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A Case of Granulomatous Mastitis due to *Corynebacterium amycolatum*

Corynebacterium amycolatum'un Neden Olduğu Granülomatöz Mastit Olgusu

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Abstract

Mastitis is a generalized cellulitis condition of breast tissue usually seen in female patients between 18-50 years of age. Granulomatous mastitis (GM), which is one of the rare types, is usually an idiopathic disease and can be caused by infectious microorganisms. In this report, a 35-year-old female patient diagnosed as having GM infected with *Corynebacterium amycolatum* was reported and the relevant literature was reviewed. The patient was treated with a combination of amoxicillin/clavulanic acid and clindamycin and no recurrence was observed at 10 months follow-up.

Keywords: *Corynebacterium*, *Corynebacterium amycolatum*, mastitis, granulomatous mastitis, MALDI-TOF MS

Öz

Mastit, genellikle 18-50 yaşlarındaki kadın hastalarda görülen meme dokusunun yaygın selülit durumudur. Nadir tiplerinden biri olan granülomatöz mastit (GM) ise genellikle idiyopatik bir hastalık olup, enfeksiyöz nedenlerle de oluşabilir. Bu olgu raporunda *Corynebacterium amycolatum* ile enfekte GM tanısı almış 35 yaşında kadın hasta bildirilmiş ve ilgili literatür bilgileri gözden geçirilmiştir. Hasta amoksisilin/klavulanik asit ve klindamisin kombinasyonu ile tedavi edilmiş, hastanın 10 aylık takibinde nüks saptanmamıştır.

Anahtar Kelimeler: *Corynebacterium*, *Corynebacterium amycolatum*, mastit, granülomatöz mastit, MALDI-TOF MS

Introduction

Granulomatous mastitis (GM) refers to a rare chronic benign inflammatory disease of the breast. It is an important clinical condition of which etiology includes infectious and non-infectious processes, which can mimic malignancy clinically and radiologically, and which may cause panic in the diagnostic process^[1,2].

The disease usually progresses with a unilateral breast mass in young women of childbearing age. Tuberculosis (most commonly

Mycobacterium tuberculosis), sarcoidosis, fungal infections, as well as autoimmune diseases such as Wegener's granulomatosis and giant cell arteritis may be the leading inflammatory etiologies of GM^[2]. These conditions are clinically, pathologically or radiologically similar and cannot be distinguished from idiopathic GM^[3].

Recently, it has been reported that the frequency of isolation of *Corynebacterium* species in patients diagnosed as having GM is gradually increasing. There are no published treatment protocols in the literature for *Corynebacterium*-associated

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breast infections^[4]. In this report, a patient with GM caused by *Corynebacterium amycolatum* who was admitted to our outpatient clinic with complaints of breast pain, mass and discharge, and was successfully treated with a combination of oral antibiotics was presented.

Case Report

A 35-year-old married woman with three children was admitted with complaints of pain, redness and swelling in the right breast. It was learned that the patient's complaints that started two months ago were accompanied by chills and shivering fever, especially at night. There was no history of travel, animal contact, trauma and oral contraceptive use in the period before the patient's complaints started. The patient, who weaned her three-year-old child eight months ago, stated that she had a slight swelling in her right breast at that time, but the swelling went away on its own after a while.

In physical examination; her general condition was good, tympanic fever was 37 °C, her pulse rate was 80/minute, her respiratory rate was 12/minute, and her arterial blood pressure was 110/75 mmHg. Inspection and palpation revealed 3 reddened and discharged lesions in the upper outer quadrant of her right breast and lymphadenopathies in the axillary region.

In laboratory examinations; hematocrit was 37%, hemoglobin was 12.8 g/dl, white blood cell count was 12000/mm³ (64.2% neutrophils), platelet count was 419.000/ul, C-reactive protein level was 2.7 mg/dl, and all other biochemical indicators were within normal limits.

In her anamnesis, it was learned that the ultrasound and mammography findings of the patient who was first admitted to the general surgery outpatient clinic were found to be suspicious for inflammatory malignancy, that a trucut biopsy was performed from the upper outer quadrant of the right breast, and that the result was reported to be consistent with GM with active chronic inflammation, inflammatory response accompanied by granulomas without necrosis, and microabscess formations. Empirical ciprofloxacin treatment was initiated in the patient and she was admitted to our outpatient clinic because there was no improvement for one month. Tissue samples were taken from the patient's lesions with biopsy. Uniform and dense *Corynebacterium* genus Gram-positive rods were produced in aerobic tissue culture and defined as *Corynebacterium amycolatum* with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) (VITEK® MS, Biomérieux, France). Antibiotic susceptibility test was performed with VITEK 2® automated system (Biomérieux, France) and was evaluated according to the Clinical and Laboratory Standards Institute 2017 guideline^[5].

Since the isolated strain was found to be resistant to ciprofloxacin and susceptible to amoxicillin/clavulanate and

clindamycin, the patient was treated with a combination of amoxicillin/clavulanate 3x1 gr po and clindamycin 3x600 mg po for three weeks. At the end of the treatment, all lesions and complaints disappeared, and the patient was free of complaints in the 10th month of follow-up.

Discussion

Corynebacterium amycolatum is an aerobic or facultatively anaerobic, non-spore-forming Gram-positive bacillus and is one of the few *Corynebacterium* species that does not contain mycolic acid in its cell wall^[6]. It was first isolated from clinical specimens in 1988 and was shown to be distantly related to other *Corynebacterium* species^[7]. *C. amycolatum* has been isolated from clinical specimens such as wound infections, pilonidal sinus, mastitis, endocarditis, and septic arthritis^[7,8].

Corynebacterium amycolatum-associated breast infections have been reported rarely^[9,10]. This is because diphtheroids are members of the skin and mucosal microbiota and their identification is difficult.

The development of new technologies such as 16S RNA sequencing and MALDI-TOF MS have enabled clinical microbiology laboratories to identify many microorganisms up to genus and species level in a short time. In the patient we followed up, the causative agent *C. amycolatum* was identified with MALDI-TOF MS in a short time and was successfully treated with a combination of antibiotics.

Although *Staphylococcus aureus* ranks first among the infectious agents of mastitis, it should not be forgotten that *Corynebacterium* species may also be causative agents. In New Zealand, Paviour et al.^[11] reported that *Corynebacterium* species were one of the factors that should be kept in mind among mastitis agents in a cohort study of 24 female patients with mastitis. They reported that *C. kroppenstedtii*, *C. amycolatum* and *C. tuberculostearicum* were the most frequently reproduced species.

In another study reported from South India, it was shown that *C. amycolatum*/*C. xerosis* was isolated in 5 samples, *C. kroppenstedtii* in 4 samples, and *C. striatum* in 1 sample, taken from 10 patients with mastitis^[12]. In addition, the examination of antibiotic susceptibility of isolated species reflects the importance of antibiogram in the treatment approach of mastitis caused by *Corynebacterium* species^[13,14].

In patients with mastitis, taking cultures and detecting the causative agent are of great importance in the treatment. Mass spectrometry is the method that is frequently used today to define the types of the determined agent after this stage. There are studies showing that MALDI-TOF MS is the most powerful method in terms of supporting the diagnosis

of *Corynebacterium* infections and its suitability for use in the clinical laboratory^[15,16].

It is also noteworthy that patients with mastitis in whom *Corynebacterium* species are produced as a factor are diagnosed as having GM. In this regard, some studies supporting that GM may be associated with *Corynebacterium* infections are also included in the literature^[17,18].

Although there was no guide on treatment and its duration in mastitis caused by *Corynebacterium* published in the literature; monotherapy or combined antibiotic protocols were used in case series^[4].

Although β -lactam and quinolones are widely used in the empirical treatment of mastitis, it has been reported that their effects in the treatment of *Corynebacterium* bacteria are weak. Therefore, from New Zealand, Dobinson et al.^[4] examined patients with *C. kroppenstedtii*, *C. tuberculostearicum*, *C. glucuronolyticum*, and *C. freneyi*-induced GM between 2002 and 2013, and they reported that these microorganisms should be treated by evaluating their lipophilicity and antibiotic susceptibility, but also they supported the use of clarithromycin and rifampicin, which were also used in the treatment of other granulomatous diseases.

Short-term antimicrobial therapy is not evaluated in favor of positive clinical results, and it is stated that the literature on treatment duration is limited^[4]. The patient's unresponsiveness to this treatment which was empirically initiated, could be explained by the low lipid solubility of fluoroquinolones and the lipophilic nature of *C. amycolatum* isolated from the patient. Therefore, low lipid solubility β -lactam and quinolones will be less effective in cases of GM caused by lipophilic *Corynebacterium*. The patient was treated for three weeks with a combination of amoxicillin/clavulanate 3x1 gr po and clindamycin 3x600 mg po, since there was no published protocol in the literature regarding the superiority of monotherapy or dual therapy over each other and *C. amycolatum* isolated from the culture taken from the patient was found to be resistant to ciprofloxacin and sensitive to amoxicillin/clavulanate and clindamycin. Since it was reported that short-term treatments resulted in clinical failure, the duration of treatment was extended to three weeks^[4].

Conclusion

The aim of this case report was to emphasize the importance of taking samples for culture from patients with suspected or confirmed mastitis and the importance of culture-grown *Corynebacterium* bacteria as the causative agent of mastitis. MALDI-TOF MS can be of great help in the effective treatment of patients with mastitis due to its rapid identification ability. With effective treatments, such conditions, which are extremely

problematic for patients, can be treated in a short time.

Ethics

Informed Consent: Verbal consent was obtained from the patient.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Z.B., M.Y., Data Collection or Processing: N.B.K., Writing: Z.B., M.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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