Prepared by Michael T.C. Ying[1] PhD, Anil T. Ahuja[2] FRCR

1 Department of Optometry and Radiography, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR, China
2 Department of Imaging & Interventional Radiology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong SAR, China

Introduction

Metastases in cervical lymph nodes are common in head and neck cancers. The presence of a metastatic node on one side of the neck reduces the 5-year survival rate of 50%, and the presence of a metastatic node on both sides of the neck reduces the survival rate to 25% [1]. Therefore, evaluation of cervical lymphadenopathy is important for patients with head and neck cancers as it helps the assessment of patient prognosis and the selection of treatment method.

Cervical lymph nodes are also common sites of involvement in lymphoma. Lymphomatous nodes are usually difficult to differentiate from metastatic nodes in clinical examinations. As the treatment for lymphoma and metastases is different, accurate differential diagnosis between the two conditions is important.

Tuberculous lymphadenitis is common in South East Asia. However, with the high prevalence of acquired immune deficiency syndrome (AIDS) in the world, the incidence of the associated tuberculous lymphadenitis is increasing worldwide. Therefore, an accurate diagnosis of tuberculous lymphadenitis is essential.

Ultrasound is a useful imaging modality in evaluation of cervical lymphadenopathy because of its high sensitivity (98%) and specificity (95%) when combined with fine-needle aspiration cytology (FNAC) [2]. With the use of power Doppler sonography, the vasculature of the lymph nodes can also be evaluated which provides additional information in the sonographic examination of cervical lymph nodes.

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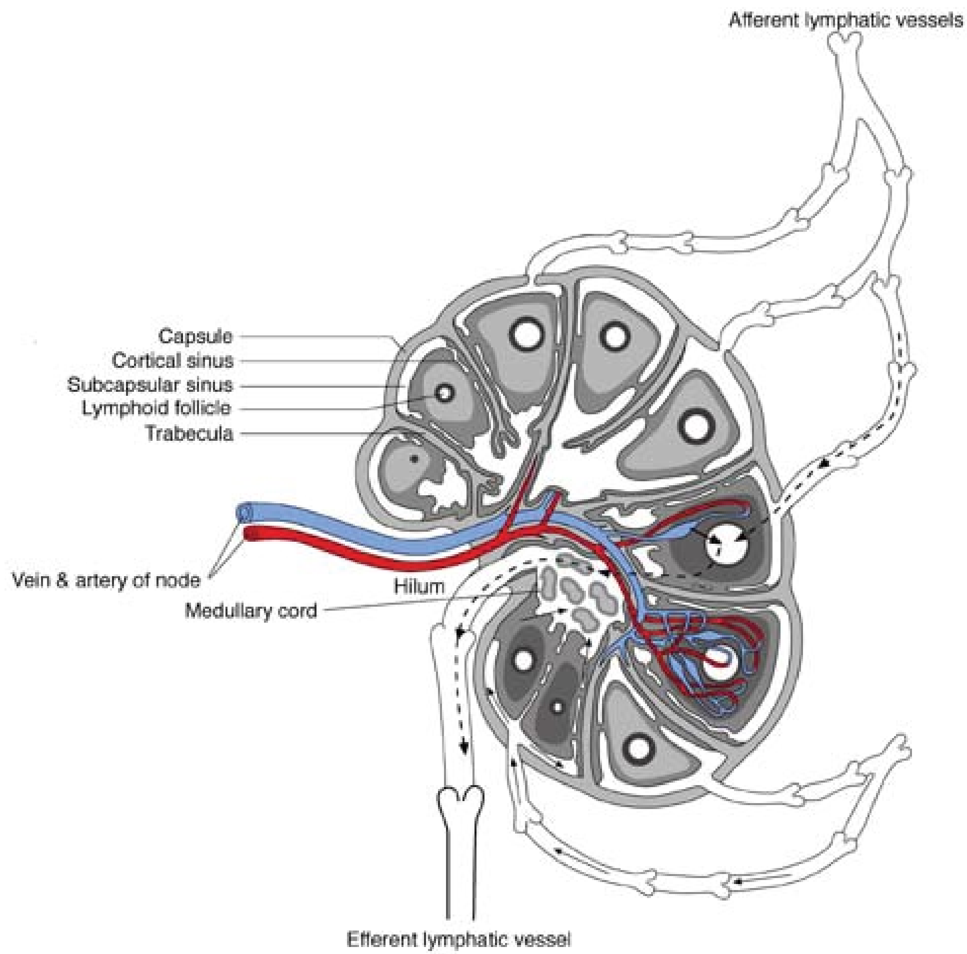
Normal anatomy

Cervical lymph nodes are composed of lymphoid tissue and are located along the lymphatic vessels in the neck. There are about 300 lymph nodes in the neck, and the lymph nodes are embedded in the soft tissues of the neck and are either partly or completely surrounded by fat [3, 4].

Each cervical lymph node is encapsulated by fibrous tissue and is divided into cortical and medullary regions. The cortex is composed of densely packed lymphocytes which group together to form spherical lymphoid follicles, and the medulla of the lymph node consists of medullary trabeculae, medullary cords and medullary sinuses. From the inner surface of the capsule, structures called trabeculae, of similar composition of the capsule, extend towards the medullary region of the lymph node. The capsule and trabeculae form a framework to maintain the shape of the lymph node. The portion of the trabeculae in the medullary region is known as medullary trabeculae, which guide blood vessels and nerves to different regions of the lymph node. The medullary cords and medullary sinuses are composed of reticulum cells. The medullary cords are arranged in a parallel pattern and most of them are long or irregular in shape and surrounded by medullary sinuses. The medullary sinuses are filled with lymph and in which the lymph drains to the efferent lymphatic vessel. The paracortex, an intermediate area between the cortex and the medulla, is a transition area where the lymphocytes return to the lymphatic system from the blood [3, 4].

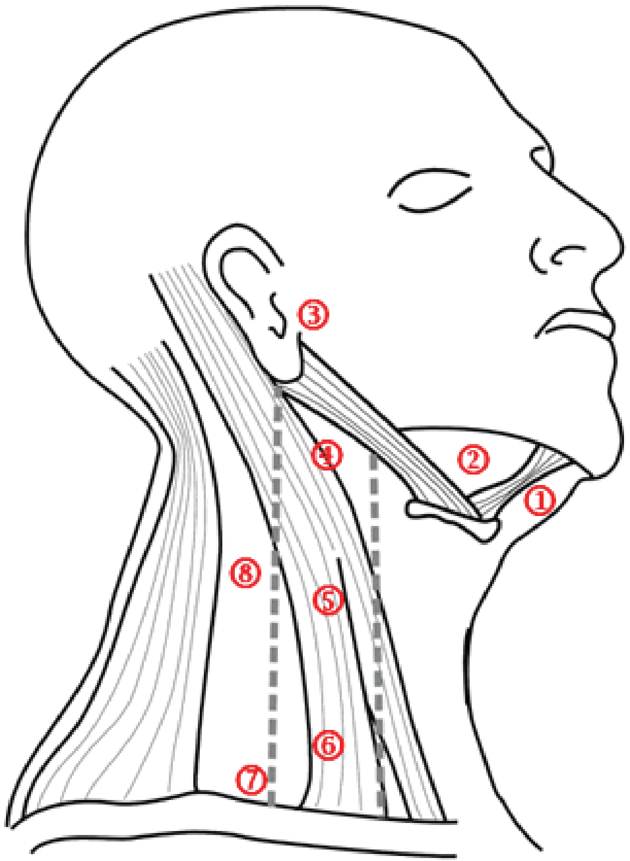


Similar to other lymph nodes, cervical lymph nodes also have blood vessels. The main artery enters the lymph node at the hilus, where it branches into arterioles. In the medulla, some of the arterioles run along the trabeculae to the cortex, while some of them supply the capillary bed of the medulla. In the cortex, the arterioles further branch into capillaries to supply the lymphoid follicles. The venous system has a similar route to the hilus as the arterial system. In the cortex, the venules converge to form small veins, which further converge to form the main vein in the medulla. The main vein then leaves the lymph node at the hilus [3-5].

Classification of cervical lymph nodes

Although the American Joint Committee on Cancer (AJCC) classification of cervical lymph nodes is commonly used, especially by surgeons and oncologists, some important lymph nodes, such as parotid and retropharyngeal nodes, are not included in this classification. As the AJCC classification is not specific for ultrasound examination, some lymph nodes in the classification such as prelaryngeal, paratracheal and upper mediastinal nodes may not be accessible with ultrasound.

Another classification of cervical lymph nodes was established by Hajek et al. [6] for ultrasound examinations. The cervical lymph nodes are classified into eight regions according to their location in the neck.



① Submental

② Submandibular

③ Parotid

④ Upper cervical, above the level of hyoid bone, and along the internal jugular chain

⑤ Middle cervical, between the level of hyoid bone and cricoid cartilage, and along the internal jugular chain

⑥ Lower cervical, below the level of cricoid cartilage, and along the internal jugular chain

⑦ Supraclavicular fossa

⑧ Posterior triangle (also known as accessory chain)

Equipment

A linear transducer of 7.5 MHz or above should be used. A 5 MHz convex transducer is sometimes useful to assess deep lesions. The standoff gel block can be used for examining large or superficial mass.

Technique

The patient is positioned supine on the examination couch with the patient's neck hyperextended. A pillow or triangular soft pad is placed under the patient's shoulders and lower neck for support. The examination is started with a transverse scan of the submental area (region 1). After that, the patient's head turns towards the opposite side and the scanning is followed with a sequence from the submandibular area (region 2) to the posterior triangle (region 8) (i.e. submandibular → parotid → upper cervical → middle cervical → lower cervical → superclavicular fossa → posterior triangle).

Table 1. Common ultrasound scan planes used in the examination of cervical nodes in different regions of the neck.

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

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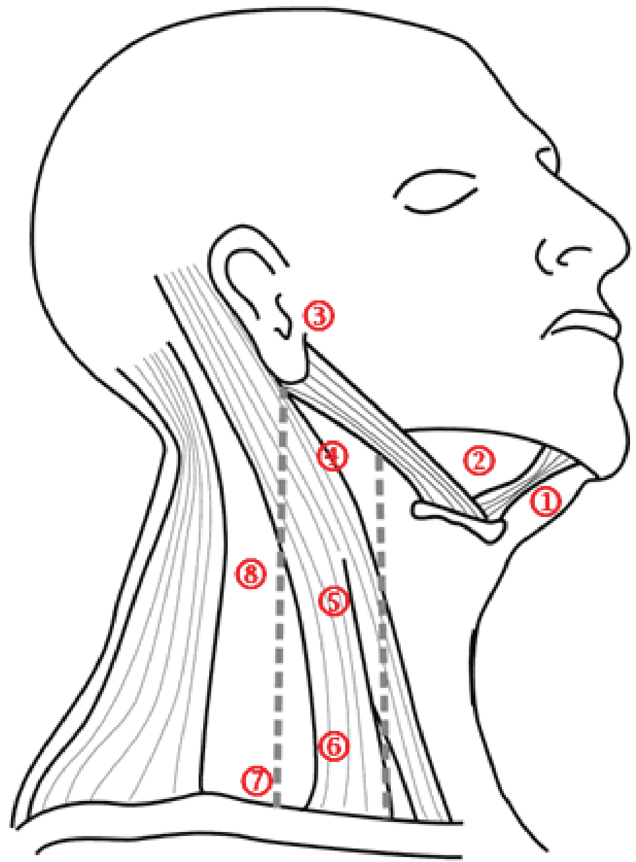


Click on the numbers to view the scanning technique and the corresponding ultrasound image

When power Doppler sonography (PDS) is used, the Doppler setting should be optimized for detecting small vessels:

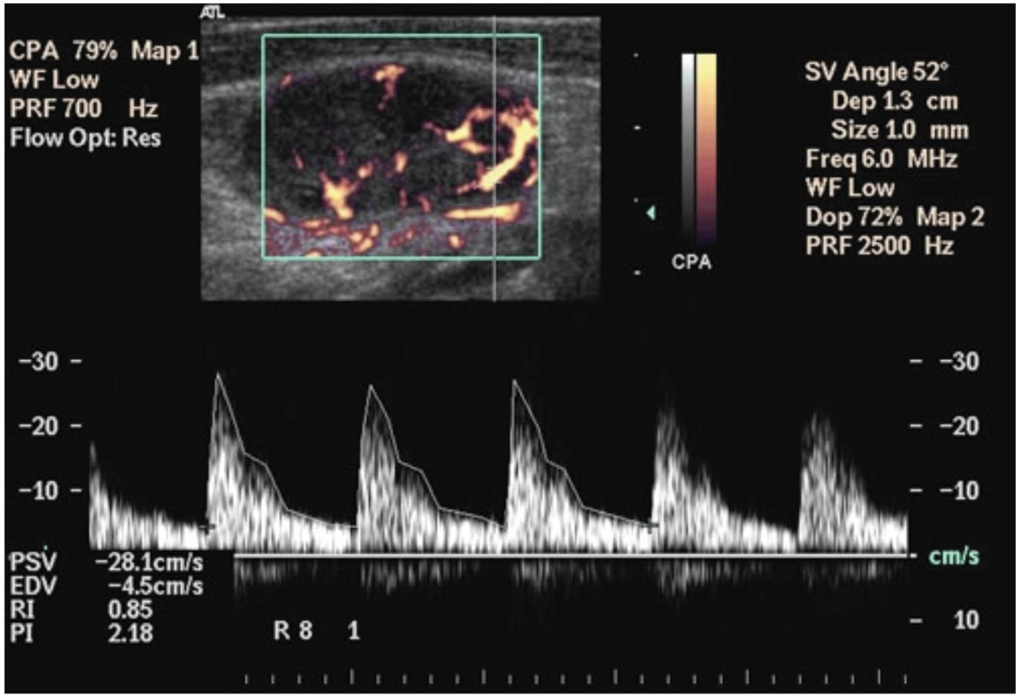
- High sensitivity
- Low wall filter
- Pulsed repetition frequency (PRF): 700 Hz
- Medium persistence
- The colour gain is initially increased to a level which shows colour noise, and then decreased to the level where the noise just disappears.

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

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

The vascularity is also assessed with whether it is displaced or not. Displacement of vascularity is usually due to intranodal cystic necrosis and tumour infiltration.

In the evaluation of the vascular resistance (resistive index RI, pulsatility index PI) of lymph nodes, spectral Doppler is used and the more prominent vessels are usually selected for the measurement. Measurements are obtained from three consecutive waveforms and the smallest sample volume should be used. If the blood flow velocity (peak systolic velocity PSV, end diastolic velocity EDV) is measured, angle correction should be made at an angle of 60 or less.



Sonographic features for diagnosis of cervical lymphadenopathy

Distribution

Normal cervical lymph nodes are usually found in submandibular, parotid, upper cervical and posterior triangle regions. Metastatic cervical lymph nodes are site-specific. In patients with a known primary tumour, the distribution of metastatic nodes helps to identify metastases and assists tumour staging. However, if the primary tumour is not identified, the distribution of proven metastatic nodes may give a clue to identify the primary. Specific distribution is also found in lymphomatous and tuberculous nodes (Table 2).

Table 2. Common sites of metastatic, lymphomatous and tuberculous nodes in the neck

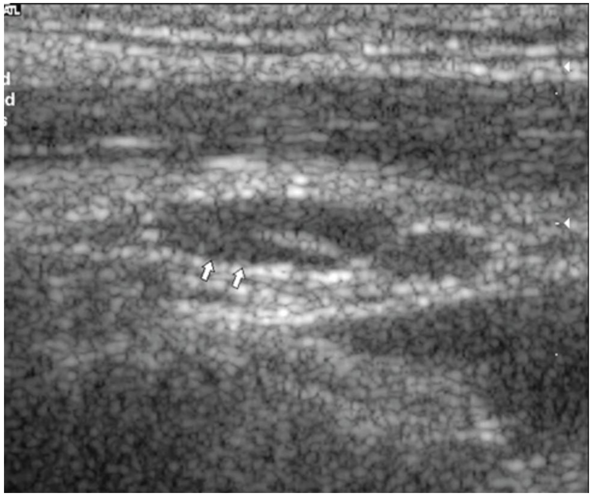
	Commonly involved nodal groups
Metastases from oropharynx, hypopharynx, larynx carcinomas	Internal jugular chain
Metastases from oral cavity carcinomas	Submandibular, Upper cervical
Metastases from nasopharyngeal carcinoma	Upper cervical, Posterior triangle
Metastases from papillary carcinoma of the thyroid	Internal jugular chain
Metastases from non-head and neck carcinoma	Supraclavicular fossa, Posterior triangle
Lymphoma	Submandibular, Upper cervical, Posterior triangle
Tuberculosis	Supraclavicular fossa, Posterior triangle

Size

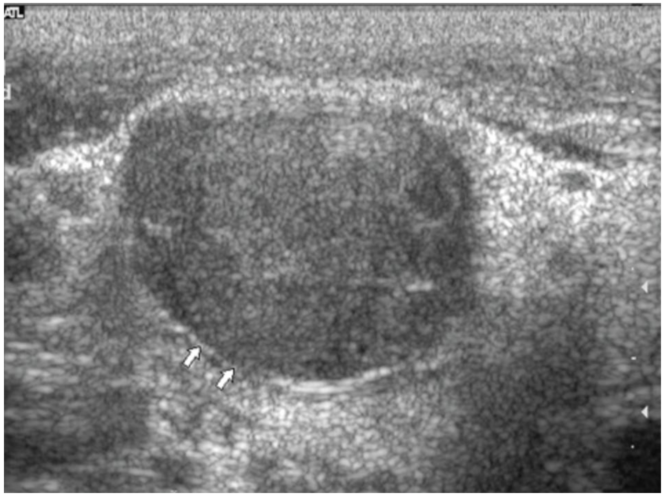
Malignant nodes tend to be large. However, inflammatory nodes can be as large as malignant nodes. Moreover, metastatic deposit can be found in small nodes. Therefore, size of lymph nodes cannot be used as the sole criterion in differential diagnosis. However, in clinical practice, size of lymph nodes is useful when there is an increase in nodal size on serial examinations in a patient with known primary tumour, which is highly suggestive for metastases. Also, serial change in size of malignant nodes is useful in monitoring patients? response to treatment.

Shape

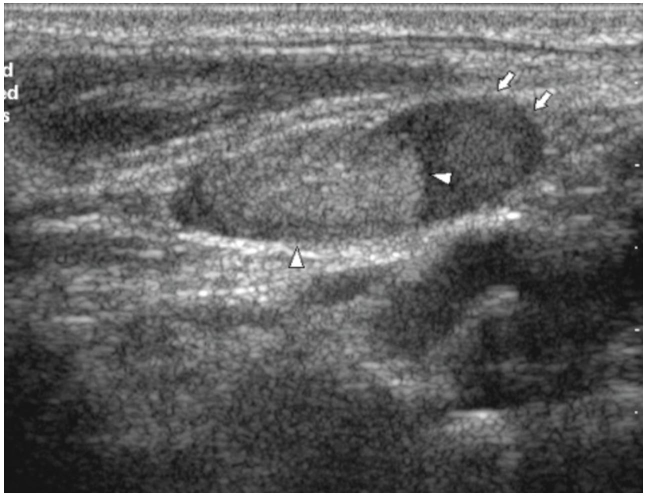
Malignant and tuberculous nodes are usually round in shape with a short axis to long axis (S/L) ratio greater than or equal to 0.5, whereas reactive and normal nodes are usually long or oval-shaped. Nevertheless, it has been reported that normal submandibular and parotid nodes tend to be round in shape. Moreover, malignant nodes may be oval in shape when they are in early stage of involvement. Therefore, nodal shape should be considered as the sole criterion in the diagnosis. However, eccentric cortical hypertrophy, which indicates focal intranodal tumour infiltration, is a useful sign to identify malignant nodes.



Grey scale sonogram showing a normal lymph node which is oval in shape (arrows).



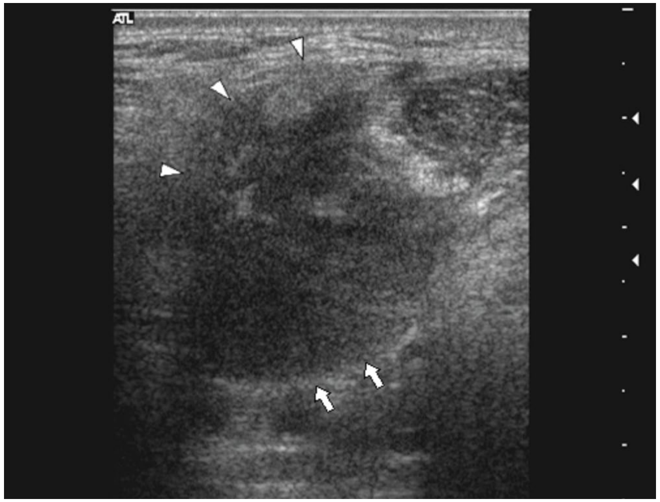
Grey scale sonogram showing a round-shaped metastatic lymph node (arrows).



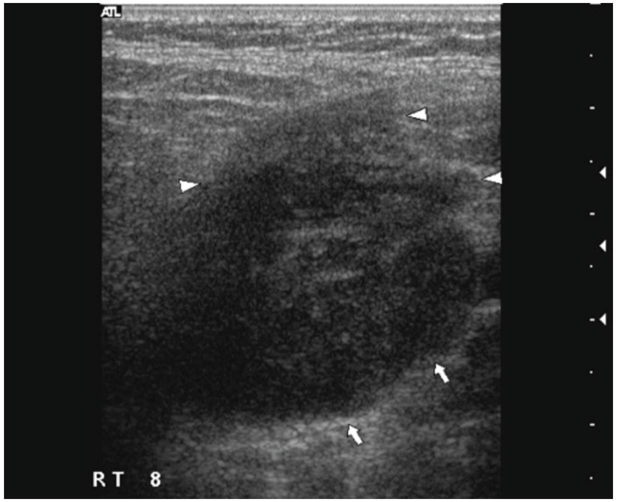
Grey scale sonogram showing a metastatic lymph node (arrows) with eccentric cortical hypertrophy (arrowheads) which indicates focal intranodal tumour infiltration.

Nodal border

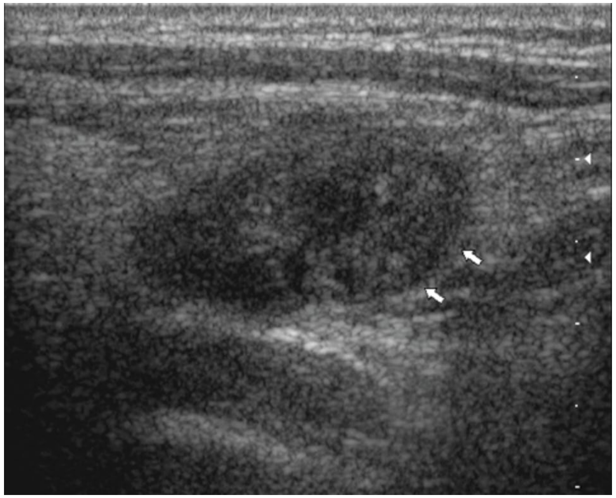
Metastatic and lymphomatous nodes tend to have sharp borders, whereas reactive and normal nodes usually show unsharp borders [7]. The sharp borders in malignant nodes are believed to be due to the tumour infiltration and the reduced fatty deposition within the lymph nodes which increase the acoustic impedance difference between the lymph node and the surrounding tissues. Unsharp borders are common in tuberculous nodes and these are due to the edema and inflammation of the surrounding soft tissue (periadenitis). In our experience, border sharpness is not helpful in differential diagnosis. However, in clinical practice, a proven malignant node with unsharp borders indicates extracapsular spread, which helps in the assessment of patient prognosis.



Grey scale sonogram of a metastatic lymph node (arrows) with ill-defined borders. Note the extracapsular spread to the adjacent soft tissues (arrowheads).



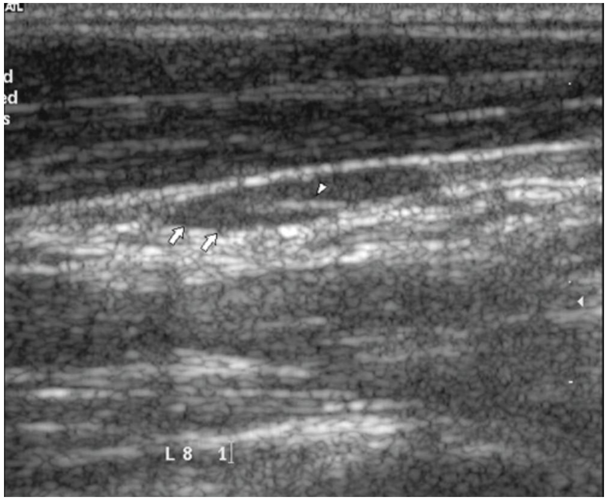
Sonogram of a tuberculous lymph node with ill-defined borders (arrows). Note the adjacent hypoechoic, ill-defined area corresponds to the edema of surrounding soft tissues, periadenitis (arrowheads).



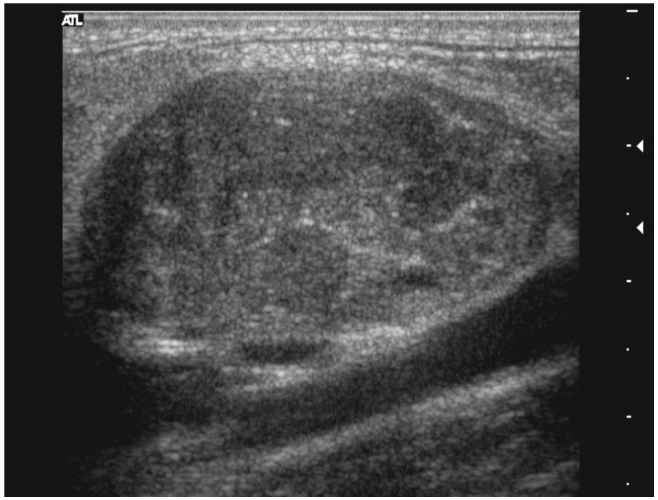
Grey scale sonogram showing a tuberculous lymph node with ill-defined borders (arrows).

Echogenic hilus

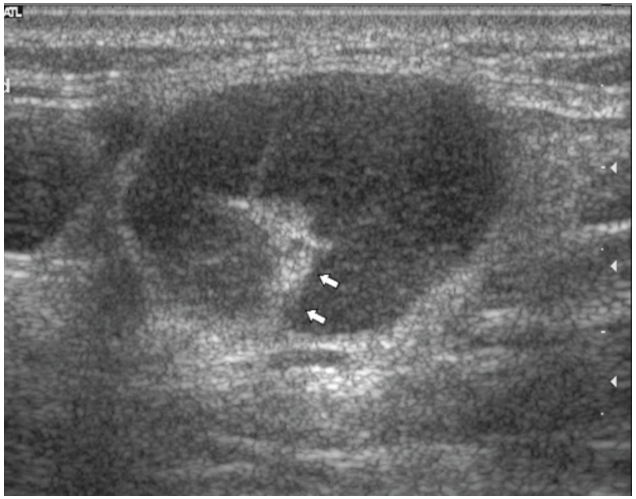
Echogenic hilus is a normal sonographic feature of most of the normal cervical lymph nodes (86%), and it is commonly seen in larger nodes [8, 9]. On ultrasound, echogenic hilus is appeared to be continuous with the adjacent soft tissues. Although metastatic, lymphomatous and tuberculous nodes tend to have absent hilus, they may present with an echogenic hilus in their early stage of involvement in which the medullary sinuses have not been sufficiently disrupted to eradicate it [10]. Therefore, the presence/absence of echogenic hilus should not be the sole criterion in the diagnosis.



Grey scale sonogram of a normal posterior triangle lymph node (white arrows) with an echogenic hilus (arrowhead). Note the echogenic hilus is continuous with the adjacent soft tissues (black arrows).



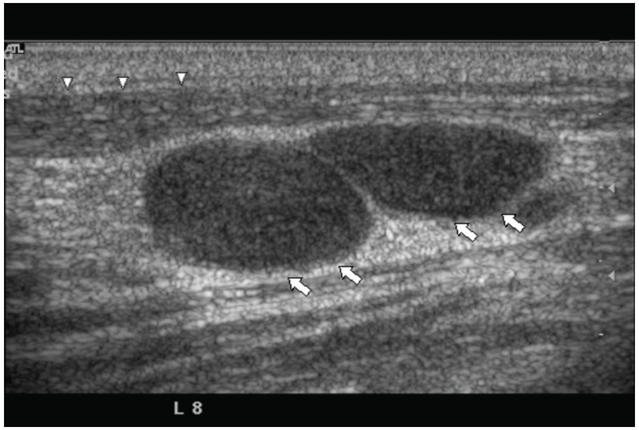
Grey scale sonogram showing a metastatic lymph node without an echogenic hilus.



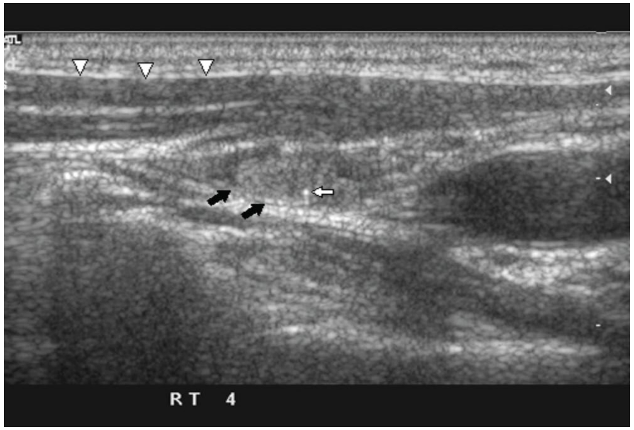
Grey scale sonogram showing a lymphomatous lymph node with the echogenic hilus (arrows) still persist in the early stage of involvement.

Echogenicity

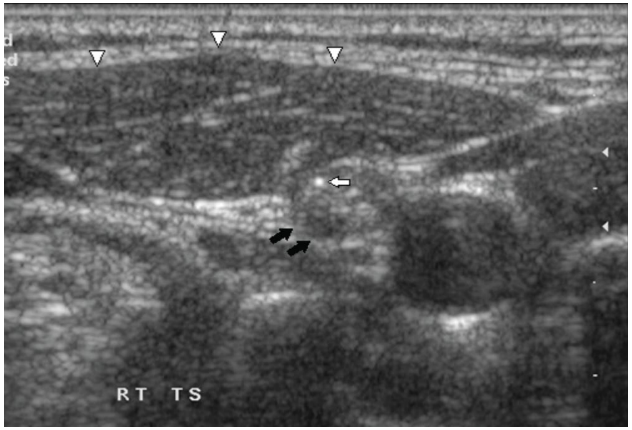
Normal, reactive, lymphomatous and tuberculous nodes are predominantly hypoechoic when compared with the adjacent muscles. Metastatic nodes are usually hypoechoic, except for metastases from papillary carcinoma of the thyroid which tend to be hyperechoic [11]. Therefore, hypereechogenicity is a useful sign to identify metastatic nodes from papillary carcinoma of the thyroid. Radiologist should scan the thyroid for a primary tumour if hyperechoic nodes are identified.



Grey scale sonogram of lymphomatous lymph nodes (arrows), which are hypoechoic when compared with adjacent muscles (arrowheads).



Grey scale sonogram showing a metastatic lymph node from papillary carcinoma of the thyroid (black arrows), which is hyperechoic when compared with adjacent muscles (arrowheads). Note the punctate calcification within the lymph node (white arrow) which is a common feature of metastatic nodes from papillary thyroid carcinoma.



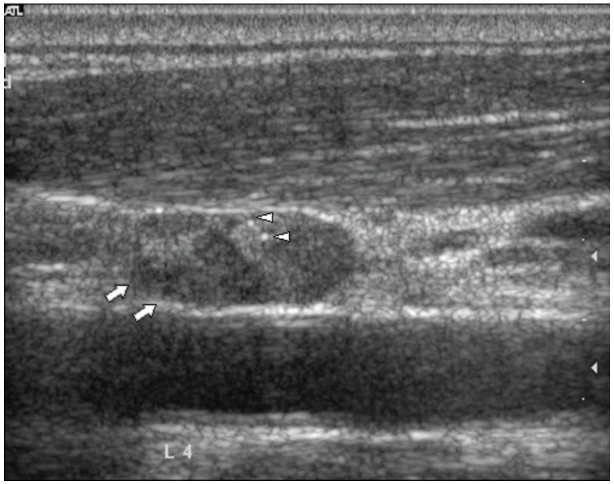
Transverse sonogram of a metastatic lymph node from papillary carcinoma of the thyroid (black arrows). The lymph node is hyperechoic when compared with adjacent muscles (arrow-heads), and has punctate calcification (white arrow).

Lymphomatous nodes were previously reported to have a pseudocystic appearance, i.e. hypoechoic with posterior enhancement [12, 13]. With the use of newer transducer, lymphomatous nodes are less likely to have the pseudocystic appearance, whereas they demonstrate a micronodular appearance [14].

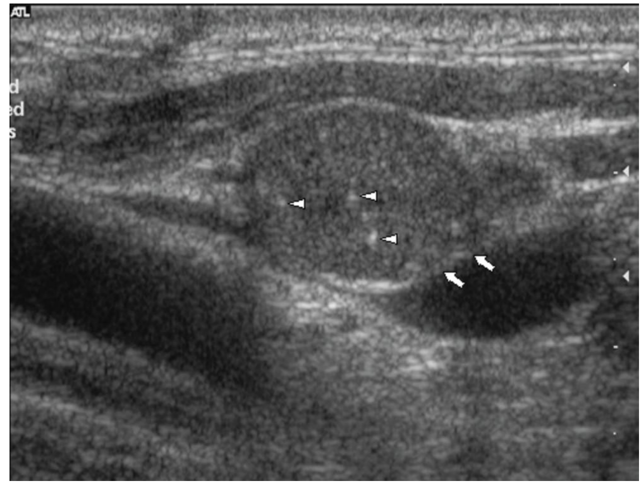
Grey scale sonogram showing a lymphomatous node with micronodular appearance (arrows). Note the cystic necrosis within the lymph node (arrowheads).

Calcification

Intranodal calcification is rarely found in cervical lymphadenopathy. However, about 50-69% of metastatic nodes from papillary carcinoma of the thyroid show calcification which is punctuate, peripherally located and may show acoustic shadowing with a high-frequency transducer [11, 15]. Therefore, the presence of characteristic calcification is a useful feature to identify metastatic nodes from papillary carcinoma of the thyroid.

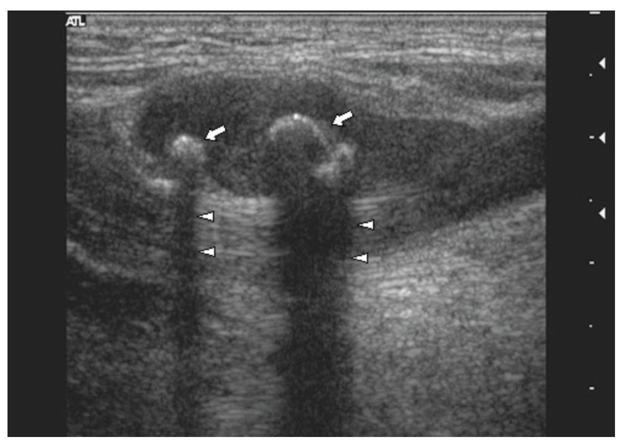


Longitudinal sonogram showing a metastatic node from papillary carcinoma of the thyroid (arrows). Note the punctate and peripherally located calcification within the lymph node (arrowheads), which is common in metastatic nodes from papillary thyroid carcinoma.



Grey scale sonogram showing a treated tuberculous node with dense intranodal calcifications (arrows) and acoustic shadowing (arrowheads).

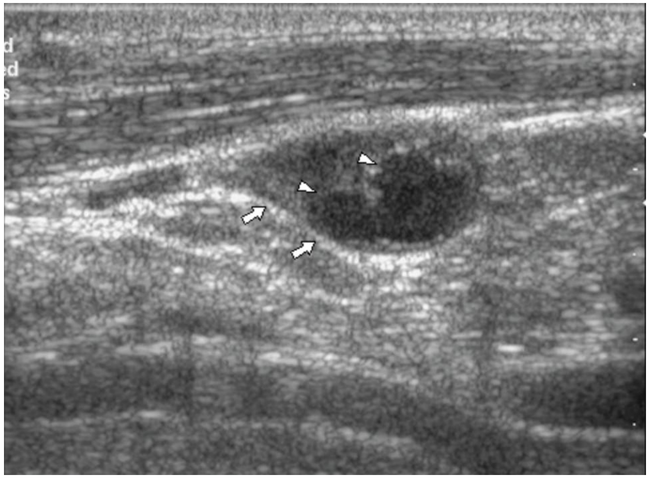
Intranodal calcification may be found in lymphomatous and tuberculous nodes after treatment but the calcification is usually dense and shows acoustic shadowing.



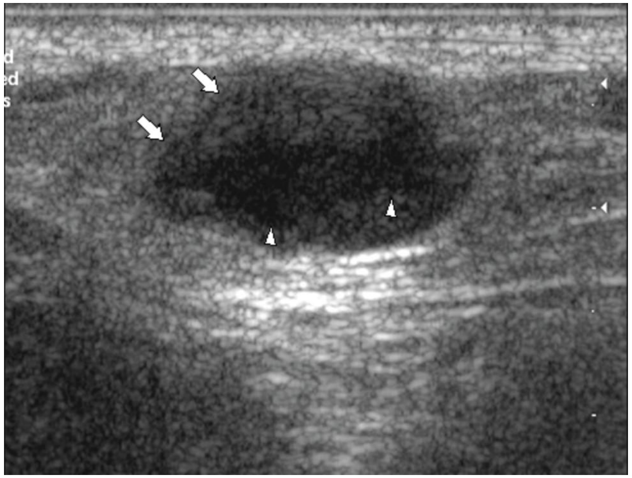
Grey scale sonogram showing a round, hyperechoic metastatic node from papillary carcinoma of the thyroid (arrows) with multiple punctate calcifications (arrow-heads).

Intranodal necrosis

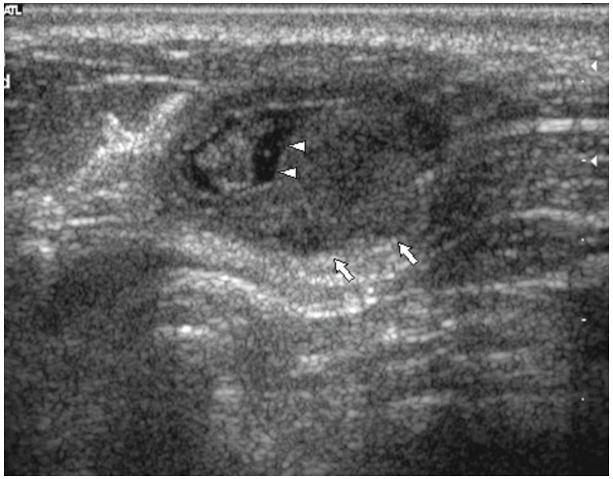
Lymph nodes with intranodal necrosis are considered to be pathologic. Intranodal necrosis can be classified into coagulation necrosis and cystic necrosis, where cystic necrosis is more common than coagulation necrosis. Coagulation necrosis appears as an intranodal echogenic focus, whilst cystic necrosis appears as an echolucent area within the lymph nodes. Cystic necrosis is commonly found in tuberculous nodes and metastatic nodes from squamous cell carcinomas and papillary carcinoma of the thyroid.



Grey scale sonogram showing a metastatic node (arrows) with intranodal cystic necrosis (arrowheads).



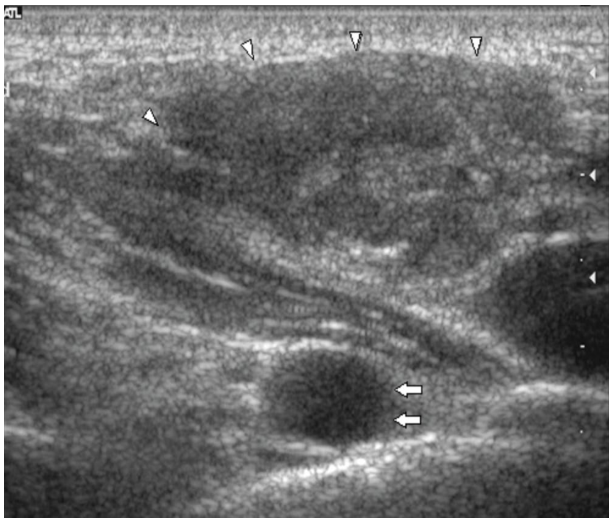
Grey scale sonogram showing a tubeculous lymph node (arrows) with intranodal cystic necrosis (arrowheads).



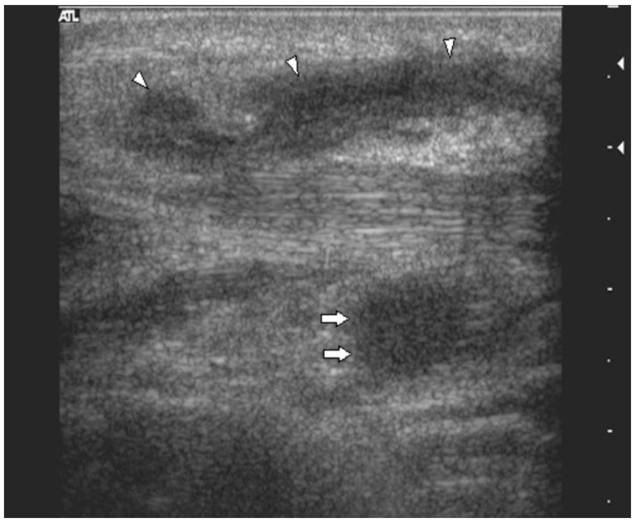
Grey scale sonogram showing an ill-defined tubeculous lymph node (arrows) with intranodal cystic necrosis (arrowheads).

Ancillary features

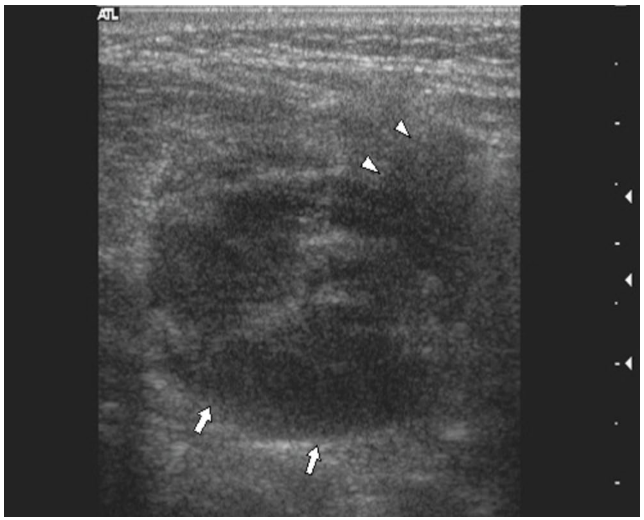
Ancillary features that help in the evaluation of cervical lymphadenopathy are adjacent soft tissues edema and matting. On ultrasound, soft tissues edema appears as an diffuse hypoechogenic area with loss of fascial planes, whereas matting is clumps of multiple abnormal lymph nodes with abnormal intervening soft tissues. Adjacent soft tissues edema and matting are common features in tuberculous nodes, whilst these features are relatively less common in metastatic and lymphomatous nodes [15]. The high incidence of adjacent soft tissues edema and matting in tubeculous nodes is believed to be due to the perinodal inflammatory reaction (periadenitis) of the nodes. However, one should note that adjacent soft tissues edema and matting may be found in patients with previous radiation treatment on the neck [16].



Grey scale sonogram of a hypoechoic tubeculous lymph node (arrows). Note the adjacent soft tissues edema which is hypoechoic, ill-defined and with loss of fascial planes (arrowheads).

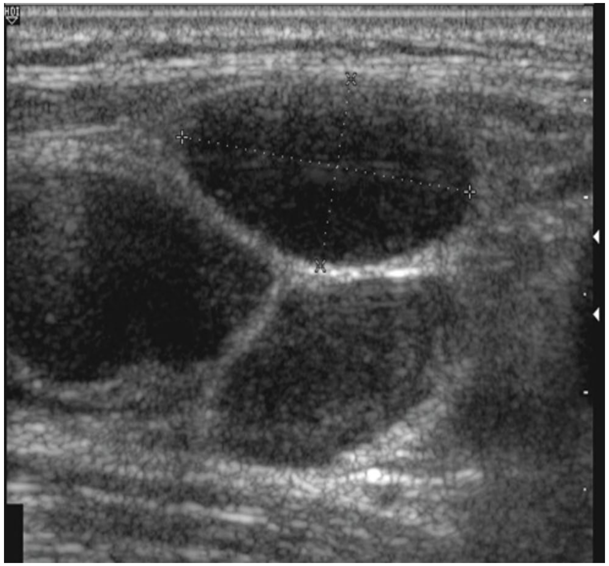


Grey scale sonogram showing a hypoechoic and ill-defined tubeculous lymph node (arrows) with adjacent soft tissues edema (arrowheads).

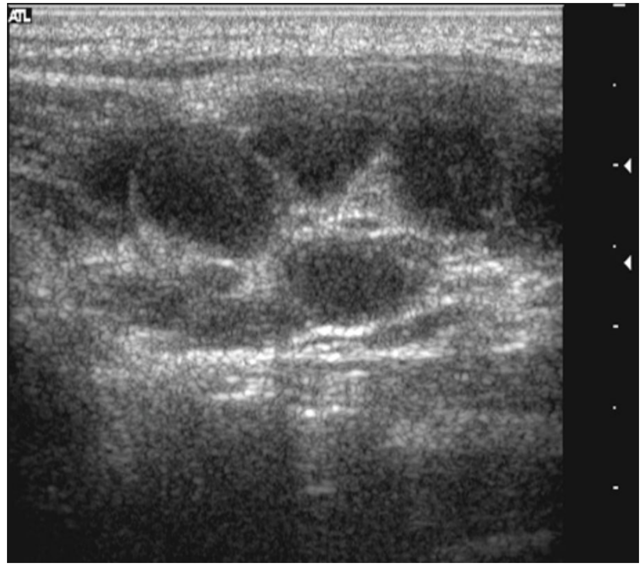


Sonogram showing a hypoechoic, ill-defined tubeculous lymph node (arrows) with adjacent soft tissues edema (arrowheads).

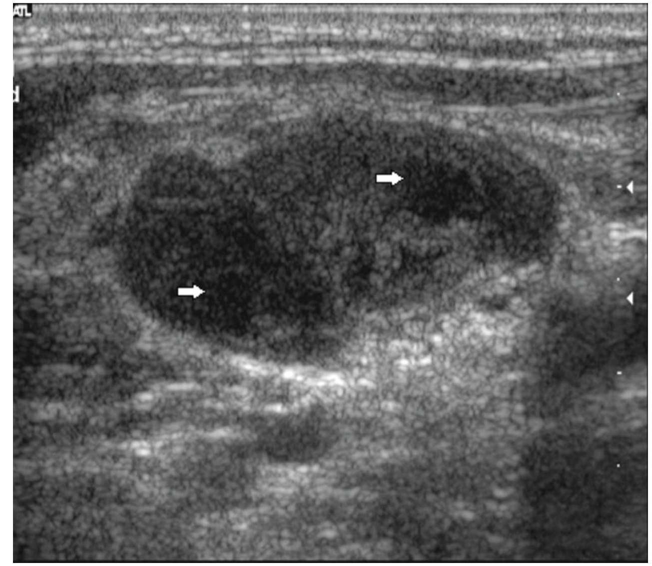
Ultrasonography of cervical lymph nodes



Grey scale sonogram showing multiple hypoechoic tubeculous lymph node clumped together, matting, which is a common feature of tuberculous lymphadenitis.



Grey scale sonogram of multiple matted tubeculous lymph node with abnormal intervening soft tissues.

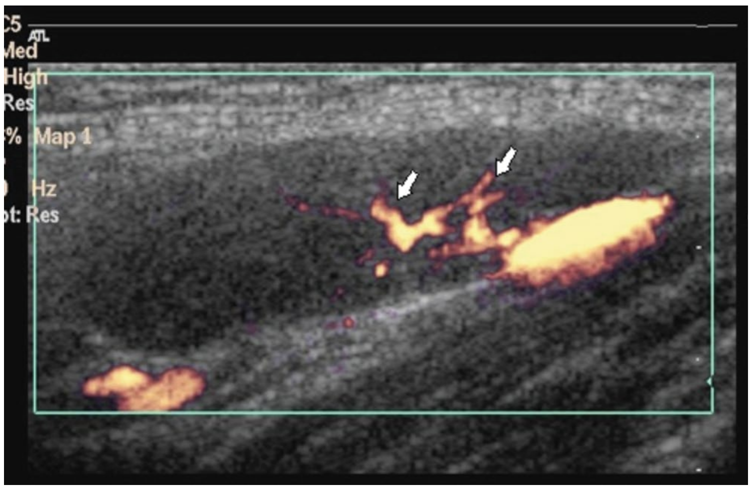


Grey scale sonogram showing two hypoechoic tubeculous lymph node matted together. Note the cystic necrosis within the lymph nodes (arrows).

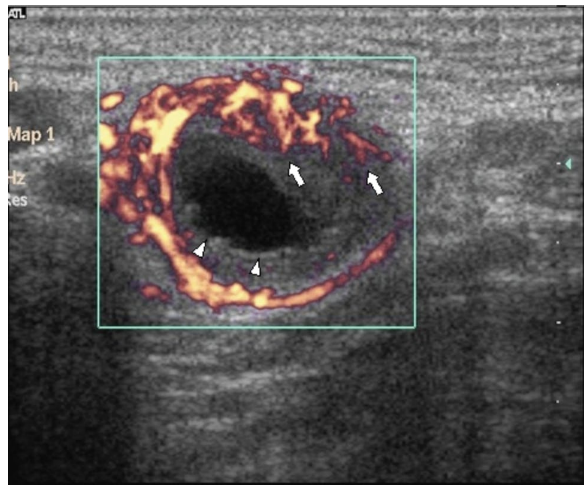
Vascular pattern

Normal and reactive lymph nodes tend to have hilar vascularity or appear apparently avascular, whereas metastatic nodes usually show peripheral or mixed vascularity, and lymphomatous nodes predominantly demonstrate mixed vascularity [17, 18]. As peripheral vascularity is not found in normal or reactive nodes, the presence of peripheral vascularity, regardless of sole peripheral or mixed vascularity, is highly suspicious of malignancy.

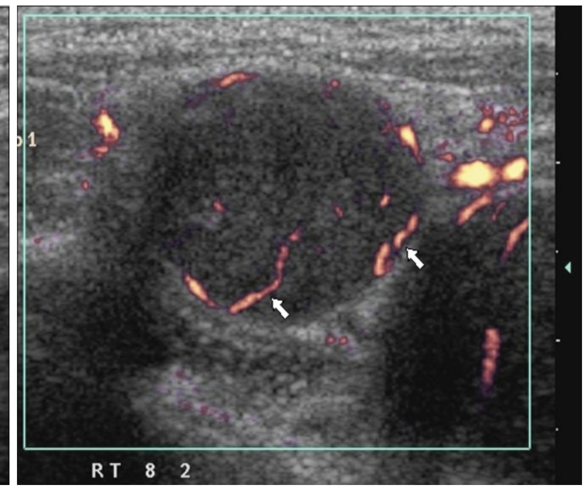
On ultrasound, tuberculous nodes have varied vascular pattern, which simulates both benign and malignant conditions [17, 19]. In spite of the varied vascular pattern, displaced vascularity and apparent avascularity are common in tuberculous nodes, which are related to the high incidence of cystic necrosis in tuberculous lymph nodes [17, 19].



Power Doppler sonogram of a reactive lymph node with hilar vascularity (arrows).

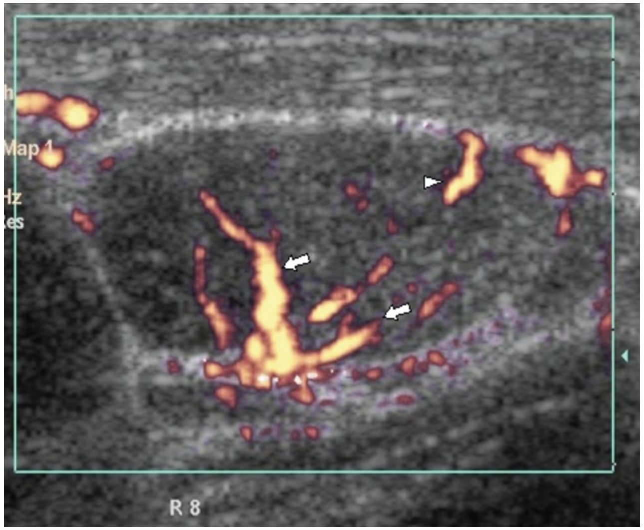


Power Doppler sonogram of a metastatic node with peripheral vascularity (arrows). Note the cystic necrosis within the lymph node (arrowheads).

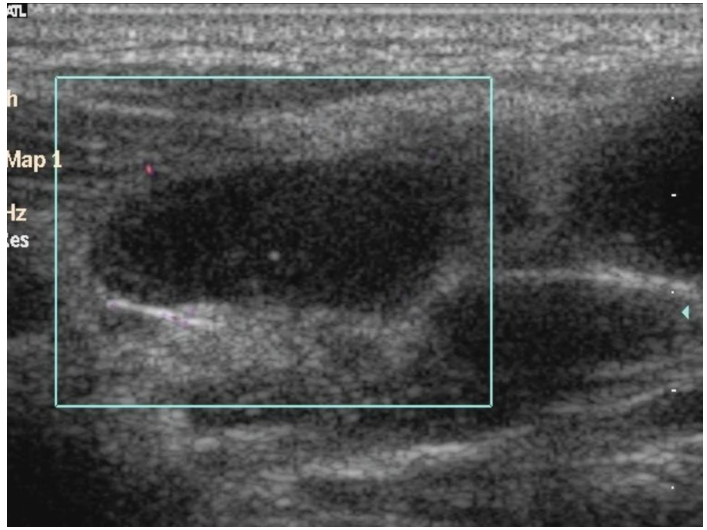


Power Doppler sonogram showing a malignant node with peripheral vascularity (arrows).

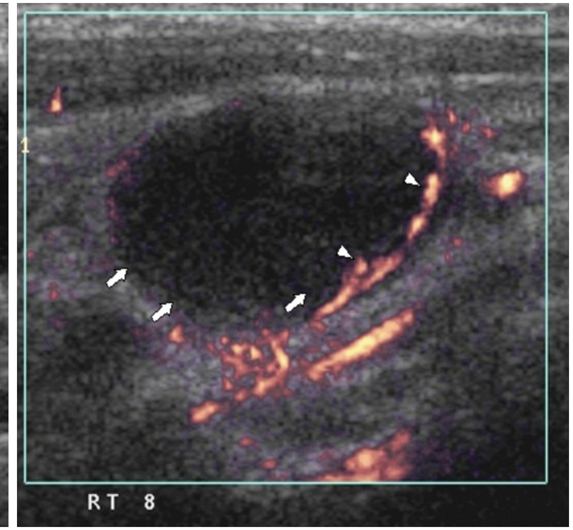
Ultrasonography of cervical lymph nodes



Power Doppler sonogram showing a malignant node with both hilar (arrows) and peripheral (arrowhead) vascularity.



Power Doppler sonogram of a hypoechoic tuberculous lymph node which appears apparently avascular.



Power Doppler sonogram showing a tuberculous node with extensive intranodal cystic necrosis (arrows), which displaces the vascularity towards the peripheral of the node (arrowheads).

Vascular resistance

In the evaluation of the vascular resistance (RI and PI) of cervical lymph nodes, the mean, highest and lowest values have been reported [20-22]. However, we found that the repeatability of measurement is higher when the mean value is used [23].

The role of RI and PI in distinguishing malignant and benign nodes is controversial. It has been reported the metastatic nodes have a higher RI and PI than reactive nodes [21, 24]. However, another study found that there was no significant difference in RI and PI between benign and malignant nodes [25]. Our studies found that metastatic nodes tend to have a higher RI and PI than reactive nodes, except for the metastatic nodes from papillary carcinoma of the thyroid which show similar RI and PI with reactive nodes [17, 26]. Nevertheless, we found that the combination of grey scale sonographic features and vascular pattern of lymph nodes already have a high accuracy in differentiating metastatic and reactive nodes [27]. Therefore, measurement of the vascular resistance of lymph nodes may not be necessary in routine clinical practice.

Conclusions

Ultrasound is a useful imaging modality in assessment of cervical lymph nodes. Distribution of nodes, grey scale and power Doppler sonographic features are useful to identify the cause of cervical lymphadenopathy. Useful grey scale features include size, shape, status of echogenic hilus, echogenicity, micronodular appearance, intranodal necrosis and calcification. Adjacent soft tissue edema and matting are particularly useful to identify tuberculosis. Useful power Doppler features include vascular pattern and displacement of vascularity

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