PET-CT in Tuberculosis

11

Key Points

Tuberculosis is one of the most common infections worldwide, which has very high morbidity and mortality. Tuberculosis is caused by *Mycobacterium tuberculosis* and having a complex pathology. It is the aerobic bacillus capable of surviving in anaerobic conditions. It can be diagnosed based on the epidemiology, symptoms, and additional tests and specific and nonspecific signs and symptoms. However, in the Indian subcontinent, it is still the commonest form of infection. It is caused by *Mycobacterium tuberculosis* (MTB) which is an aerobic bacillus that survives in anaerobic conditions for a very long time. PET-CT has become an important imaging modality for diagnosis staging and assessing therapy response.

11.1 Introduction

Molecular imaging is based on PET-CT, which can provide a three-dimensional view of the disease in the entire body at a time. The role of PET-CT is now commonly used to differentiate between tuberculosis and malignant concurrent conditions at same time.

Tuberculosis remains the biggest threat to humans, especially due to various causes, multidrug resistance, and immune-compromised status are one of the commonest. TB has one of the highest mortalities [1–3]. The commonest reason for the increased morbidity and mortality is multidrug-resistant TB (MDRTB) and immune-compromised status [4].

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11.2 Pathophysiology

Mycobacterium tuberculi is an aerobic intracellular microorganism with thick cell walls having long chain of fatty acids called mycolic acids. This MTB has the peculiarity to persist in the host cells dormant for a long time [5]. The commonest mode of spread of this is through droplets as aerosol generated through the respiratory system. The risk of development of pulmonary tuberculosis is based on endogenous and exogenous factors. Exogenous factors will have a role from exposure to infection while endogenous factors have a role from infection to active disease. Again, it depends on the PTB and extra PTB were a lot of factors are influencing. The activation of the immune system cells boosts the cell glycolysis even in the scenario of the immune suppression. With this, there will be increased glycolysis resulting in the increased FDG uptake. MTB can be defined clinically by tuberculin skin test, which is still not sensitive. The characteristic feature of MTB is slow growth and dormant, latent persistent state. MTB is transmitted by aerosol generated by the respiratory tract and is primary source of infection, which is labeled as primary tuberculosis. The commonest location for primary tuberculosis is the lung, which has varied features imaging wise and shows different phases depending on the treatment.

11.3 Clinical Symptoms

The classical clinical features are chronic cough, weight loss, fever, night sweats, and hemoptysis. The predisposing factors are mal-rotation, tobacco smoking, and pollution. The extrapulmonary TB occurs in 10% to 42% and depends on the age presence or absence of underlying disease, human status of an individual, and strain of MTB. Diagnosis of tuberculosis is done by Mantoux tuberculin skin test. Imaging in a tuberculosis chest radiograph is the most commonly used diagnostic imaging modality for pulmonary tuberculosis. Varied presentations are seen depending on the various factors. This can be patchy opacities, cavitation's, fibrosis, nodal involvement, and with or without caseation necrosis. Conventional radiograph is also used in other extrapulmonary tuberculosis, which is not highly sensitive [6]. For these other modalities like ultrasound, CT, and MRI are used depending on the organ or systemic involvement.

11.4 PET-CT

PET-CT is a combination of molecular and anatomical information with this it has an ability to evaluate the various aspects of the disease [7, 8]. FDG PET-CT is to evaluate the anatomical, microbiological, immunologic, and pharmacological components related to tuberculosis. FDG PET-CT is nonspecific for the

evaluation as many malignant pathologies and inflammatory conditions which has an overlap of many conditions, they also demonstrate similar uptake patterns. Tuberculosis is classified into two major groups: Pulmonary tuberculosis and Non-Pulmonary tuberculosis. The role of PET-CT now is well established and documented to detect the tuberculosis disease activity [9–13] and extent of disease. The capacity of FDG PET to distinguish between benign and malignant lesions is being evolved with encouraging results. FDG PET shows diffuse increased uptake in both pulmonary and extrapulmonary lesions and helps to assess the extent of the active disease. PET has an advantage though not sensitive to distinguish between malignancy and other granulomatous conditions. Thus, there is a significant overlap between the SUV values in malignant, benign, and other granulomatous lesions, but recent studies that show the dual time point imaging which is a delayed PET imaging to distinguish between benign and malignant lesions. The concept theory is after doing dual point imaging, the SUV values will be falling in cases of infective inflammatory, tuberculosis, and granulomatous pathologies. However, malignant tissues will have a capacity to retain the radiotracer, which is the characteristic feature of the malignant pathology [14]. Now tuberculosis involving the cerebral parenchyma known as tuberculomas or sometimes difficult to differentiate between malignant gliomas, fungal infections, and other granulomas. FDG uptake can be quantified to evaluate the intracerebral lesions and meningeal and Dural involvement in phases like tuberculous meningitis or tubercular meningoencephalitis [15]. Diffuse uptake will be noted in the lesion along the meninges or the dura. Same applies to the spinal cord that can be involving the spinal cord parenchyma and the arachnoid space.

Other radiotracers like 11C Choline, 68 Ga-Citrate, and 18 F FLT are in pipeline and will be used in coming years.

Another set of newer radiotracers that are in the preclinical stage are 11C Rifampicin, 11C Pyrazinamide, 11C Isoniazid, and 18F NaF and these radiotracers will be more specific and precise for the evaluation of MDRT or extrapulmonary tuberculosis. Hypoxia PET imaging will also be a promising radiotracer in the future.

11.5 Head and Neck Tuberculosis

Intracranial tuberculosis is one of the common pathologies, which shows features similar to neoplastic lesions. Ring enhancing lesion with perilesional edema is one of the common features. These lesions show increased metabolic activity (Figs. 11.1 and 11.2).

The commonest tubercular involvement in the neck is in form of lymph nodes. The presentation of nodal involvement depends on the stage of the disease activity within the node [16]. Again the SUV value varies according to the stage and phase of tuberculosis. In suspected cases, dual point imaging can be used to distinguish between tuberculosis vs. malignant pathologies (Fig. 11.3).

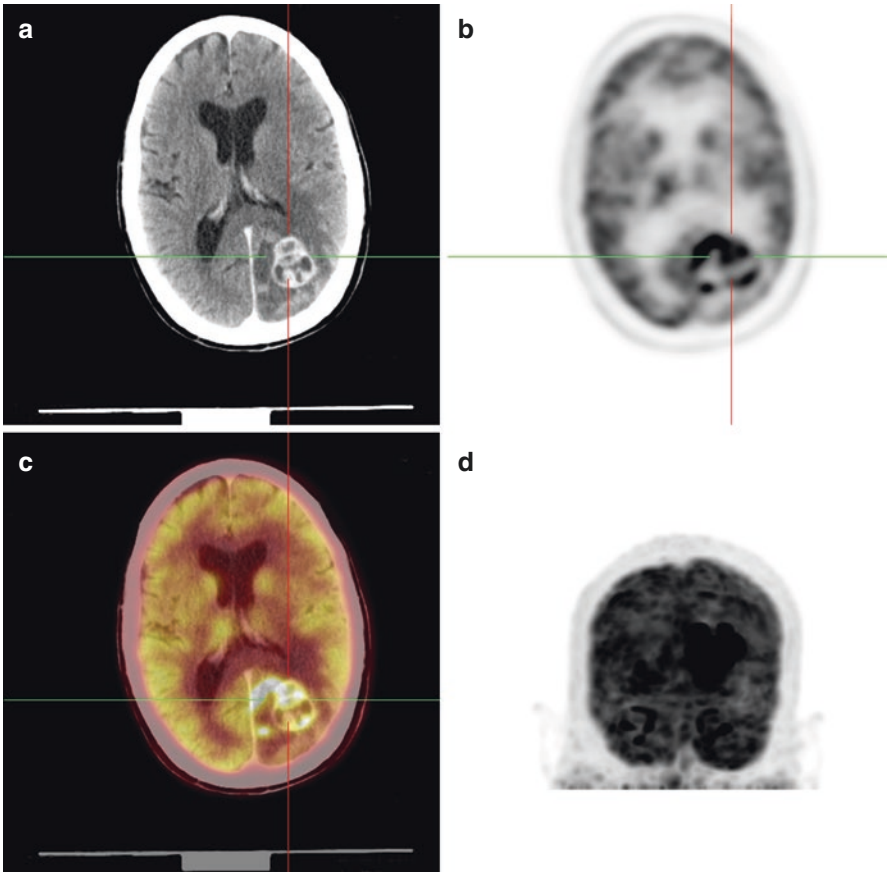

Fig. 11.1 Brain PET-CT, CT image (**a**) showing lobulated ring-enhancing lesion with irregular soft tissue component in the left parieto-occipital region increased metabolic activity in PET images (**b**, **d**) and fused image (**c**) with SUV max of 5.8 suggestive of tuberculoma

11.6 Chest

The commonest tuberculosis presentation is pulmonary tuberculosis. Varied presentations in the form of patchy infiltrates, nodules, consolidations, collapse, focal pleural thickening, cavitation's, ectatic changes, ground glass opacities, honeycombing, pleural effusion, mediastinal nodes, and combination of the above-mentioned entities. The presentation of especially mediastinal nodes depends on the phase of the disease, active disease, caseation necrosis, or calcifications. Tuberculosis involving the chest wall muscles is also equally common in the Indian subcontinent. Tuberculosis involving the pericardium is quite common and presents clinically in the form of pericarditis and severe cases of pericardial tamponade [17]. It can be focal pleural involvement or diffuse pleural involvement with or without pericardial

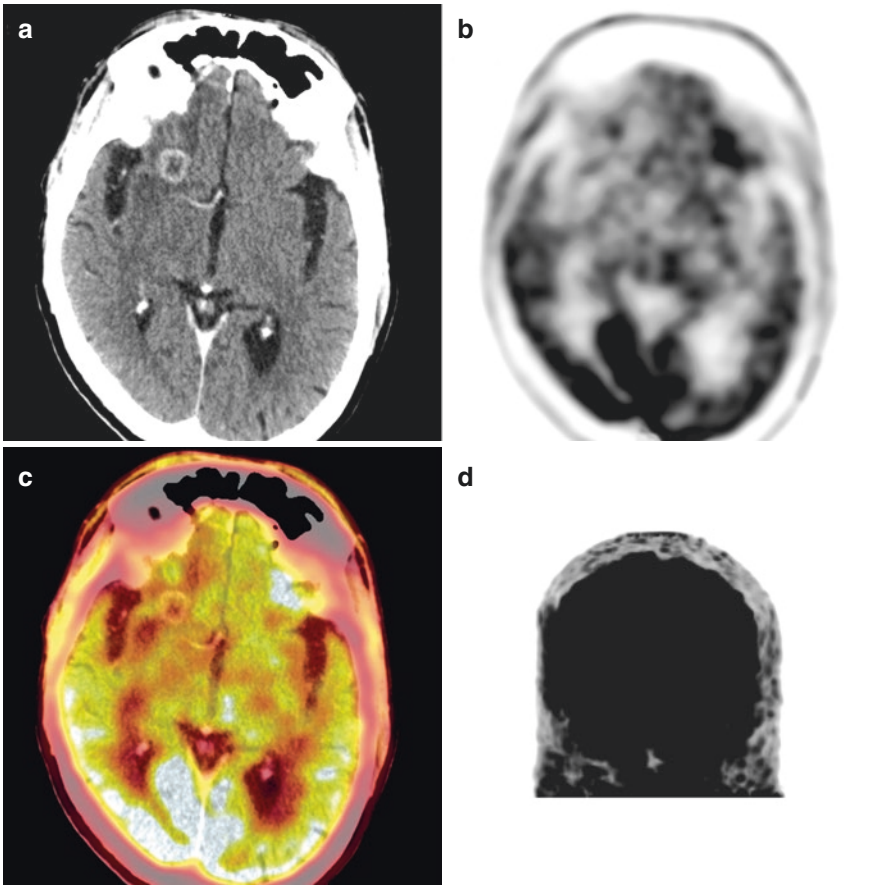

Fig. 11.2 Small ring-enhancing lesion on CT image (**a**) with mild peripheral uptake on PET and fused images (**b**, **d**, **c**) with SUV max of 2.5. This was later diagnosed as tuberculoma

effusion. In chronic cases, there will be calcification of the pericardium representing as constrictive pericarditis. The role of PET-CT is to evaluate the active disease and to differentiate between other neoplastic differentials [18, 19] (Figs. 11.4, 11.5, 11.6, and 11.7).

11.7 Abdomen

Tuberculosis involving the abdomen is mostly confined to GI tract and GUT. GIT stomach is very rarely involved [20]. Small intestine is not common except ileocecal junction, which is very commonest cause of GI tuberculosis. Colon is not commonly involved by tuberculosis. The ileocecal Koch's is the commonest form of tuberculosis with close differential with Crohn's disease, ulcerative colitis, and

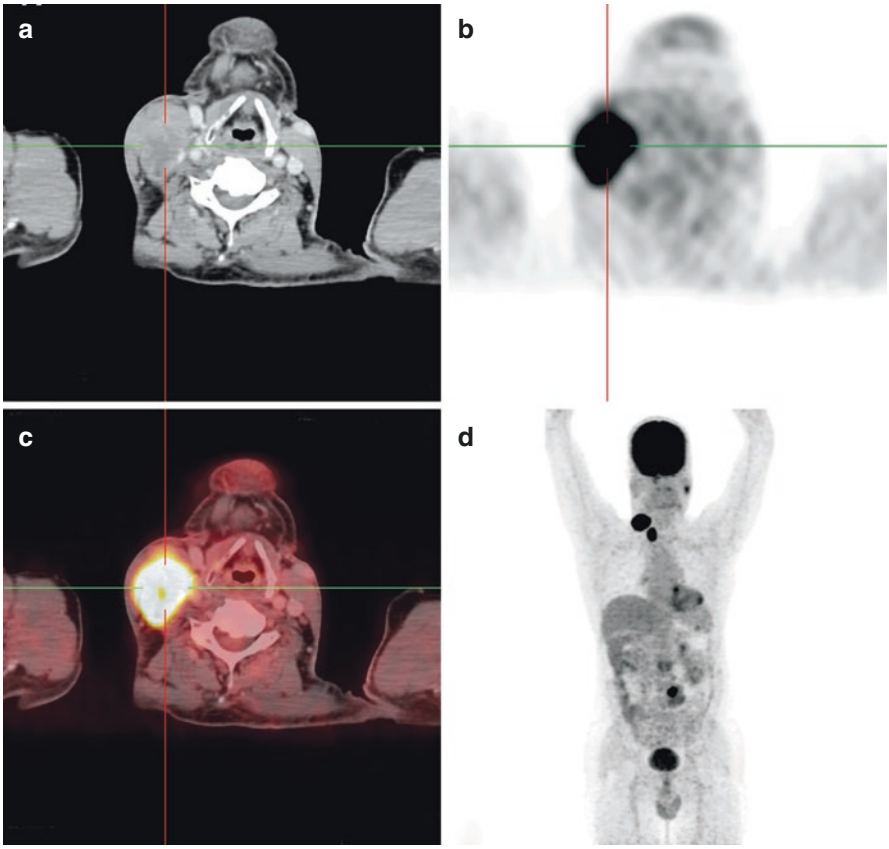

Fig. 11.3 Enlarged patchily enhancing lymph nodes in CT image (**a**) in right level-III and IV with significantly increased uptake on PET images (**b**, **d**) and fused image (**c**) with SUV max of 9 suggestive of necrotic caseating tuberculous nodes

ileocecal malignancies [21]. PET-CT has an important role in quantification of the SUV values. Again, dual point imaging is based on important role in differentiating between Koch's and malignant pathologies.

11.8 Genito Urinary Tract

Renal tuberculosis is also an important and common cause with varied presentations. The presentations involving the focal or diffuse renal involvement that can be acute or chronic depending on the stage and time of the disease [22, 23]. Renal pelvicalyceal system is also involved with varied presentations. Tuberculosis involvement of ureter is not common, but literature and PET-CT shows diffuse increased uptake involving the ureter, which can be focal, diffuse stricture, or hydronephrosis [24]. One of the commonest forms of tuberculosis is involving the

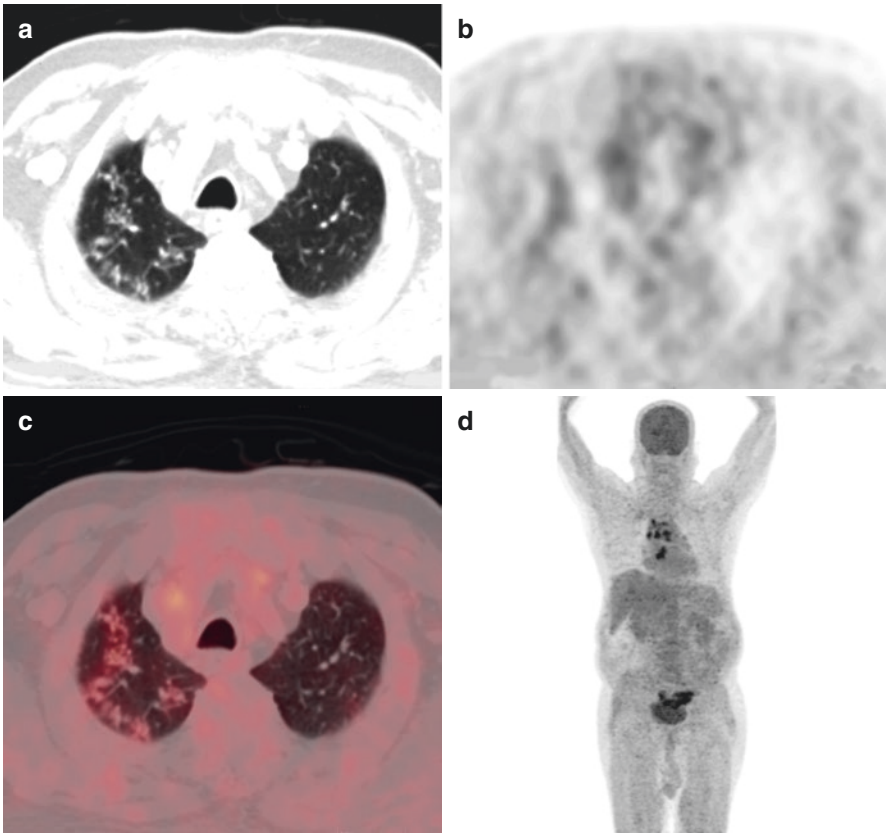

Fig. 11.4 Whole-body PET-CT, CT image (**a**) showing patchy parenchymal infiltrates with mild metabolic activity in the right upper lobe in PET (**b**, **d**) and fused images (**c**), respectively, with SUV max of 3.4. Small metabolically active mediastinal nodes. Findings are suggestive of pulmonary tuberculosis

urinary bladder. It can be focal or diffuse with perivesical involvement. Tuberculosis involving prostate which can be focal or diffuse. Small nodule, abscess, or may present as prostatitis. PET has an important role to differentiate between nodular lesions that can be tubercular or malignant [25, 26]. FDG PET-CT has extremely low sensitivity for prostatic malignancies [27]. The newer radiotracer Prostate-Specific Membrane Antigen (PSMA) is being widely used for prostatic malignancies and has remarkably high sensitivity compared to FDG PET [28]. This is very sensitive for infective inflammatory and tubercular lesions, which can be quantified by SUV max values. Tuberculosis of the urethra is an important entity in the Indian subcontinent. The commonest presentation is in the form of stricture and urethritis. PET-CT plays an important role in the quantification of tuberculosis pathology (Fig. 11.8).

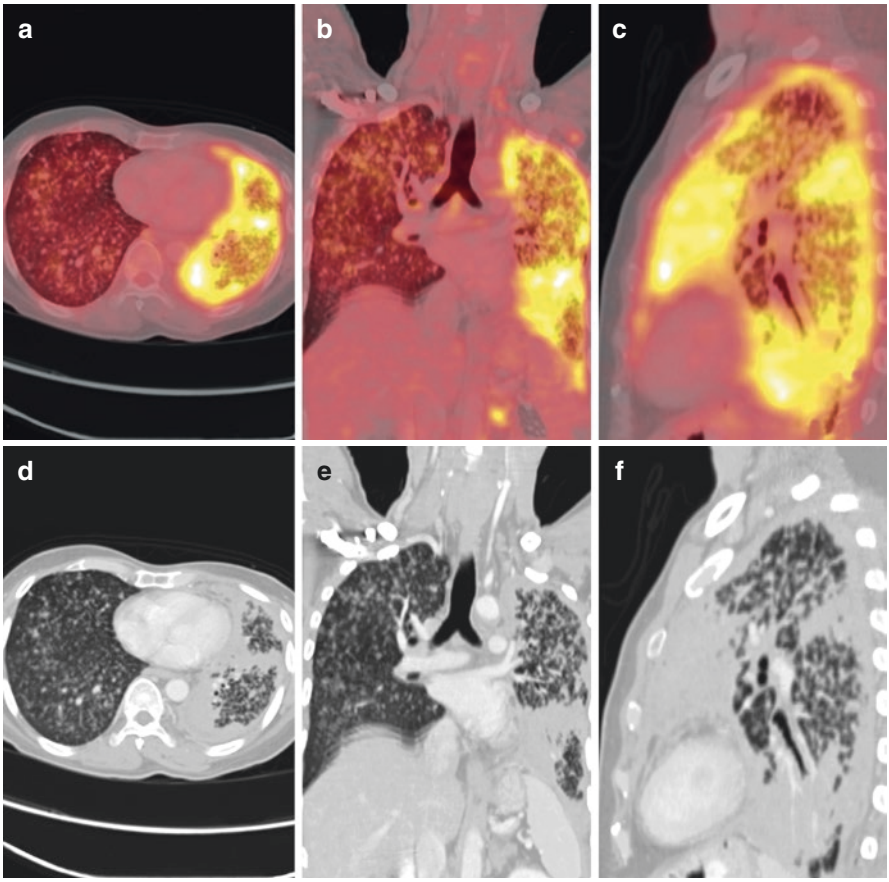

Fig. 11.5 Whole-body PET-CT showing a significant loss of left lung volume with diffuse nodular pleural thickening on left side with significant metabolic activity in PET-CT fused images (**a**–**c**) with SUV max of 7.8. Diffuse miliary mottling noted in both lungs also seen in both lungs in CT images (**d**–**f**)

11.9 Female Pelvis

Female genitourinary tuberculosis is the commonest cause involving non-oncological pathologies that can be in the form of salpingo-oophoritis, which is the commonest cause of tuberculosis. PET-CT shows diffuse increased uptake in the organs of involvement and in the post ATT evaluation. Uterine tuberculosis is not that much common but endometrial involvement is the commonest form. PET-CT plays an important role in differentiating endometrial malignancy, endometritis, endometriosis, and endometrial tuberculosis [24, 29].

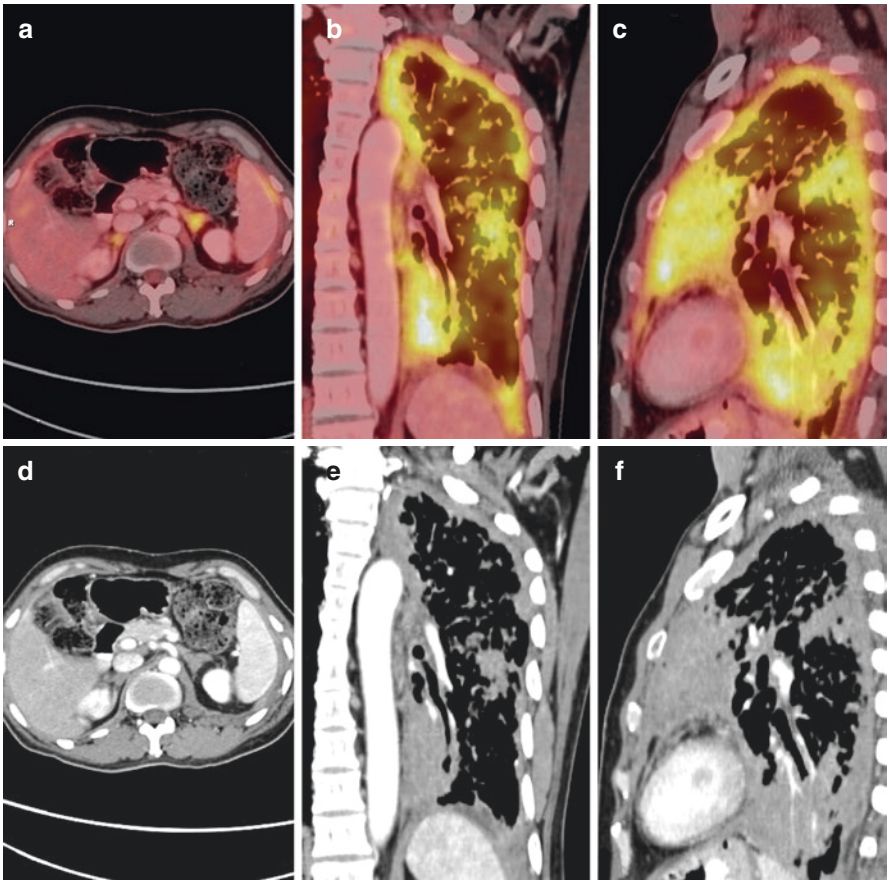

Fig. 11.6 Whole-body PET-CT showing a significant loss of left lung volume with diffuse nodular pleural thickening on left side with significant metabolic activity in PET-CT fused images (**a**–**c**) with SUV max of 7.8. Diffuse miliary mottling noted in both lungs also seen in both lungs in CT images (**d**–**f**)

11.10 Peritoneum

Peritoneal tuberculosis is one of the important commonest causes of abdominal tuberculosis. It can be focal or diffuse nodular or mass lesions with or without ascites. The PET-CT plays an important role in differentiating between pseudomyxoma peritonei (which is a primary peritoneal tumor) vs. peritoneal tuberculosis [30] (Fig. 11.9).

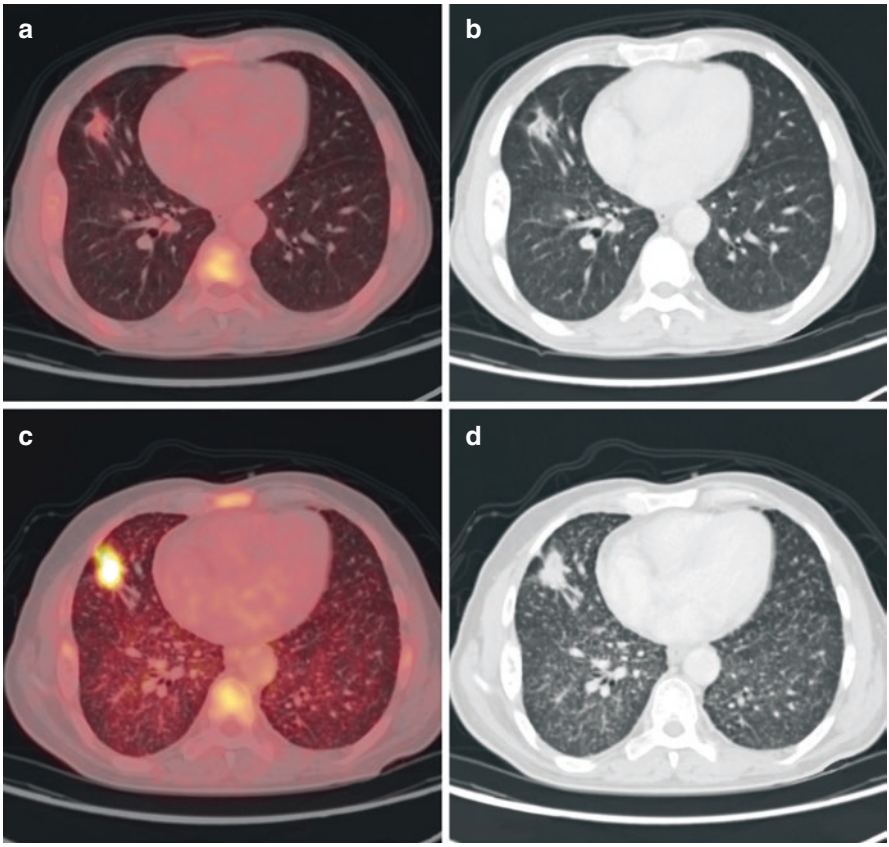

Fig. 11.7 PET-CT at the level of chest showing small nodular lesion with significant FDG uptake in right upper lobe with SUV max of 5.8 in PET-CT fused images (**a**, **c**). Associated miliary mottling in both lower lobes seen in the CT images (**b**, **d**). Findings are suggestive of pulmonary Koch's

11.11 Musculoskeletal

Musculoskeletal tuberculosis is one of the important extrapulmonary forms of tuberculosis. It can involve the axial or appendicular skeleton.

11.11.1 Axial Skeleton

Axial skeleton which can be seen in the form of tubercular discitis, psoas abscess, vertebral body involvement, prevertebral, paravertebral, and epidural soft tissue component with abscess formations depending on the stage of the disease. Vertebral

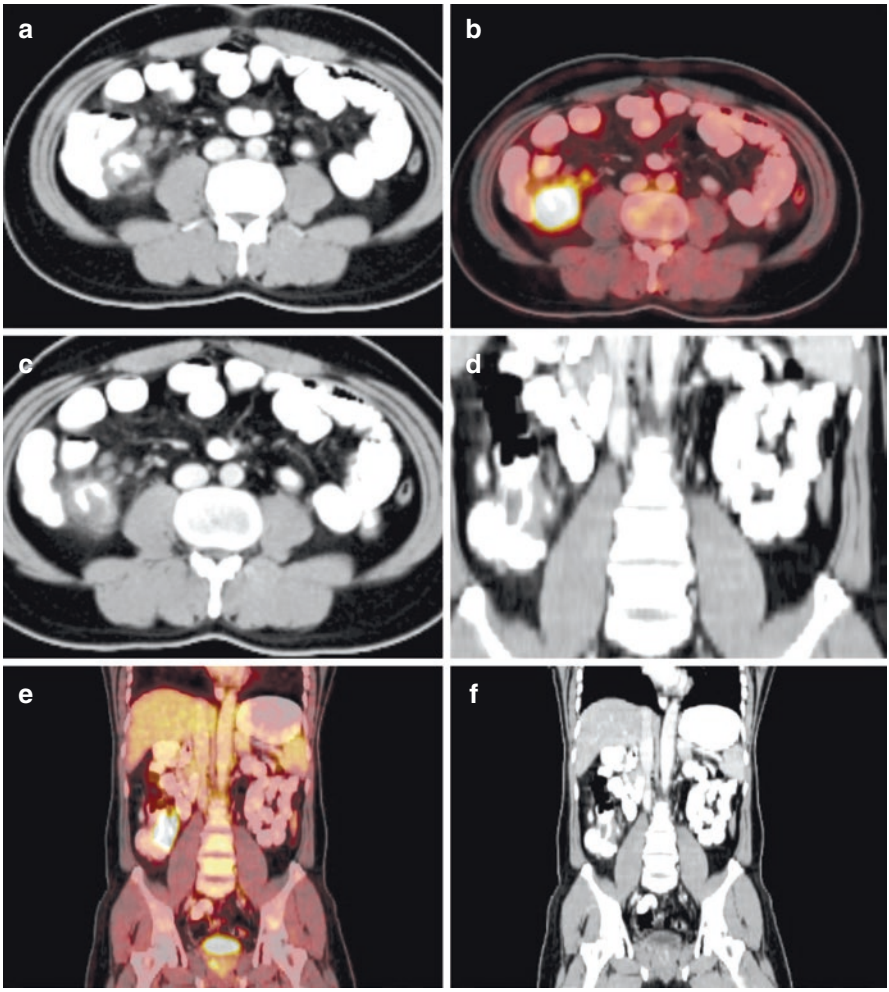

Fig. 11.8 Whole-body PET-CT with abdominal images showing mild irregular wall thickening involving the ileocecal junction and adjacent small nodes in CT images (**a**, **c**, **d**, and **f**). This wall thickening shows increased uptake with SUV max of 6.9 in fused images (**b**, **e**) suggestive of ileocecal tuberculosis

involvement may lead to destruction of the vertebral bodies, collapse compression fractures and spinal cord involvement, and cervical and dorsal regions. There can be associated involvement of the spinal canal and spinal cord. FDG PET-CT is an excellent modality to evaluate the tuberculosis involving axial skeleton. One of the commonest forms is lumbar vertebral tuberculosis with psoas abscess [31] (Fig. 11.10).

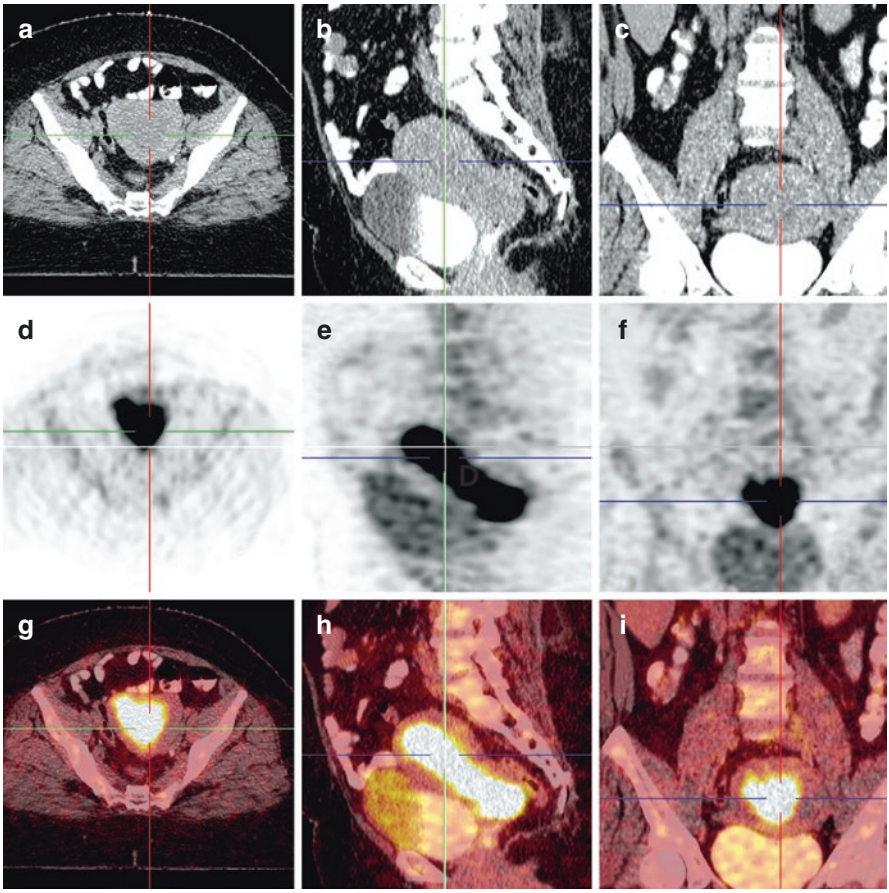

Fig. 11.9 Limited abdomen PET-CT of the pelvis showing bulky uterus with subtle ill-defined hypodense soft tissue in the endometrial cavity on CT images (**a**–**c**). PET (**d**–**f**) and fused images (**g**–**i**) show diffuse extensive metabolic activity corresponding to the hypodense lesion in the endometrium with SUV max of 11.8. Histopathologically suggestive of endometrial tuberculosis

11.11.2 Appendicular Skeleton

11.11.2.1 Hip Joint

The commonest form of tuberculosis are joint involvement, synovial thickening, joint effusion, bony erosions, bony destructions, and associated features like soft tissue and neural involvement. PET-CT has an important role in quantifying the amount of uptake by SUV values [32].

11.11.2.2 Knee Joint, Shoulder Joint, Ankle Joint, and Elbow Joint

The commonest form of tuberculosis joint involvement, synovial thickening, joint effusion, bony erosions, bony destructions, and associated features like deformities.

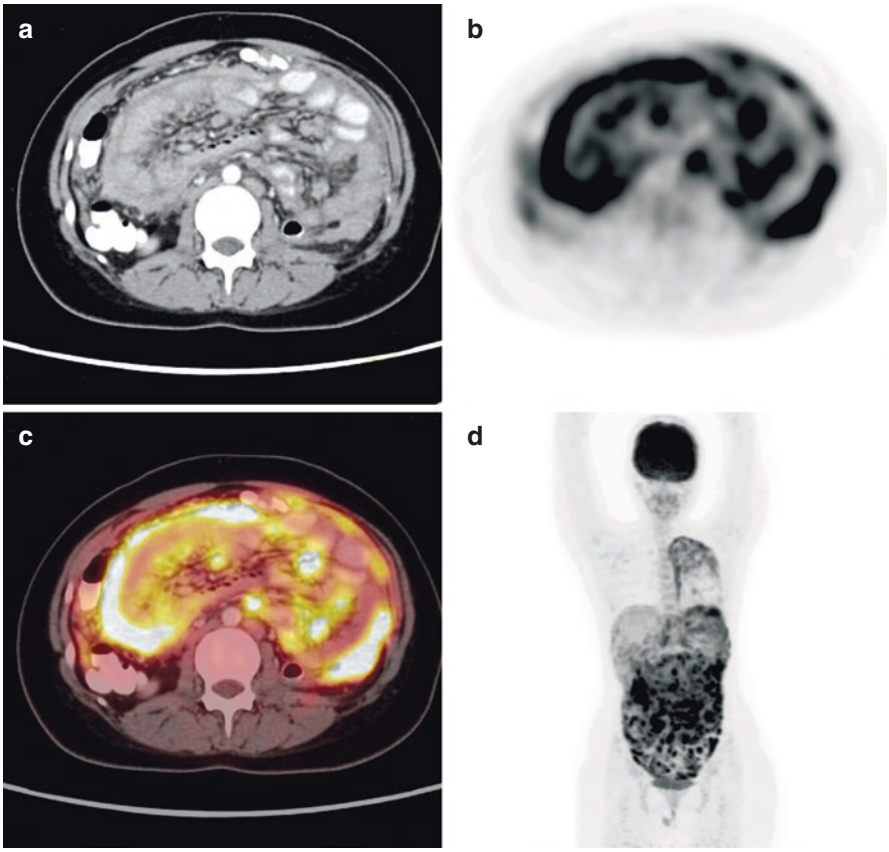

Fig. 11.10 Whole-body PET-CT at the level of abdomen CT image (**a**) showing diffuse irregular peritoneal thickening with cocoon formation with metabolic uptake in PET images (**b**, **d**) and fused image (**c**) showing SUV max of 7.7. Findings are suggestive of peritoneal tuberculosis

A small joint tuberculosis are rarely involved. PET-CT has an important role to differentiating between the associated pathologies involving the joints [33–37].

11.11.3 Muscles

The commonest presentation of tuberculosis involving the muscle is the psoas abscess. Other features presenting the muscles are focal bulkiness and small collections or abscess involving the muscles. The PET has an important role in quantifying the SUV values [38]. However, clinical correlation is important to differentiate between infective inflammatory and tubercular pathologies (Fig. 11.11).

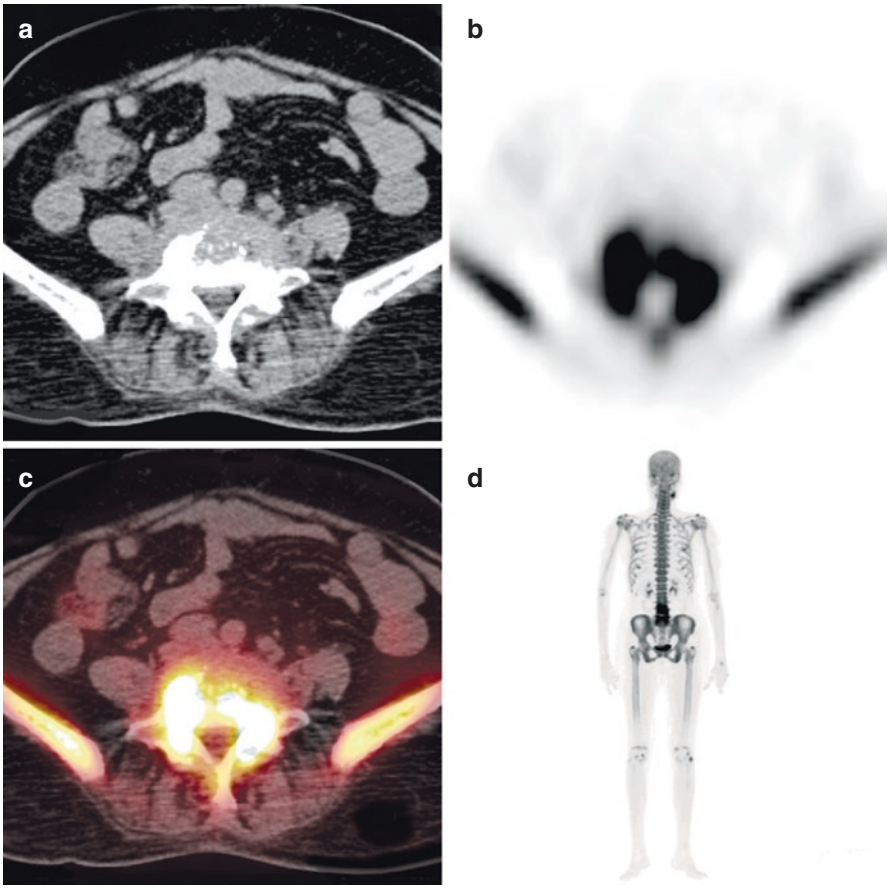

Fig. 11.11 Whole-body F-18 bone scan showing CT image (**a**) patchily enhancing small soft tissue component in the prevertebral and bilateral paravertebral locations with significant uptake in fused (**c**) and PET images (**b**, **d**) at L4–L5 level suggestive of Pott's spine

11.12 Conclusion

PET-CT is a sensitive biomarker for detection, staging, accessing the disease activity, and monitoring response to therapy since tuberculosis has long treatment regimes. PET-CT offers the early option for the posttreatment evaluation, especially in relation to the short regimes as the drugs can be modified if needed thus reducing the morbidity and mortality. With the advent of MDRT and newer radiotracers, the role of PET-CT is more consolidated in the future.

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