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Imaging Features and Recent Advances in Lymph Node Tuberculosis

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Abstract

The burden of tuberculosis in our country persists, with diverse presentations affecting various organ systems, most commonly manifesting as pulmonary tuberculosis followed by nodal tuberculosis. While pulmonary involvement is frequently observed, nodal tuberculosis can present in isolation, commonly affecting cervical lymph nodes. Various imaging modalities play pivotal roles in diagnosis and assessment. Radiographs serve as initial screening modality in thoracic lymphadenopathy. Ultrasound is mostly used in cervical lymphadenopathy. Cases of thoracic and abdominal lymphadenopathy are usually evaluated with computed tomography but magnetic resonance imaging can be a radiation-free alternative. The role of fluorodeoxyglucose-positron emission tomography and newer modalities like shear-wave elastography and contrast-enhanced ultrasound are briefly discussed.

Keywords
- tuberculosis
- lymphadenopathy
- imaging
- computed tomography
- MRI

Introduction

Tuberculosis (TB) remains one of the leading contributors of disease burden in our country with varied presentations involving various organ systems. It can involve a single organ system or present in disseminated form. Pulmonary TB is by far the most common form, followed by nodal TB. Nodal TB is the most common form of extrapulmonary TB.

Patients of nodal TB often have a past history of inadequately treated or clinically silent pulmonary TB. Although most patients may also show pulmonary involvement on further examination and investigations, it is not uncommon to have isolated regional lymphadenopathy, most commonly seen in the cervical region.[1] Nodal TB can practically involve any region in the body.

Imaging Modalities

It is critical to use the imaging modalities judiciously, keeping in mind the issue of availability, as well as economic and radiation costs.

Radiographs

Chest radiograph (CR) is useful in the evaluation of thoracic lymphadenopathy for which it is the primary initial modality. A lateral radiograph improves the diagnosis of enlarged lymph nodes at several sites including hila. Large cervical lymph nodes can also be appreciated on radiographs of the neck.

Ultrasonography

It is a very useful modality when the target region is superficial/easily accessible and thus plays a major role in

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cervical lymphadenopathy. Abdominal lymphadenopathy can also be evaluated and subjected to guided-sampling on ultrasound (US). In specific situations, ultrasonography (USG) can be used in visualizing upper mediastinal lymph nodes (right and left paratracheal, prevascular, subaortic, subcarinal). In addition to superior characterization of nodal characteristics, it can be used as a valuable tool in guided sampling and follow-up of patients.

Computed Tomography

Contrast-enhanced computed tomography (CECT) is the most important imaging modality in intrathoracic diseases. The nature of contrast enhancement, presence or absence of calcification, and conglomeration are some of the parameters that need to be assessed on CT images. Characteristic appearance on CT includes necrotic nodes with peripheral rim enhancement, conglomerate lymphadenopathy, perinodal fat streakiness, and calcification (more prominent on treated nodes). Additional advantage includes the ability to evaluate the lungs and the osseous structures. CECT abdomen and CT enterography are useful in abdominal involvement.

Magnetic Resonance Imaging

On magnetic resonance imaging (MRI), three patterns can be seen—discrete, matted, and confluent. Necrosis is seen as an area of T2 hyperintensity and T1 hypointensity. Contrast administration is crucial, as presence or absence of necrosis can be confidently commented upon only on a CE-MRI. Most of the patients suffering from tubercular lymphadenopathy have to undergo repeated imaging. While superficial lymphadenopathies can be followed up on US, deeper lesions need alternate imaging modality. MRI can fit in this situation, in both abdominal as well as thoracic lymphadenopathies.

Fluorodeoxyglucose-Positron Emission Tomography CT

It can help in mapping the extent of the disease accurately before the initiation of therapy and also aid in confirmation of TB. Maximum standardized uptake value can be useful in monitoring treatment response.[2,3] Major drawback of fluorodeoxyglucose-positron emission tomography (FDG-PET) imaging is that it fails to distinguish between other similar etiologies of lymph node involvement like metastases, sarcoidosis, and lymphoproliferative disorders. Lymphoma is the most common misdiagnosis. However, it can suggest the site for successful biopsy and differentiate between active and inactive nodes.[4]

Imaging Characteristics and Differentials in Tubercular Lymphadenopathy

The imaging findings and differentials are discussed sitewise (cervical, thoracic, and abdominal lymphadenopathy) below.

Cervical Lymphadenopathy

Tubercular cervical lymphadenopathy, like any other sites, classically presents with matted/conglomerated lymph nodes with or without necrosis. The main differential diagnoses include other infective causes (bacterial/viral), malignant causes (lymphoma, metastases), Kimura's disease, histiocytic disorders (Rosai–Dorfman disease), and inflammatory causes (Kawasaki disease).

While imaging is not fool proof, several imaging characteristics have been described for differentiating tubercular lymphadenopathy from other causes (►**Fig. 1**). Besides gray scale USG, color Doppler USG has also proved to have diagnostic benefits in differentiating tubercular lymphadenopathy from other causes. Pattanayak et al studied the US characteristics of cervical lymph nodes in predicting the benign and malignant etiologies. Statistically significant features are listed in ►**Table 1**.[5]

Newer imaging modalities such as shear wave elastography (SWE) and CEUS have been studied for their applications in tubercular lymph nodes. Patterns of enhancement in CEUS is studied for its utility in US classification of tuberculous lymph nodes to aid in better assessment of the disease stage.[6] More than half area of nonenhancement was found to be predictor for lymph node rupture in cervical tubercular

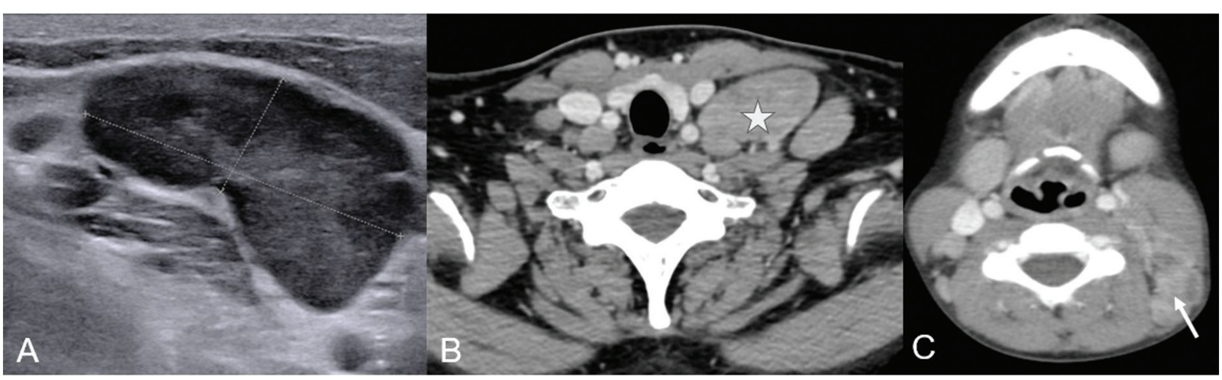

Fig. 1 (**A–C**) Variable appearances of cervical lymphadenopathy in tuberculosis in three different patients. Gray scale ultrasound (US) (**A**) of a 24-year-old male showing nonnecrotic supraclavicular lymphadenopathy. Axial contrast-enhanced computed tomography (CECT) in a 17-year-old male showing enlarged homogeneous left supraclavicular lymph nodes (asterisk in **B**). Another patient, 24-year-old male showing multiple conglomerate necrotic cervical lymphadenopathy (arrow in **C**).

Table 1 Imaging differentiation of tubercular versus other causes of cervical lymphadenopathy

Etiology	Ultrasound characteristics
Tuberculous lymph nodes	• Absent hilum • Unsharp nodal border • Hypoechoic echotexture • Intranodal necrosis • Presence of ancillary features like soft tissue edema and matting • Peripheral vascularity
Reactive lymph nodes	• Oval shape • Presence of hilum • Unsharp nodal border • Absence of ancillary features like soft tissue edema, matting • Absence of intranodal necrosis • Central vascularity
Lymphomatous nodes	• Round shape • Absent hilum • Sharp nodal borders • Hypoechoic echotexture • Soft tissue edema • Peripheral vascularity
Metastatic	• Round shape • Hypoechoic echotexture • Soft tissue edema • Peripheral vascularity

lymphadenopathy.[7] SWE along with conventional US can help in differentiating benign from malignant lymph nodes.[8,9]

Thoracic Lymphadenopathy

Thoracic lymphadenopathy is the most common site involved in lymph nodal TB. Both mediastinal as well as hilar lymph nodes can be affected. Uncommon sites include internal thoracic, epicardial, and intercostal lymph nodes.

Chest Radiograph

CR can detect mediastinal and hilar lymphadenopathy. Right paratracheal lymphadenopathy is evident by widening of right paratracheal stripe; subcarinal adenopathy is reflected by widening of the carinal angle (►**Table 2**, ►**Fig. 2**). One of the nonspecific and less described signs on lateral radiograph, "dough nut sign" refers to the radiopaque ring formed in the presence of enlarged subcarinal and hilar lymph nodes where the trachea/upper lobe bronchi form the central radiolucency. Aortic arch and pulmonary arteries form the superior and anterior aspect of the ring which is completed by the presence of enlarged lymph nodes inferiorly.

Ultrasonography

USG has an additive value in differentiation of lymph nodes from a normal or enlarged thymus. Although the lower mediastinal stations are not amenable to USG evaluation. Upper stations (4A, 4B, 3, 5, and 7) can be visualized under USG using proper technique[10] (►**Fig. 3**). The technique of USG in the chest is described in ►**Table 3**.

CECT

CECT remains the workhorse of imaging in intrathoracic lymphadenopathy (►**Fig. 4**). Intrathoracic lymphadenopathy, in addition to the causes listed elsewhere in the body, has a few unique differential diagnoses such as enlarged thymus or developmental cysts.

MRI

As described earlier, necrosis and peripheral rim enhancement can be appreciated in MRI (►**Fig. 5**).

Table 2 Radiographic features of tubercular lymphadenopathy (►**Fig. 2**)

Nodes involved	Imaging finding
Right paratracheal	Widening of right paratracheal stripe ($>$ 5 mm)
Hilar	Increased density and outward convex contour of hila
Subcarinal	Widening of carinal angle, straightening of the left main bronchus
Azygo-esophageal	Displacement of the azygo-esophageal line

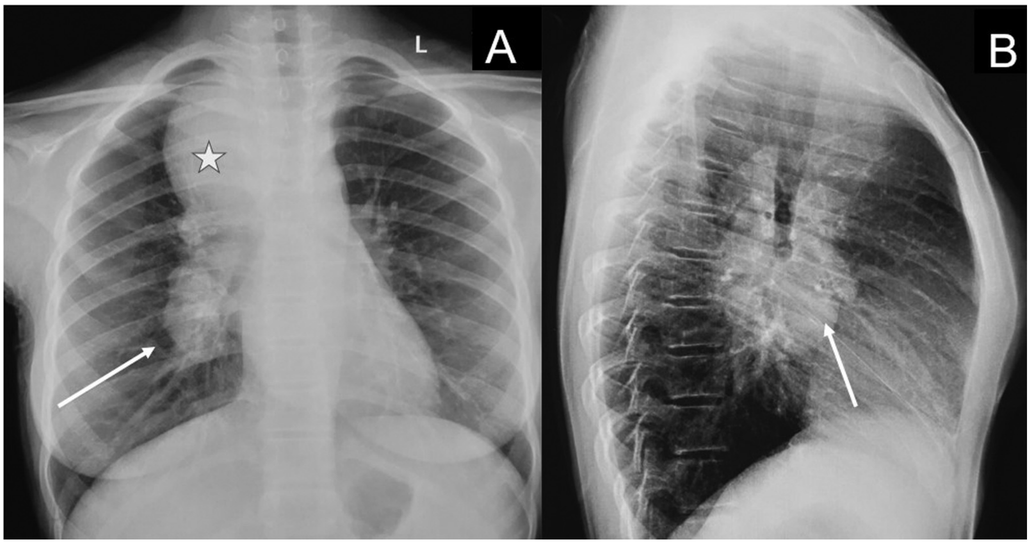

Fig. 2 (**A**, **B**) Thoracic lymphadenopathy in tuberculosis. (**A**) Right paratracheal (asterisk) lymphadenopathy seen as widening of right paratracheal stripe. Right hilar adenopathy seen as hilar enlargement on postero-anterior (PA) projection (arrow in **A**) and "doughnut sign" on lateral radiograph (arrow in **B**).

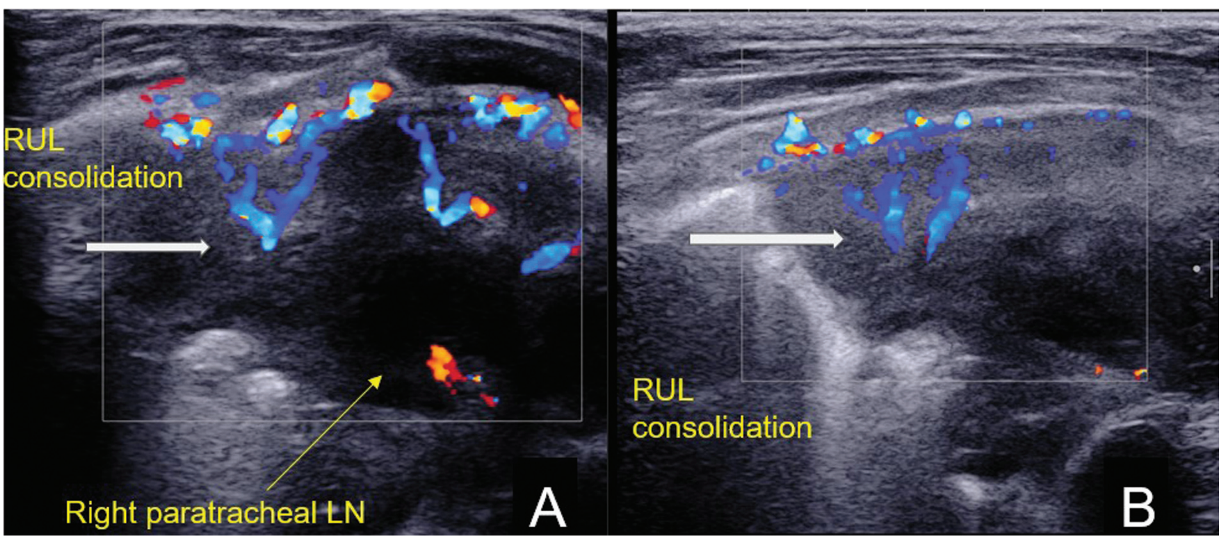

Fig. 3 (**A**, **B**) Mediastinal ultrasonography for lymph node assessment. Right parasternal approach with linear transducer. Color Doppler images (**A**) and (**B**) show vascularity within consolidated lung. Hypoechoic (necrotic) right paratracheal lymph node with hilar vascularity is shown (**A**).

Table 3 Mediastinal ultrasound technique

Surface location	Supraclavicular	Parasternal	Suprasternal	Suprasternal with caudal tilt
Anatomic landmark	Triangle between • IJV • SCV termination • BCV	• Sternum • trachea • Heart and aortic origin	Trachea	• Aortic arch and branches • Carina
Transducer	Linear probe axial - station 1	Linear probe axial - station 3A longitudinal - station 4, 3A (medial)	Linear probe - axial - station 2, 3P Endocavitatory probe axial oblique - station 4	Endocavitatory probe longitudinal - station 3A, 5, 6 (lateral sweeps)

Abbreviations: BCV, brachiocephalic vein; IJV, internal jugular vein; SCV, subclavian vein.

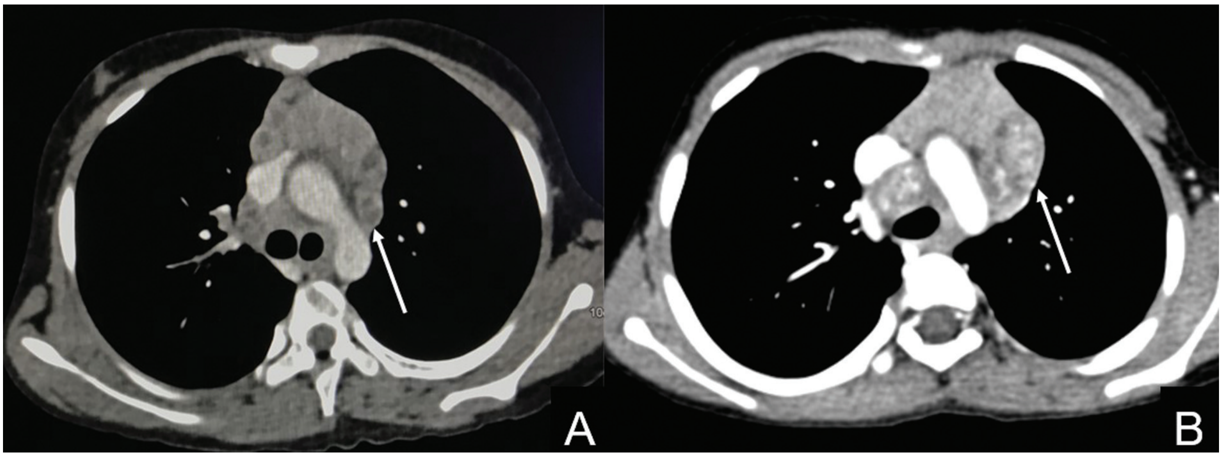

Fig. 4 (A, B) Thoracic tubercular lymphadenopathy on computed tomography (CT). Two different patients, 15-year-old female showing conglomerate nodes with central nonenhancing (necrotic) areas (arrow in **A**). Stippled calcification in mediastinal lymph nodes (arrow in **B**) in another patient, 10-year-old male with microbiologically proven tuberculosis on treatment.

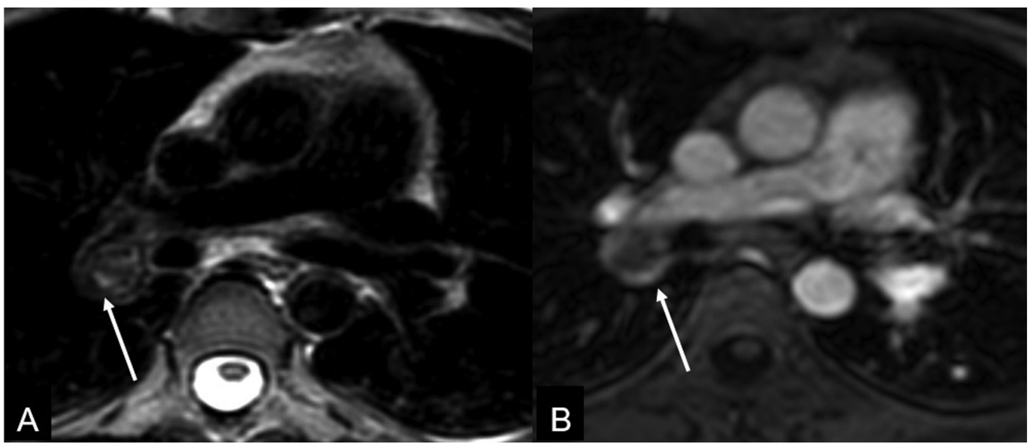

Fig. 5 (A, B) Thoracic lymphadenopathy on magnetic resonance imaging (MRI) in a 25-year-old male. Axial T2-weighted image (T2WI) showing hypointense nature with central focus of hyperintensity (arrow in A). Axial postcontrast T1W image showing rim enhancement (arrow in **B**).

Table 4 Imaging differentials in thoracic tubercular lymphadenopathy (►**Figs. 6** and **7**)

	Size	Findings on ultrasound	Findings on CT
Tuberculosis	Enlarged	• Central hypoechoic/anechoic areas of necrosis • Conglomeration • Loss of fatty hilum • Calcification	• Perinodal fat streakiness • Peripheral rim enhancement • Conglomeration • Calcification
Normal lymph node	Solitary < 15 mm Multiple < 10 mm	Can be oval or round. Homogeneously hypoechoic with presence of fatty hilum	Well-defined margin with clear perinodal fat, preserved hilar fat
Reactive lymphadenopathy	Enlarged	Can be oval or round. Homogenously hypoechoic with presence of fatty hilum	Well-defined margin with clear perinodal fat, preserved hilar fat
Lymphoma	Enlarged	• Homogeneous, no necrosis • Compression/encasement of adjacent structures	• Nonnecrotic • Mass effect/compression on adjacent structures
Metastases	Enlarged	• Can be either homogeneous or necrotic • Solid components may appear similar to primary mass	• Can be either homogeneous or necrotic

Abbreviation: CT, computed tomography.

Differential Diagnoses

There is a myriad of etiologies leading to thoracic lymphadenopathy including the common bacterial, viral, and fungal infections. TB being the most common reason for thoracic lymphadenopathy that commonly undergoes cross-sectional evaluation. Malignant etiologies include metastases from esophageal, breast, and thyroid malignancies. Lymphoma can involve any site in the body including the mediastinum.

Detailed discussion of all differentials is beyond the scope of this article. ►**Table 4** describes the imaging differentials in intrathoracic lymphadenopathy (►**Figs. 6** and **7**).

Sarcoidosis remains the major imaging differential in intrathoracic tubercular lymphadenopathy. The major differentiating points include the distribution, presence/absence of necrosis, and pattern of calcification. The most common nodes affected in thoracic TB are right paratracheal, hilar, and subcarinal; while bilateral hilar and right paratracheal are the most common nodes involved in sarcoidosis. Sarcoid lymphadenopathy is typically symmetrical, unlike TB. Lymph nodes in TB can show conglomeration and peripheral rim enhancement whereas sarcoidosis shows discrete homogeneous nodes. Pattern of calcification in tubercular lymph nodes after treatment is usually homogeneous while it is rim-like/egg-shell or punctate in sarcoidosis.[11] Although less evaluated, "cluster of black pearls" is a finding in thin CECT sections considered specific for sarcoidosis where multiple small (1–2 mm) hypodense sarcoid nodules are seen within the homogenously enhancing lymph nodes.[12] This feature is evaluated in a single study limited to thoracic and abdominal lymphadenopathy. Classical "garland triad" or "1-2-3 pattern" is described in CRs where triad consists of enlarged right paratracheal, right hilar, and left hilar lymph nodes. Further, additional presence of left-sided mediastinal/aorticopulmonary window lymph nodes is considered as "1-2-3-4" pattern.[13]

Abdominal Lymphadenopathy

Abdominal lymphadenopathy in TB can be mesenteric or retroperitoneal.

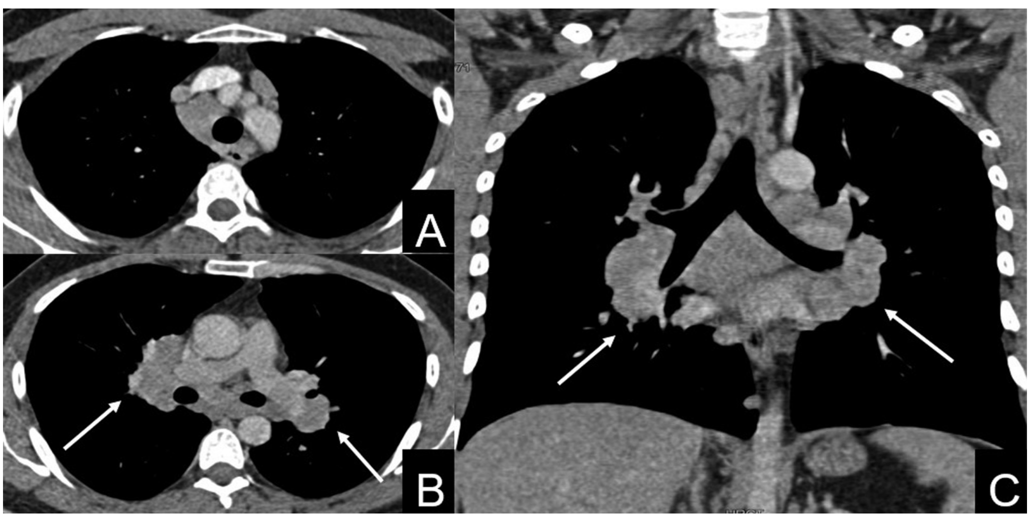

Fig. 6 (**A–C**) Imaging differential: Sarcoidosis. Axial (**A**, **B**) and coronal multiplanar reconstruction (MPR) (**C**) contrast-enhanced computed tomography (CECT) images showing conglomerate homogeneous right paratracheal and symmetrical bilateral hilar nodes.

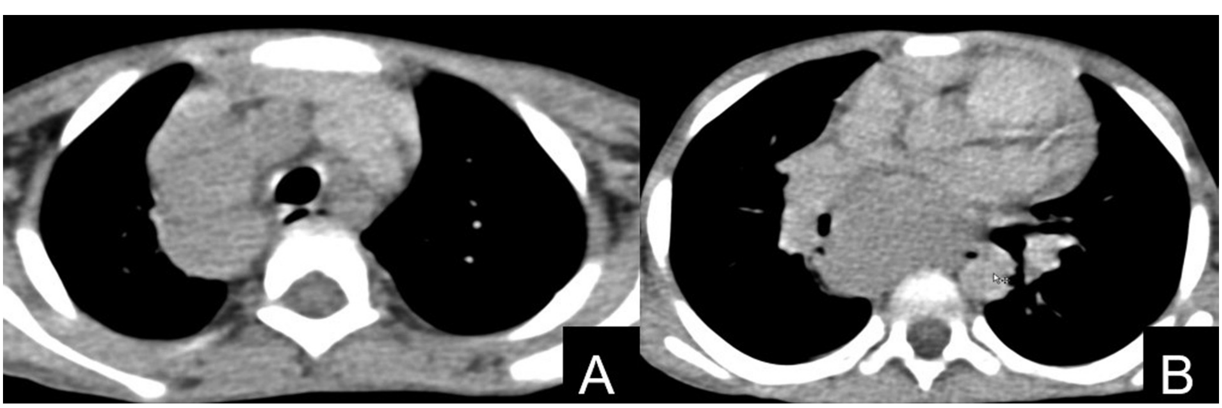

Fig. 7 (**A**, **B**) Imaging differentials: Non-Hodgkin's lymphoma in a 10-year-old male. Axial contrast-enhanced computed tomography (CECT) images showing conglomerate homogeneous lymph nodal mass in the visceral compartment (**A**, **B**).

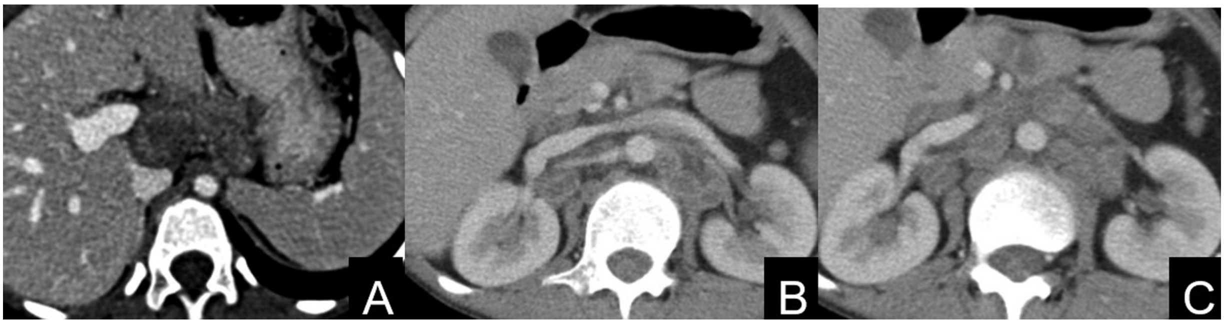

Fig. 8 (A–C) Abdominal lymphadenopathy in an 11-year-old girl with tuberculosis. Axial contrast-enhanced computed tomography (CECT) images showing conglomerate necrotic nodes in periportal, para-aortic, and aortocaval area.

Mesenteric Adenitis

The list of differential diagnosis of mesenteric lymphadenopathy includes a vast range of abdomino-pelvic inflammatory disorders and malignant lymphadenopathy in metastases or lymphoma. While differentiating lymph nodes of lymphoma from TB, it can be done based on the presence of necrosis and calcification in the latter. One of the characteristic signs described in CT imaging of mesenteric lymphoma is "sandwich/hamburger sign" where there are homogenous large lymphonodal masses (resembling buns) interspersed between the mesenteric vessels and mesenteric fat (akin to sandwich filling) with no necrosis/calcification. It is specially described in non-Hodgkin lymphoma; however, in patients with history of transplant, possibility of posttransplant lymphoproliferative disorder needs to be considered.[14] Differentiating TB from various other causes of infective/inflammatory lymphadenopathy may not be possible on imaging alone but useful associated imaging findings such as bowel wall thickening and ileocaecal junction involvement can point toward a tubercular etiology.

Retroperitoneal Lymph Nodes

Similar to mesenteric adenopathy, metastases, lymphoma, and other infective/inflammatory processes remain the main differential diagnosis in retroperitoneal adenopathy. Tubercular lymph nodes classically tend to involve the upper retroperitoneal nodes, whereas lymphoma can involve infrarenal nodes as well (►**Fig. 8**).

CT remains the preferred modality in evaluation of abdominal TB as it allows adequate assessment of ascites, peritoneal, and solid organs as well.[15] MRI is a useful alternative, however, with the drawback of lengthy acquisition times, motion artifacts, and relative difficulty in detection of calcified lymph nodes.[16]

Complications

Long-term caseous necrosis in tubercular lymphadenopathy can result in:

- Sinus or fistula formation in neck (►**Fig. 9**)
- Vascular thrombosis/narrowing: can involve arterial thrombosis, portal vein, or superior vena cava thrombosis
- Pseudoaneurysm
- Fibrosing mediastinitis
- Erosion of bronchi (node-bronchial fistula, airway narrowing, or stenosis)

Response Assessment

Assessing response to treatment is an integral part of any treatment. Ever since the emergence of the drug-resistant strains, it has become even more important. While clinical

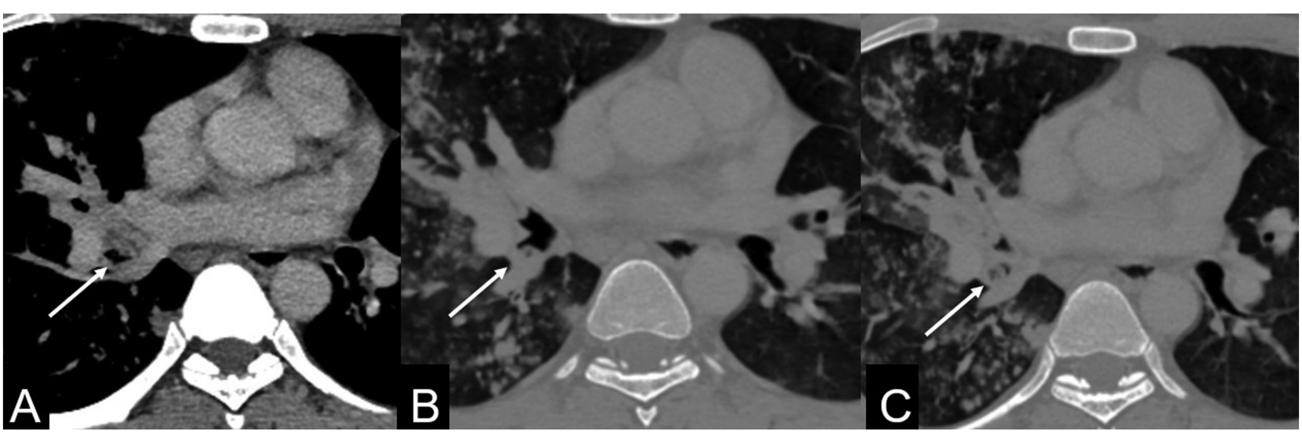

Fig. 9 (A–C) Complications: Node-bronchial fistula in tuberculosis. Axial contrast-enhanced computed tomography (CECT) mediastinal window image (A) showing necrotic right hilar lymph node (LN) (arrow in A). Axial lung window images (B, C) showing extrinsic impression on right lower lobe bronchus (arrow in B) and air density within the lymph node (arrow in C), suggesting fistula.

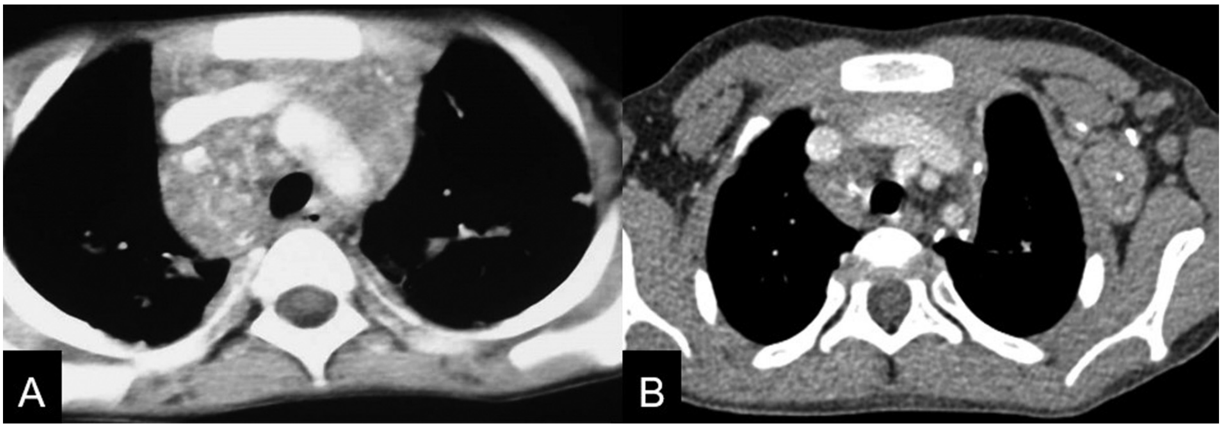

Fig. 10 (**A**, **B**) Follow-up imaging on computed tomography (CT) in tubercular lymphadenopathy in a 7-year-old male. Initial imaging (**A**) showing prevascular and right paratracheal lymphadenopathy. Follow-up imaging (**B**) showed reduction in size and development of coarse calcification.

assessment is helpful, isolated nodal disease may be difficult to assess on clinical examination alone. Therefore, imaging remains crucial in such situations. Assessing the number and size of lymph nodes has been the traditional method of response assessment.

On CR, response assessment is done based on a reduction in size and appearance of calcification.

On US, the nodes may show a reduction in size and area of anechoic necrotic area, and appearance of calcification on treatment. After adequate treatment, on CT, there may be appearance of calcification (diffuse, coarse, eggshell) and lack of perinodal fat streakiness (►**Fig. 10**). The presence and pattern of calcification, however, does not always denote good response to therapy.[17]

On MRI, decrease in T1 and T2 signal intensities and change of enhancement pattern from peripheral/rim to solid or nonenhancement can suggest response to treatment (►**Fig. 11**). Some recent studies have explored the importance of nodal signal characteristics on T1- and T2-weighted images, without the use for CE sequences. It was observed that with treatment, there is a decrease in T1 and T2 signal in the nodes, along with size reduction. Additional imaging with apparent diffusion coefficient values were not contributory in the assessment.[18] Since these patients require repeated imaging, an imaging modality with no radiation burden as in MRI can be an effective alternative to CT in appropriate cases.

18F-FDG-PET can prove useful in equivocal treatment response, or persistent nodal disease.

Take Home Points

- In conclusion, assessment of tubercular lymphadenopathy requires a multimodality approach; depending on the site involved.
- USG is the most commonly used modality in cervical lymphadenopathy with its role in mediastinal lymphadenopathy briefly explained.
- CT is the most used modality in thoracic and abdominal lymphadenopathy and one must be familiar with the posttreatment features.
- MRI can be a suitable alternative to repeat CT scans on follow-up imaging.

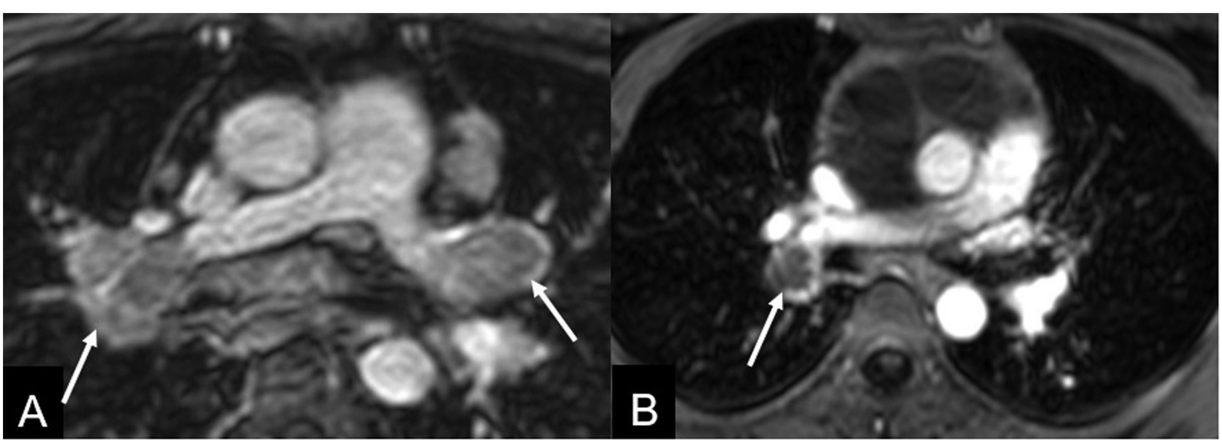

Fig. 11 (**A**, **B**) Follow-up magnetic resonance imaging (MRI) in tubercular lymphadenopathy in a 23-year-old male. (**A**) Initial imaging showed bilateral hilar lymph nodes with homogeneous enhancement (arrows). Follow-up imaging (**B**) showed a reduction in size and rim enhancement (arrow).

Conflict of Interest
None declared.

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