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RESEARCH ARTICLE

Tuberculous mastitis: A masquerading face of granulomatous mastitis

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ABSTRACT

Tuberculous mastitis: A masquerading face of granulomatous mastitis

Introduction: *Tuberculosis (TB) mastitis is a rare form of granulomatous mastitis. We aimed to evaluate the clinical characteristics and prognosis of patients diagnosed with TB mastitis.*

Materials and Methods: *A descriptive study was carried out on patients who were reported to national tuberculosis control authorities as having TB mastitis between 2003 and 2021. Demographic, histopathological, and radiological data including mammography, ultrasonography (US), and magnetic resonance imaging (MRI) were reviewed. All were followed up to 24 months and prognosis was also evaluated.*

Results: *This study identified 29 TB mastitis patients who had been diagnosed using excisional biopsies. The mean age was 33.5 ± 10.1, all were premenopausal women. The most common symptom was breast mass (n= 24, %82.8), nearly half of the patients also had ipsilateral axillary lymphadenopathy (n= 14, 48.3). One-fourth of the patients had bilateral involvement (n= 7, 24.1%), and half of the patients (n= 16, 55.2%) presented with multiple masses. One patient had co-existing pulmonary TB. Predisposing factors for TB were not identified in any of the patients. Nearly half of the patients received prior mastitis treatment. The most common radiological finding was mass in both mammography and US. All patients received anti-tuberculosis treatment of a standard regimen for six to 21 months, three patients had a relapse but were finally cured.*

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Conclusion: *TB mastitis should be suspected in young and premenopausal women presenting with a breast mass and axillary lymphadenopathy in an endemic region. Radiological findings could not identify the diagnosis. A multidisciplinary approach including bacteriology and histopathology should be performed. Anti-tuberculosis treatment can be implemented successfully.*

Key words: *Mastitis; tuberculosis mastitis; granulomatous mastitis; breast abscess*

ÖZ

Tüberküloz mastit: Granülomatöz mastitin maskeli yüzü

Giriş: *Tüberküloz (TB) mastiti, granülomatöz mastitin nadir görülen bir formudur. Bu çalışmada TB mastit tanısı alan hastaların klinik özelliklerini ve prognozunu değerlendirmeyi amaçladık.*

Materyal ve Metod: *2003-2021 yılları arasında ulusal tüberküloz kontrol sistemine TB mastiti olduğu bildirilen hastaların dahil edildiği tanımlayıcı bir çalışma yapıldı. Mamografi, ultrasonografi (US) ve manyetik rezonans görüntüleme (MRG) dahil olmak üzere radyolojik, demografik ve histopatolojik veriler gözden geçirildi. Hastalar 24 aya kadar takip edildi ve prognozları da değerlendirildi.*

Bulgular: *Çalışmada eksizyonel biyopsiler kullanılarak teşhis edilen 29 TB mastit hastası belirlendi. Ortalama yaş 33,5 ± 10,1 idi, hepsi premenopozal kadındı. En sık görülen semptom meme kitlesiydi (n= 24, %82,8), hastaların yaklaşık yarısında aynı zamanda aynı tarafta aksiller lenfadenopati de vardı (n= 14, 48,3). Hastaların dörtte birinde (n= 7, %24,1) iki taraflı tutulum vardı ve hastaların yarısında (n= 16, %55,2) birden fazla kitle mevcuttu. Bir hastada eşlik eden pulmoner TB vardı. Hiçbir hastada TB için predispozan faktörler saptanmadı. Hastaların yaklaşık yarısı mastit için önceden tedavi görmüştü. Hem mamografide hem de ultrasonografide en sık radyolojik bulgu kitleydi. Tüm hastalar altı ila 21 ay boyunca standart bir rejimle tüberküloz tedavisi aldı, üç hastada nüks görüldü ancak sonunda iyileşti.*

Sonuç: *Endemik bir bölgede meme kitlesi ve aksiller lenfadenopati ile başvuran genç ve premenopozal kadınlarda TB mastitisten süphelenilmelidir. Radyolojik bulgular tanıyı belirlemede yetersizdir. Bakteriyoloji ve histopatolojiyi içeren multidisipliner bir yaklaşım uygulanmalıdır. Anti-tüberküloz tedavi başarıyla uygulanabilmektedir.*

Anahtar kelimeler: *Mastit; tüberküloz mastit; granülomatöz mastit; meme apsesi*

INTRODUCTION

Tuberculosis (TB) is still the world's major leading infectious cause of mortality, with 10 million infected people worldwide and 1.5 million deaths every year. Türkiye is a country with a relatively low TB incidence of 13/100000, following the successful implementation of a directly observed therapy strategy (1).

Lungs are the primary site of both primary and post-primary TB and only five to fifteen percent of the infected people develop active TB disease. Breast TB is relatively rare even in the low- and middle-income countries where most of the infected people live. In studies also including data from Türkiye, the prevalence of breast TB among all breast lesions was reported between less than one to four percent (2,3,4). Breast tissue is naturally resistant to the survival and growth of tuberculous bacilli (4,5).

Due to the non-specific clinical and imaging characteristics and rarity of the disease, its diagnostic workup, and management can be challenging. Most patients are premenopausal breastfeeding women with breast mass (6). However, patients may also present with skin ulcers, thickening, abscesses, and sinus tracts (7). Therefore, it may be difficult to differentiate from pyogenic abscesses or breast cancer (8).

In the present study, 29 patients with TB mastitis were reviewed and the significant characteristics of this rare disease are described and discussed to highlight an optimal diagnostic modality.

MATERIALS and METHODS

This is a retrospective and descriptive evaluation of 29 TB mastitis patients who have been registered to local national tuberculosis control health authorities between 2003-2021. The evaluations were made after local ethics committee approval was obtained (2021/23-07).

All patients presented with breast-related symptoms. Demographic data and clinical presentations of the patients (breast mass, skin changes, palpable axillary lymphadenopathy, nipple retraction, nipple discharge and constitutional symptoms) were reviewed. Imaging data were obtained for 25 in the form of mammography and/or ultrasonography depending on age. When applicable, magnetic resonance imaging (MRI) of the breast was also evaluated.

According to clinical and radiological findings patients were classified into nodular, disseminated, and sclerosing/tubercular TB mastitis groups. Breast masses, with/without associated sinus tracts and/or skin ulcers are called nodular type, diffuse coalescent

multiple inflammation foci and hypo-echoic imaging with sinus tract and/or skin ulcer were called disseminated type and liquefied breast lesions with skin ulcer or sinus tracts are called tubercular/sclerosing type (9).

All patients underwent excisional biopsy. They were considered positive for breast TB if records demonstrated histological findings in favor of TB infection and other diagnoses were excluded. Standard anti-tuberculosis treatment was administered to all with variable durations.

RESULTS

The study population included 29 relatively young and pre-menopausal female patients who ranged from 27 to 48 years. Most of them had at least one prior parity (n= 14, 48.3%). The most common presenting symptom was breast mass (n= 24, 82.8%), and nearly half of the patients also had ipsilateral axillary lymphadenopathy (n= 14, 48.3%). Patients did not report constitutional symptoms such as fever, night sweats, or weight loss. One-fourth of the patients had bilateral involvement (n= 7, 24.1%), and half of the patients (n= 16, 55.2%) presented with multiple masses. One patient had also co-existent pulmonary TB. Prior tuberculosis or exposure to TB was not detected in any of the patients. Predisposing factors for TB such as congenital or acquired immunosuppression and diabetes mellitus were not identified in any of the patients. Bacteriological detection of *Mycobacterium tuberculosis* was not performed, and tuberculin skin test (TST) was positive in two patients who were the only ones who had undergone this test. Nearly half of the patients received prior treatment for mastitis. Most of the patients had the disseminated form of the disease. The findings are summarized in Table 1.

The most common radiological finding was mass in both mammography and ultrasonography. Axillary lymphadenopathy was observed in approximately 10% of the patients (Table 2). Breast MRI was performed on eight patients (27.6%) and six of them (75%) represented peripheral contrast-enhanced density, and two parenchymal edema (20%). Radiological imaging features of two selected patients presented with a mass are shown in Figures 1 and 2.

All patients underwent an excisional biopsy that revealed the presence of granulomas and caseous necrosis in the histological examination.

Anti-tuberculosis treatment of a standard regimen consisting of isoniazid, rifampicin, ethambutol, and pyrazinamide was administered to all patients for a median duration of nine months, with a minimum of six months to 12 months. Only one patient received treatment for 21 months and had to interrupt her treatment due to drug allergies. There were two other patients with relapses, one of them received a retreatment regimen and the other one had a prolonged treatment, and all were cured in the end. All patients were followed up for a median duration of 12 months (min= 6, max= 36) and all were clinically and radiologically stable during the follow-up period.

DISCUSSION

TB may develop in any part of the body and should be considered in the differential diagnosis of granulomatous mastitis. Here, we presented 29 TB mastitis cases of childbearing age mostly presented with a breast mass that was histologically diagnosed as granulomatous necrosis, and all were cured by anti-tuberculosis treatment.

TB mastitis is a rare form of TB, firstly defined in 1829. Akbaba et al. were the first to summarize TB mastitis cases that had been reported in Türkiye until 2007 (10). They also reported two cases. The summary included 29 TB mastitis cases with a mean age of 37.5 and only one was male. Most of them presented with a painless unilateral breast mass and the most common pre-diagnosis was breast cancer. Five patients also had pulmonary TB. All were treated by anti-TB treatment; however, abscess drainage (n= 3) and simple mastectomy (n= 2) were other therapeutic modalities. Following them, one radiological and five clinical reports of TB mastitis were published from Türkiye, with similar features (4,11). Soon after, in 2010 Tanrıkulu et al. analyzed 27 patients in southeast Türkiye (12) and in 2016 Kılıç et al. reported their experience of 46 TB mastitis cases (2). All cases were female with a mean age of 31.5/36.4 years respectively. Similarly, unilateral breast mass was the most common symptom, mastalgia was also present in 18.5-41% of the patients. The diagnostic method preferred was ultrasonography for most of the patients, however, a definitive diagnosis was mainly made by histopathology. In both studies, all cases were treated with standard anti-TB treatment for six months which was extended to nine months when there was an inadequate response. The clinical and

Table 1. Demographic and clinical characteristics of the TB mastitis patients

	n (%)
Age, years (mean ± standard deviation)	33.5 ± 10.1
Premenopausal	29 (100)
Prior parity	14 (48.3)
Current breastfeeding	2 (6.9)
Clinical symptoms	
Breast mass	24 (82.8)
Mastalgia	19 (65.5)
Nipple discharge	16 (55.2)
Ipsilateral axillary lymphadenopathy	14 (48.3)
Location	
Right side	10 (34.5)
Left side	12 (41.4)
Bilateral	7 (24.1)
Single breast mass	16 (55.2)
Coexistent pulmonary tuberculosis	1 (3.4)
Prior tuberculosis contact/infection	0/0
Chest X-ray compatible with TB	0
Median duration of symptoms, months (min-max)	3 (1-36)
Prior treatment of mastitis	13 (45.9)
Systemic antibiotics	8 (27.6)
Local antibiotics/steroids	3 (10.3)
Local surgery	2 (6.9)
TB mastitis pattern	
Nodular	11 (37.9)
Disseminated	13 (44.8)
Trabecular/Sclerosing	5 (17.3)

Data are expressed as numbers and percentages unless mentioned otherwise.
min: Minimum, max: Maximum, TST: Tuberculosis skin test, TB: Tuberculosis.

Table 2. Radiological findings (mammography/ultrasonography) of the TB mastitis patients

Mammography (n= 8, 27.6)	n (%)	Ultrasonography (n= 24, 82.8)	n (%)
Mass	6 (75.0)	Hypoechoic mass	17 (70.0)
Oedema, skin thickening	2 (25.0)	Oedema, skin thickening	7 (29.1)
Tissue distortion	1 (12.5)	Ductal ectasia, fluid collection	15 (62.5)
Areolar distraction	1 (12.5)	Abscess	3 (12.5)
Fistula	0 (0)	Fistula	2 (8.3)
Axillary lymphadenopathy	2 (25.0)	Axillary lymphadenopathy	3 (12.5)

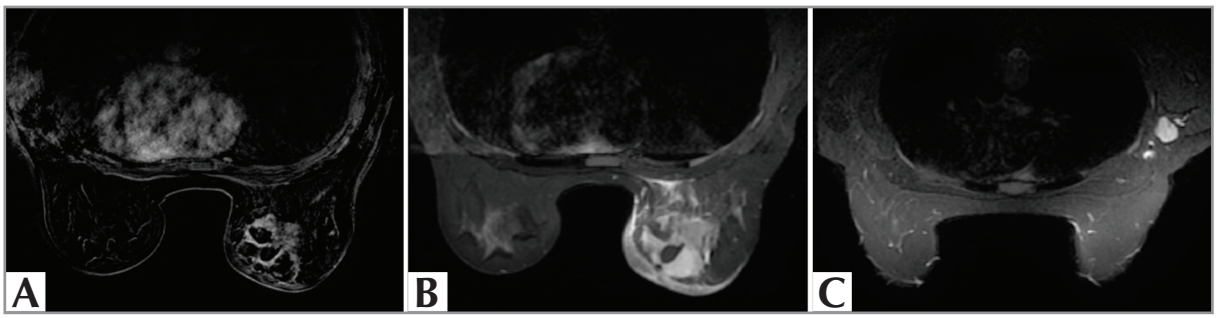


Figure 1. Magnetic resonance images of tuberculosis mastitis in a 33-year-old woman with a painful mass of six months duration in the inner region of the right breast.
A. Gradient echo (GE)-post-contrast subtraction magnetic resonance image shows clustered ring enhancement (arrows). **B.** T2-weighted images (T2WI) with fat saturation reveal the abscess (arrowhead) and skin thickening (arrows) and parenchymal edema. **C.** Enlarged lymph nodes appear on the right axillary region (arrow).

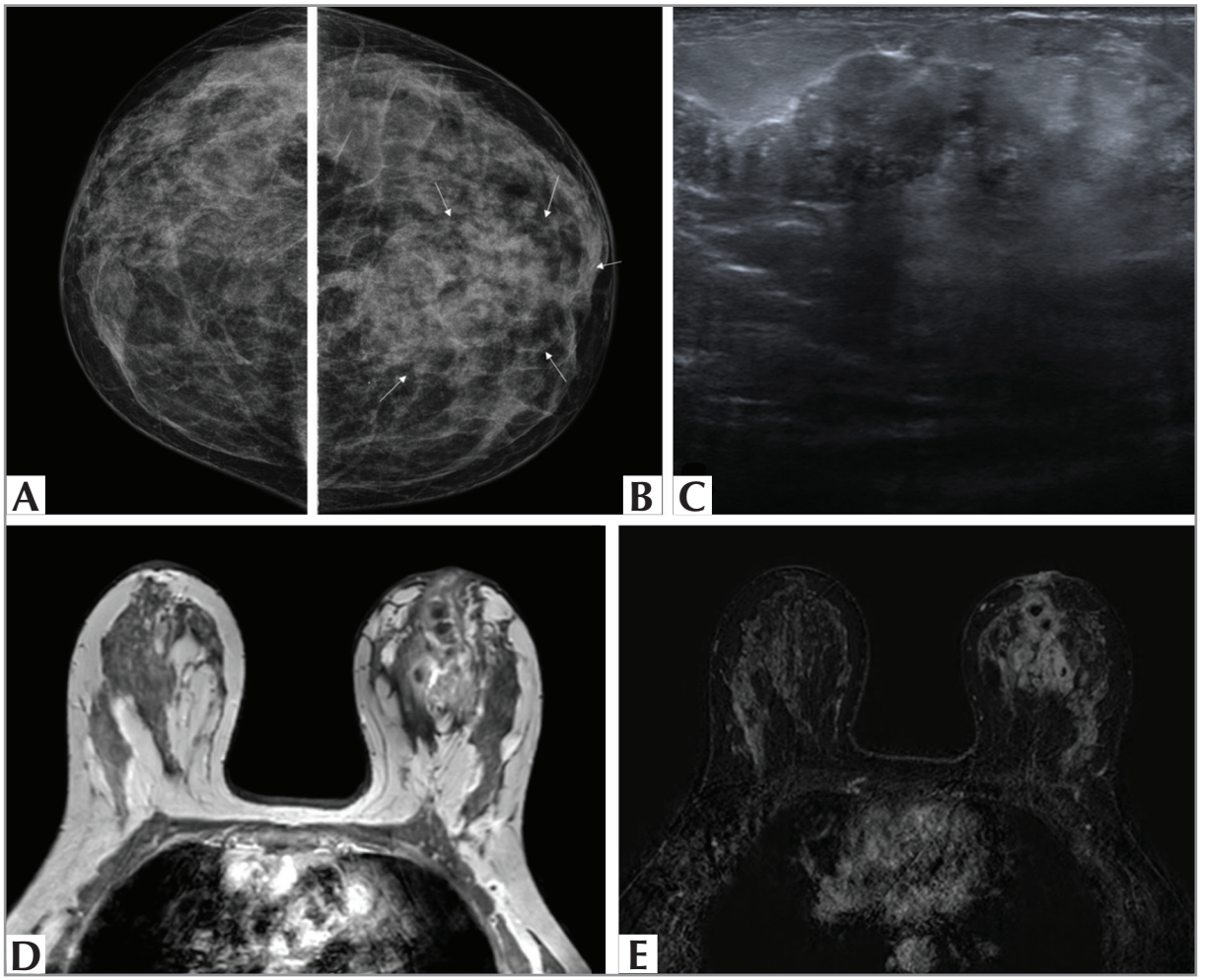


Figure 2. Radiological images of tuberculosis mastitis.
A. Mammographic craniocaudal (CC) view of the left breast shows focal asymmetry (arrows) in the left upper inner region and trabecular thickening. **B.** Mammographic craniocaudal view of the right breast does not reflect structural abnormality. **C.** Targeted ultrasound (US) image of the upper inner region of the left breast shows a heterogeneously hypoechoic parallel mass with hypoechoic tubular extensions and surrounding inhomogeneous breast tissue (arrow). **D,E.** Gradient echo (GE)-post-contrast subtraction magnetic resonance images show clustered ring enhancement in the same region of the left breast (arrows).

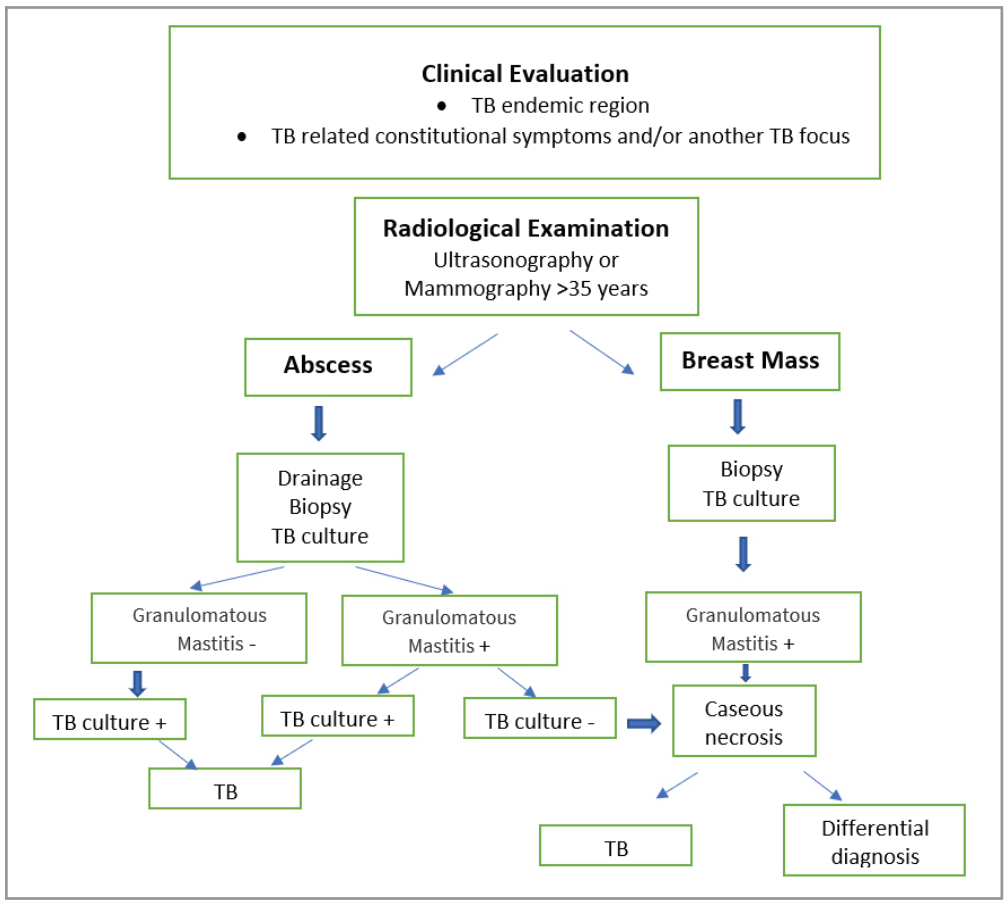


Figure 3. Diagnostic algorithm for breast lesions (adapted from reference 16).

demographical features of our TB mastitis cases were similar to the previous literature for age, presenting symptoms, and diagnostic methods (Table 1).

Breast tissue is resistant to *Mycobacterium tuberculosis*, however, during breastfeeding, high vascularization of the breast tissue facilitates TB infection. The rate of lactating patients has been reported at around ten percent in previous studies (2,9,13), we found it seven percent in our TB mastitis series. Primary TB mastitis may develop from direct inoculation of bacilli through skin abrasions, while secondary TB mastitis is the most prevalent form and occurs by direct invasion, hematogenous extension, or retrograde axillary lymph node dissemination. We found axillary lymph node involvement in approximately half of the patients. Concomitant TB in other sites had been reported in approximately one-fifth of the patients (9), there was only one patient (3.4%) with pulmonary TB in our study. In our series, axillary lymph nodes were the primary focus in most of the cases (Table 1).

TB involvement of the breast presents with solitary or multiple breast masses, abscesses, sinus tracts, skin thickening, or ulceration in any quadrant of the breast. In our TB mastitis series breast mass was the most frequent symptom, and mastalgia was also frequently reported. The duration of symptoms was reported between zero to 180 days. This period ranged from one to 36 months in our study. Granulomatous mastitis, breast cancer, and breast abscess are other diagnostic challenges that should be distinguished. Granulomatous mastitis is diagnosed by exclusion from other diagnoses and unilateral and retro areolar region involvement is more common (14). Breast cancer is associated with skin or nipple retraction and can be diagnosed histopathologically. In the case of antibiotic-resistant breast abscess, TB mastitis should be considered. In our study, nearly half of the patients had been previously treated for mastitis mostly with antibiotics or steroids (Table 1).

TB mastitis is diagnosed with a combination of radiological, microbiological, or histopathological methods. Radiological procedures including mammography, US, and/or MRI are the first steps in the diagnostic algorithm. US can detect multiple communicating breast lesions and fistulas, tracts, and sinuses, which are associated with breast TB and idiopathic granulomatous mastitis (15). However, imaging does not help in distinguishing between other diagnoses (16). A diagnostic algorithm has been introduced for breast masses (Figure 3). In our series, hypoechoic mass and fluid collection were the most prevalent features.

Isolating *Mycobacterium tuberculosis* (MT) in bacteriological culture or using Ziehl Neelsen stain is the gold standard, therefore, all specimens obtained should also undergo acid-fast bacilli (AFB) staining and culture and/or Ziehl Neelsen staining for identifying *M.tuberculosis*. Polymerase chain reaction (PCR) analysis should also be considered when available (2,17).

However, AFB positivity has been reported to be around 10% in aspiration materials and 30% in histology specimens. (18,19).

There are three predefined types of clinically, pathologically, and radiologically TB mastitis. The most common form is the nodular type followed by the disseminated form, which is characterized by multiple TB foci and sinus formation. The sclerosing form is less observed and fibrosis and nipple retraction are characteristic. In our study, the most common form was the disseminated form both clinically and radiologically, which is a rather interesting finding.

Standard Anti-TB treatment is the treatment option. Surgical intervention might be required, in case of failure with anti-TB treatment. In our series, there were three relapses which were all cured with prolonged anti-TB treatment or retreatment and there was no need for other treatment options.

CONCLUSION

The diagnosis of TB mastitis is challenging. Clinical signs and imaging are nonspecific. When a woman of childbearing age presents with a breast mass and axillary lymphadenopathy in an endemic region, TB mastitis should be considered, and a multidisciplinary team, including bacteriology and histopathology, should take a diagnostic approach.

Ethical Committee Approval: This study approval was obtained from Dokuz Eylül University Non-invasive Research Ethics Committee (Decision No: 2021/23-07, Date: 18.08.2021).

CONFLICT of INTEREST

The authors declare that they have no conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: ESU, PB, AÖA

Analysis/Interpretation: ESU, AÖA

Data acqusition: MRY, MK, OZ, DGK

Writing: AÖA, BT, DGK

Clinical Revision: AÖA, BT, DGK

Final Approval: AÖA, ESU

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