narrow hilus. In our study, 87% of metastatic nodes and 71% of lymphomatous nodes had absent hilus, while only 28% of tubercular nodes had absent hilus and 90% of reactive nodes had widened hilus (Figs 10 and 11).
- Echotexture—Normal, tubercular, reactive, and lymphomatous nodes are hypoechoic in comparison to surrounding structures, usually of homogenous echotexture. Malignant nodes are also hypoechoic but may have heterogeneous echotexture. The exception to it is metastasis from papillary carcinoma of thyroid, which are hyperechogenic, and majority showing punctate calcifications. Intranodal calcification may also be found in lymphomatous or tubercular nodes. In our study, only 14% of tubercular and 6% of metastatic nodes showed intranodal calcification (Figs 6 to 8).
- Intranodal necrosis—Intranodal necrosis of lymph nodes is pathologic. There are two types: cystic or liquefaction necrosis and echogenic or coagulation necrosis. Cystic necrosis is more common than echogenic necrosis. Cystic necrosis gives the appearance of a hypoechoic area inside lymph node, whereas coagulation necrosis appears as intranodal echogenic focus. Metastatic nodes from papillary carcinoma of thyroid and squamous cell carcinoma commonly show intranodal cystic necrosis.[13,14] Metastatic and tubercular lymphadenopathy may have intranodal necrosis. In a study done by Komma et al.[9] 40% of malignant nodes and tubercular showed cystic necrosis and only 12% of reactive nodes showed cystic necrosis. In our study, 71% of tubercular and 68% of metastatic nodes had intranodal necrosis with cystic necrosis being commoner, and only 13% of reactive nodes showed intranodal cystic necrosis.
- Matting—Matting is a common feature of tubercular lymph nodes but is uncommon in metastatic and lymphomatous lymphadenopathies. The soft tissue edema and matting in tubercular lymphadenopathy is due to peri-adenitis resulting in fusion of lymph nodes that are adjacent to each other. A study done by Komma et al.[9] showed matting in 100% of the nodes of tubercular origin. In our study, 82% of tubercular and 75% of metastatic nodes had matting (Figs 5, 12 and 13).
- Vascular Pattern—Hilar vascular pattern is seen in normal, benign, or reactive lymph nodes. It is due to increased blood flow as infection progresses. Peripheral or mixed vascularity is usually seen in metastatic nodes. Lymphomatous nodes predominantly

have mixed vascularity. Tubercular lymph nodes have variable vascularity pattern. Vascular displacement and avascularity is commonly seen in these nodes, and they are related to cystic necrosis in tubercular nodes. Peripheral vascularity is highly suspicious of malignancy. A study done by Na et al.[11] showed 97% of reactive nodes had hilar vascular pattern and only 18% of malignant nodes had hilar vascular pattern, 6% of metastatic and 24% of tubercular nodes showed peripheral vascularity, and 85% of malignant nodes and 76% of tubercular nodes showed mixed vascular pattern. In another study done by Komma et al.[9] 10% of malignant, 13% of tubercular, and 76% of reactive nodes showed hilar vascularity; 8% malignant and 17% tubercular nodes showed peripheral vascularity; and 76% of malignant, 60% tubercular, and 6% reactive nodes showed mixed vascularity. In our study, 12% of metastatic nodes and 28% of tubercular nodes showed peripheral vascularity, whereas 87% of metastatic nodes and 71% of tubercular nodes showed mixed vascularity, and 60% of reactive nodes showed hilar vascularity. Displacement of vascularity in the node signifies tumor infiltration and intranodal cystic necrosis (Figs 12 to 17).

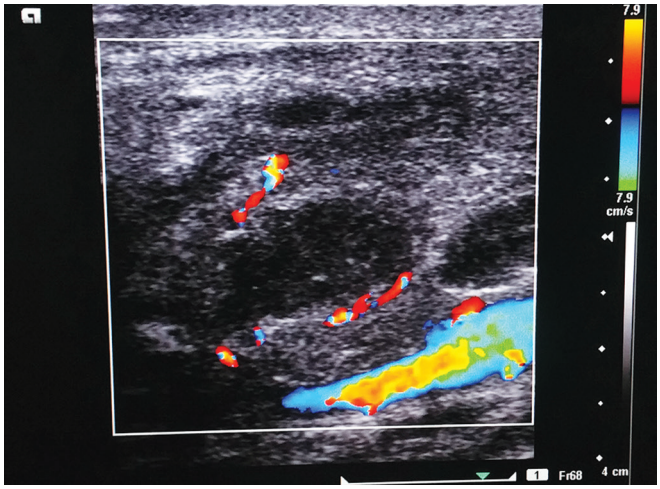


Fig. 12: Color Doppler ultrasonography study showing enlarged lymph node with absent hilum and peripheral vascularity

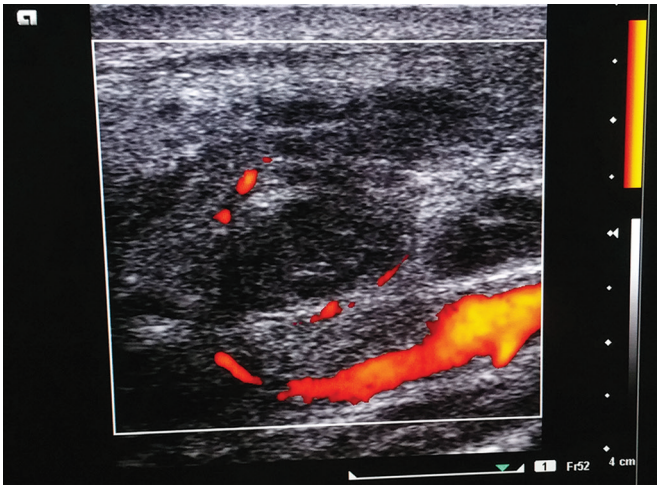


Fig. 13: Power Doppler ultrasonography study showing enlarged lymph node with absent hilum and peripheral vascularity

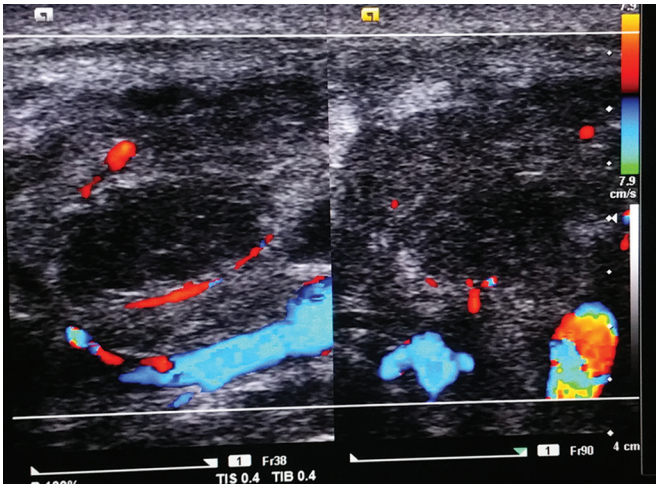


Fig. 14: Color Doppler study showing enlarged lymph node with absent hilum and peripheral vascularity in longitudinal and transverse sections

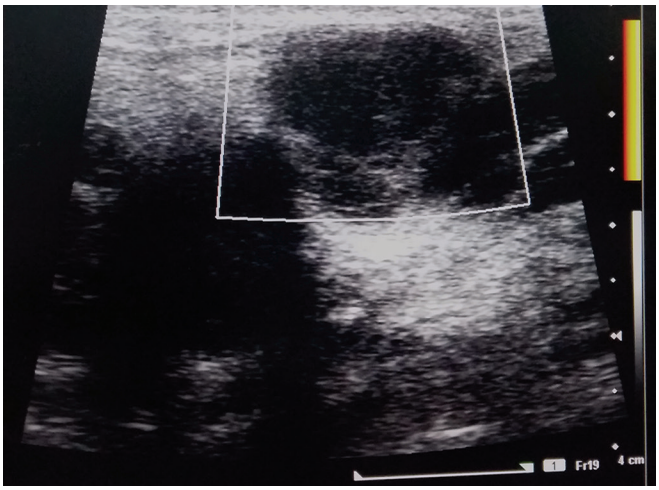


Fig. 15: Power Doppler ultrasonography study showing enlarged and heterogeneous lymph node with loss of nodal architecture and absent hilum and no obvious vascularity

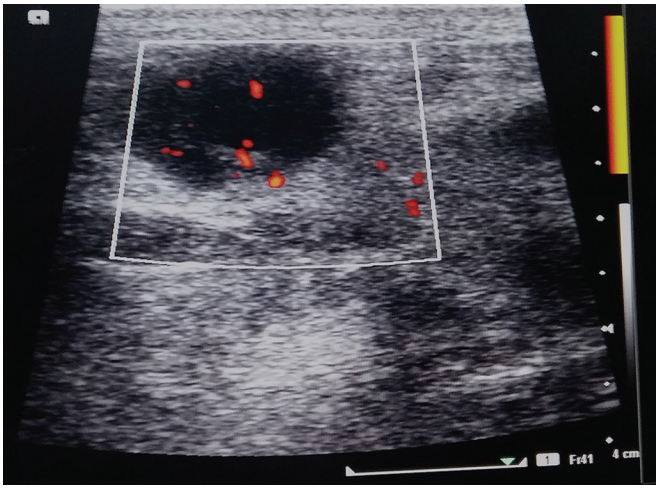


Fig. 16: Power Doppler ultrasonogrpahy study showing enlarged lymph node with absent hilum and peripheral vascularity suggestive of abnormal node

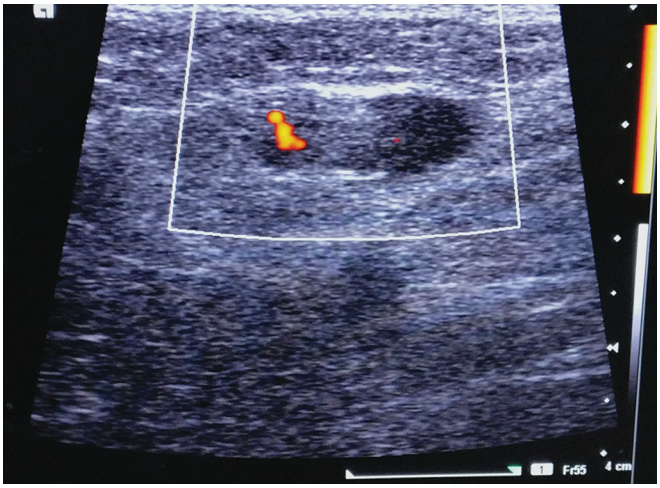


Fig. 17: Power Doppler ultrasonogrpahy study showing enlarged lymph node fatty hilum and normal hilar vascularity

- Vascular Resistance—For evaluating vascular resistance, i.e., resistive index (RI) and pulsatility index (PI) of lymph nodes, the more prominent vessels are used for assessment. RI is calculated as RI = [(PSV – EDV)/PSV], and PI is calculated as PI = [(PSV – EDV)/TAV]. Peak systolic velocity (PSV), end diastolic velocity (EDV) and time averaged velocity (TAV). It has reported a 88% sensitivity in metastatic nodes and 67% sensitivity in lymphomatous nodes with 100% specificity.[15] A higher resistivity index (>0.8) and pulsatility index (>1.5) is seen in metastatic nodes than reactive nodes.[16]

Conclusion

Ultrasonography with Doppler examination of cervical lymphadenopathy yields important information for diagnostic purpose. It has proved to be a primary investigation for identification and differentiation of neoplastic and non-neoplastic lymph nodes. The etiology of cervical lymphadenopathy can be identified by use of gray scale, color Doppler, and power Doppler sonographic features. The useful lymph node features such as size, shape (L/S ratio), border, hilus, echotexture, intranodal necrosis, and calcification can be determined by gray scale. A tubercular lymph node can be identified by adjacent soft tissue edema and presence of matting. The vascular pattern and displacement of vascularity can be determined by power Doppler. Ultrasound evaluation is a nonionizing, noninvasive, safe, and cheaper method in diagnosis of cervical lymphadenopathy.

Ethical and Humane Considerations

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all the participants to be included in the case study.

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