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Image-guided biopsy-proven lung and skeletal tuberculosis cases mimicking malignancy

Görüntüleme eşliğinde biyopsi ile kanıtlanmış olan, maligniteyi taklit eden akciğer ve iskelet tüberkülozu vakaları

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Abstract

Aim: Tuberculosis diagnosis may be challenging and percutaneous biopsy may be required for definitive diagnosis. In this study, we aimed to investigate the utility of percutaneous biopsy in diagnosis of tuberculosis and radiological features of the tuberculosis cases diagnosed by image-guided biopsy.

Methods: The patients who were diagnosed with tuberculosis by image-guided biopsy between 2016 and 2020 in our institution were reviewed retrospectively in these case series. Histories of malignancy or immune deficiency, age and genders of the patients, localizations and radiological imaging findings of the lesions, needle types, imaging methods used for the biopsies and presumptive diagnoses before the biopsies were noted.

Results: A total of 16 patients (5 Females, 11 Males) with a mean age of 41 years (range: 17-74 years) had image-guided biopsy with presumptive diagnosis of infection or malignancy. Four patients had transthoracic core-needle-biopsy for lung masses, 12 had curettage-bone-biopsy for lytic lesions of vertebral and pelvic bones under CT-guidance. Four of the patients had immune deficiency and one had a history of malignancy. All patients were diagnosed with tuberculosis by both histopathological and culture analysis.

Conclusion: Image-guided-biopsy is safe and useful in the diagnosis of tuberculosis cases who could not be diagnosed by laboratory and sputum tests or those with presumptive diagnoses of malignancy. Tuberculosis should be kept in mind during percutaneous biopsy of radiologically suspicious cases as a differential diagnosis, even though they are clinically negative.

Keywords: Tuberculosis, Polymerase chain reaction, Biopsy, Diagnosis

Öz

Amaç: Tüberküloz tanısı bazı hastalarda zor olabilir ve kesin tanı için perkütan biyopsi gerekebilir. Bu çalışmada, görüntüleme eşliğinde biyopsi ile tanı alan tüberküloz olgularının radyolojik özelliklerini ve tüberküloz tanısında perkütan biyopsinin tanı koymadaki faydasını paylaşmayı amaçladık.

Yöntemler: Kurumumuzda 2016-2020 yılları arasında görüntüleme eşliğinde biyopsi ile tüberküloz tanısı alan hastalar, bu vaka serisi çalışmasında retrospektif olarak incelendi. Hastaların yaş ve cinsiyet bilgileri, biyopsi öncesi malignite veya immün yetersizlik öykülerinin olup olmadığı, lezyonların lokalizasyonları ve radyolojik görüntüleme bulguları, biyopsi için kullanılan iğne tipleri ve görüntüleme yöntemleri ile biyopsi öncesi ön tanıları not edildi.

Bulgular: Toplam 16 hastaya (5 Kadın, 11 Erkek; ortalama yaş 41; yaş aralığı 17-74), enfeksiyon veya malignite varsayımıyla birlikte görüntü rehberliğinde biyopsi yapıldı. Dört hastaya BT kılavuzluğunda akciğer kitleleri için transtorasik kalın iğne biyopsisi, 12 hastaya vertebral ve pelvik kemiklerdeki litik lezyonlar için kemik-küretaj biyopsisi uygulandı. Hastaların dördünde immün yetmezlik ve birinde malignite hikayesi vardı. Tüm hastalara hem histopatolojik hem de kültür analizi ile tüberküloz tanısı kondu.

Sonuç: Görüntüleme rehberliğinde biyopsi, laboratuvar ve balgam testleri ile teşhis edilemeyen veya malignite ön tanısı olan tüberküloz vakalarının tanısında güvenli ve yararlıdır. Radyolojik olarak şüpheli vakaların perkütan biyopsi işlemi sırasında, klinik olarak negatif de olsa, ayırıcı tanı olarak tüberküloz akılda tutulmalıdır.

Anahtar kelimeler: Tüberküloz, Polimeraz zincirleme reaksiyonu, Biyopsi, Teşhis

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Introduction

Tuberculosis (TB) is an important public health issue all over the world [1]. It has a higher incidence among people with immunodeficiency. A well-known and frequent form of the infection is lung TB. In some cases, TB bacillus can also affect many other systems and organs such as the lymphatics, central nervous system, urogenital tract, and the musculoskeletal system [1,2].

Diagnosis involves positive blood and sputum tests for active tuberculosis, that are supported by clinical history. Sometimes, the diagnosis of tuberculosis may be challenging, and it may mimic malignancy [3]. Due to the steadily decreased incidence in many countries, differential diagnosis of TB may be overlooked. That can cause overuse of diagnostic tests, delay in diagnosis and even death [4]. Thus, being familiar with common radiological features of TB is important for differential diagnosis and treatment.

Tuberculosis infection (TBI) in the bones and lungs may mimic primary or secondary involvement of malignancy [5-10]. The bone (especially spinal bones) and the lungs are the most frequent sites of metastasis in patients with a primary cancer. Both typical TBI and cancer may show similar radiological findings in the lungs and bones: Solitary or multiple nodular lesions in the lung parenchyma with or without cavitation, consolidations with irregular margins and thick-walled cavities may be present in both. In some cases, differentiating one from another by imaging is challenging. In spinal vertebral bodies, paraspinal soft tissue and intervertebral disc involvement may accompany destructive-lytic lesions with or without compression fractures [11,12]. Continuous vertebral body involvement with skip lesions may be present in both TBI and malignancy due to hematogenous spreads. Thus, especially when the patient has ambiguous laboratory findings and clinical symptoms, Computed Tomography (CT)-guided percutaneous biopsy is a valuable diagnostic tool to confirm the diagnosis by pathological and microbiological tests [13,14].

Diagnostic yield of image-guided biopsy for tuberculosis has been investigated in a few studies [13,14]. However, these studies investigated lung or bone tuberculosis cases separately. We have not encountered any studies evaluating lung and bone cases together. To the best of our knowledge, this is one of the very few studies investigating both in one study. We aimed to share the utility of percutaneous biopsy in the diagnosis of lung and bone tuberculosis and review the radiological features of the tuberculosis cases diagnosed by image-guided biopsy in our institution.

Materials and methods

This retrospective study was approved by our institution's ethical committee (Sisli Hamidiye Etfal Education and Research Hospital; Number: 2506; Date: 9/3/2019). The patients who had a diagnosis of tuberculosis by image-guided biopsies between 2016 and 2020 in our institution were reviewed retrospectively. Regardless of underlying immunodeficiency or a history of cancer, male and female patients of all age groups were included in the study. Informed patient consent was obtained from all patients before image-guided biopsy interventions. Coagulation profile, antiplatelet-anticoagulant medication usage and capability for the procedure of the patients were evaluated before the biopsies. Preprocedural radiological examinations were reviewed before planning the biopsies. A semi-automatic core needle (18 Gauge, 15 cm) was used for trans-thoracic lung mass biopsies, a bone biopsy needle (11 Gauge, 10 cm) was used for curettage bone biopsies and a 20 Gauge Chiba was used for Fine Needle Aspiration Biopsies (FNAB). Same sized needles were used for every patient to prevent a potential source of bias. The biopsies were performed under CT (Toshiba, Alexion, Japan and Siemens, Somatom Emotion, Germany) guidance in the CT room or under ultrasound (US) (Mindray, China) guidance in outpatient clinic room in our institution. All the biopsies were performed under local analgesia and aseptic conditions. The biopsy samples were obtained from the most suspicious and solid parts of the masses. The samples were fixed in formalin for core needle and curettage biopsies. Those obtained by FNAB were prepared as cell blocks fixed in 96% alcohol. As a routine procedure in our clinic, in case of any suspicion of infection, samples were obtained for culture analyses. All patients had histopathological and microbiological analysis (including polymerase chain reaction (PCR) for tuberculosis) for either malignancy or infection. After the biopsy, patients were observed in the hospital for about 2 hours for complications. Radiological images, histopathological results and laboratory tests were reviewed from picture archiving communication system (PACS) and hospital information system (HIS) retrospectively. Localizations, sizes and multiplicity of all the lesions were evaluated. For lung masses, presence of cavitation, involvement of surrounding lung parenchyma, presence of lymphadenopathy in the mediastinum and pleural effusion was noted. For bone lesions, involvement of adjacent joint, intervertebral disc or surrounding soft tissue was noted. History of malignancy or immune deficiency, age and gender of the patients, localizations and radiological imaging findings of the lesions, needle types, imaging methods used for the biopsies and presumptive diagnosis before the biopsies were recorded. The demographical characteristics of the patients, localizations of the lesions and histories of malignancy or immune deficiency is presented in Table 1.

Statistical analysis

For statistical analysis, Statistical Package for the Social Sciences (SPSS) for Windows (Version 21.0, Chicago, SPSS Inc.) program was used. Descriptive statistics were presented as number and percentage for categorical variables and as mean, standard deviation, minimum, maximum, and median for numerical variables. Ratios in independent groups were tested by Chi-Square Analysis.

Results

A total of 16 patients (5 Females, 11 Males) with a mean age of 41 years (range: 17-74 years) had image guided biopsies with presumptive diagnoses of infection or malignancy. Four patients had transthoracic core needle biopsy for lung masses, and 12 had curettage-bone-biopsy for lytic lesions of vertebral and pelvic bones under CT-guidance. Four of the patients had immune deficiency and one had a history of malignancy (Table 1). All patients were diagnosed with

tuberculosis by both histopathological and culture analysis with positive PCR tests**.**

Among 4 lung lesions, 75% presented as solitary cavitary nodular lesions while 25% were non-cavitary multiple nodular lesions (in the patient with a history of nasal squamous cell cancer and differential diagnosis of metastasis) (Figure 1 and 2). Mediastinal lymphadenopathy accompanied 75% of the lung lesions while pleural effusion was present in 25%. All bone lesions, which presented as osteolytic lesions, were localized in the axial skeleton (67% in spinal vertebra columns, 33% in pelvic bones) (Figure 3, 4 and 5). All the bone lesions were multifocal except the four that were localized in pelvic bones. Intervertebral disc or adjacent joint involvement was present in all bone lesions. Four patients had immune deficiency (1 had tuberculous spondylodiscitis previously, 2 were Human Immunodeficiency Virus (HIV) positive, 1 had Systemic lupus erythematosus (SLE) disease) and 1 had a history of nasal squamous cell cancer. A total of 19% of the patients were immigrants. None of the patients with spine lesions had a history of disc operation.

A total of 80% of the patients had pain that was unresponsive to medical treatment. Seventy-six percent had weight loss. Three patients with lung lesions had cough while the fourth one, whose lung lesions were incidentally detected during cancer follow-up imaging, did not. White blood cell (WBC) and C-reactive protein (CRP) counts were in normal ranges in 81% and 43% of the patients, respectively. In our hospital, since the patients were not referred for anti-TB therapy without a definite diagnosis proven microbiologically, the patients with presumed to have infection. Those who did not improve with routine antibiotherapy and anti-inflammatory drugs were referred for percutaneous biopsy to find out the causative pathogen and rule out a malignancy. No significant complication was observed during treatment or the recovery period according to Society of Interventional Radiology (SIR)-complication criteria [15].

Table 1: List of patients with lesion localizations

Patients	Gender	Age	Lesion localization	Malignancy or immune deficiency history in background
1	M	62	Right lung, lower lobe	No
2	M	71	Left lung, lingular segment	Yes, nasal squamous-cell carcinoma
3	M	74	Right lung, lower segment	No
4	M	41	Right lung, apex	No
5	F	19	Bone, L3 spine vertebra	No
6	F	33	Bone, right sacroiliac	No
7	F	34	Bone, L4 spine vertebra	No
8	M	37	Bone, L3 spine vertebra	No
9	M	30	Bone, D10 spine vertebra	No
10	M	33	Bone, L4 spine vertebra	No
11	M	37	Bone, iliac bone	Yes, HIV (+)
12	F	40	Bone, ischium	Yes, Systemic lupus erythematosus
13	M	45	Bone, L4 spine vertebra	Yes, HIV (+)
14	F	42	Bone, acetabulum	No
15	M	39	Bone, L5 spine vertebra	Yes, tuberculosis spondylodiscitis
16	M	17	Bone, L5 spine vertebra	No

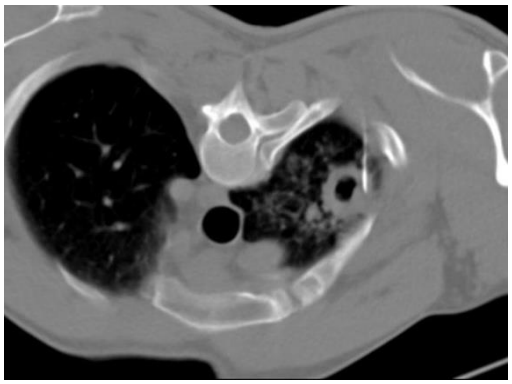
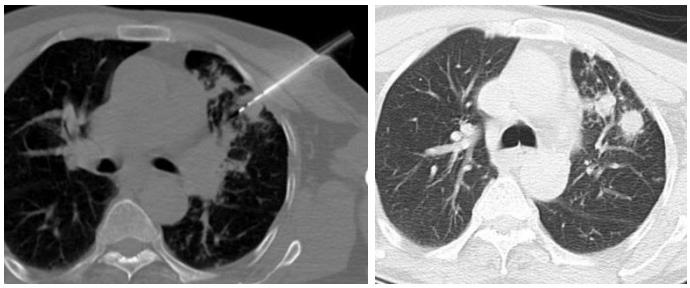


Figure 1: A 41-year-old heavy smoker male without any malignancy history. The patient was referred with the presumptive diagnosis of malignancy. Axial CT scan shows the thick walled cavitated lesion with irregular margins and ground glass opacity in surrounding lung parenchyma. He was diagnosed with tuberculosis with a positive PCR test both microbiologically and histopathologically after CT-guided transthoracic biopsy.



Figures 2: A 71-year-old patient with nasal squamous cell cancer history. The patient was referred with the presumptive diagnosis of metastasis. Axial CT scan shows the multi-nodular lesions with irregular margins and ground glass opacity in surrounding lung parenchyma. The patient had CT-guided percutaneous core needle biopsy. Histopathological and microbiological test results revealed tuberculosis infection with a positive PCR test after CT-guided transthoracic biopsy.

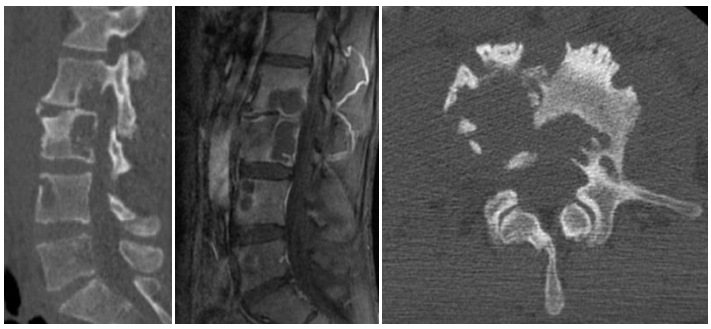
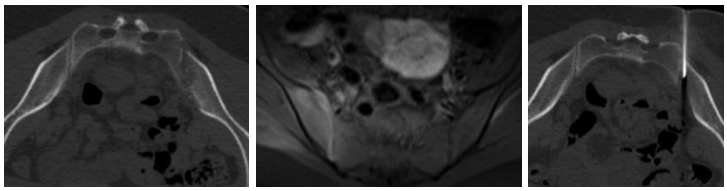


Figure 3: A 33-year-old male with spondylitis. CT (a) and contrast enhanced T1-weighted MR (b) images demonstrating the skip vertebral body lesions of lumbar spine. In axial CT image (c) destruction of the vertebral body is clearly seen. Pay attention to the destruction of the right pedicle in the vertebral body, which may be assumed as a sign of malignancy. Histopathological and microbiological test results revealed tuberculosis infection with a positive PCR test after CT-guided transpedicular biopsy.



Figures 4: A 31-year-old female with sacroiliitis that did not heal with medication. Axial CT (a) and non-contrast enhanced T2-weighted MR (b) images demonstrating the destruction in cortical bone adjacent to the joint and bone marrow edema. CT guided biopsy and the laboratory results revealed tuberculosis infection (c).

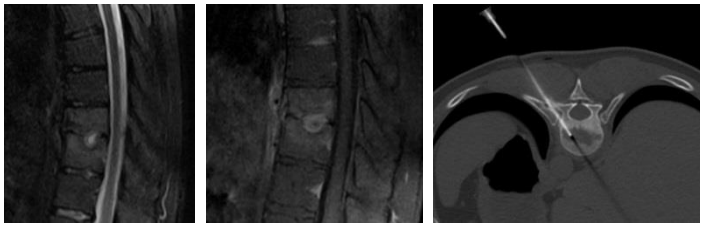


Figure 5: A 30-year-old male with spondylitis in dorsal vertebral bodies. Non-contrast enhanced T2-weighted (a) and contrast enhanced T1-weighted MR (b) images demonstrate the destruction of vertebral body endplates and involvement of the adjacent intervertebral disc. Since the patient had negative clinical history and laboratory tests for TBI, he was referred with presumptive diagnosis of malignancy. The patient had CT-guided percutaneous-transpedicular bone biopsy (c). Histopathological and microbiological test results revealed tuberculosis infection.

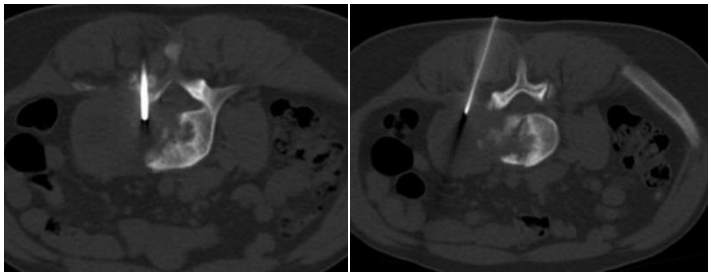


Figure 6: A 37-year-old male patient with spondylitis. Axial CT image shows vertebral body and left pedicle destruction. Since the enlargement of the left psoas muscle was highly suspicious for a Pott abscess, CT guided bone biopsy from vertebral body (a) and needle aspiration from adjacent soft tissue (b) were performed. Histopathological and microbiological test results revealed tuberculosis infection.

Discussion

There has been an increase in the prevalence of tuberculosis, especially among the patients with immunodeficiency and immigrant populations. Early diagnosis promotes effective treatment of the disease [1-3]. A positive sputum or tuberculin skin test support the diagnosis of TBI. Nevertheless, a negative result does not rule it out [16]. Thus, being familiar with the common radiologic features of tuberculosis may prevent wasting time until diagnosis and accordingly, reducing the morbidity.

Tuberculosis usually involves the respiratory system and lungs. However, any organ system may be affected, particularly in the patients with immunodeficiency [1-3]. In lungs, TBI and malignancy may show typical imaging features. In some cases, cavitated nodular masses with thick, irregular walls, mediastinal lymphadenopathy and pleural effusion may mimic lung cancer. Also, clinical symptoms present in TB, such as fever, hemoptysis, and weight loss, may be seen in malignancy as well. Consequently, definitive diagnosis of these two diseases remain a diagnostic dilemma in the clinic. In our study, among 4 lung lesions, 75% presented as solitary cavitary nodular lesions while 25% were non-cavitary multiple nodular lesions (in the patient with a history of nasal squamous cell cancer (SCC), in which differential diagnosis of metastasis was needed) (Figure 1 and 2). Of the 3 cavitary masses, only one was localized in apical segment of the right lung, while the 2 others were localized in lower lobes. Mediastinal lymphadenopathy accompanied 75% of the lung lesions, which was not consistent with usual radiological presentation of post-primary TBI. Pleural effusion was present in 25% of the patients. On the other hand, in one patient, who had a history of nasal SCC, multiple nodular lesions in the lingular lobe was assumed as metastasis. Therefore, malignancy was presumed; and biopsy was required to prove the diagnosis. All lung lesions were diagnosed with tuberculosis with both histopathological and culture analysis by CT guided biopsy, and malignancy was excluded in all.

In musculoskeletal involvement, bone and joint destruction may result in severe morbidity [9,10]. Especially in patients with spinal involvement, severe neurological deficit may be seen. Almost 50% of musculoskeletal tuberculosis affects the spine. Usually, the lower thoracic and upper lumbar vertebral bodies are involved due to hematogenous spread via the Batson's paravertebral venous plexus. Infection usually spreads to the intervertebral disc from the involved part of the vertebral body close to the end plate. Also, it may disseminate into adjacent spinal segments, resulting in skip lesions as well as into the paraspinal tissues that results as paravertebral Pott abscess (Figure 6). TBI tends to involve the anterior part of the vertebral body, while metastasis tends to involve the posterior part and pedicles. Nevertheless, radiological findings are nonspecific in the early stages. In our study, all bone lesions were osteolytic lesions that were localized in axial skeleton (67% in spinal vertebra columns, 33% in pelvic bones) (Figure 3, 4 and 5). They were all multifocal, except the four that were localized in pelvic bones. Intervertebral disc and adjacent joint involvement were present in all bone lesions. Involvement of the posterior part of the vertebral body was present in 5 of 8 vertebral body lesions (Figure 3) and cortical lysis was present in all. Pott abscess accompanied prominent spondylodiscitis in two patients (Figure 6). In suspected patients, if TBI cannot be diagnosed with noninvasive techniques, percutaneous biopsy should be performed for histologic analysis and culture [13,14]. The interventional radiologist may not be informed of the possible diagnosis prior to intervention many times and the malignancy or metastasis may be the only presumptive diagnosis for reason of referring the patient for biopsy. We should be aware of the possibility of TBI according to common radiological features and obtain an additional sterile sample for culture analysis during the biopsy to get prevent an additional biopsy procedure and delaying the diagnosis. Specimens should be placed in a sterile container and referred to the laboratory for culture analysis, as well as in a formalin cup for histopathological analysis.

Limitations

The are some limitations in this study. Due to its retrospective nature, we could not reach the files of all patients. Some of the patients were referred for biopsy only from different centers. Thus, the physical assessments were performed in different centers by different physicians for every patient. We did not know if sputum tests were repeated for the patients who had clinically high suspicion of TBC disease. Also, the number of the patients was small. Nevertheless, we think this study will contribute to the literature by presenting the utility of percutaneous biopsy to shorten time until diagnosis with a positive PCR test. Further research with a considerable number of patients is needed to emphasize the diagnostic yield of image-guided biopsy for tuberculosis.

Conclusion

The diagnosis of tuberculosis may be challenging, and it may mimic malignancy. Image-guided-biopsy is safe and useful in diagnosis of tuberculosis cases who could not be diagnosed by laboratory and sputum tests or those with presumptive diagnoses of malignancy. Tuberculosis should be kept in mind during percutaneous biopsy procedures of radiologically suspicious cases as a differential diagnosis, despite being clinically negative.

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