

## A Case of Erosive Polyarthriti s in a Patient Diagnosed With a Suspicion of Atypical Mycobacteria

Hani Almoallim<sup>\*,1,2,3</sup>, Laila Alharbi<sup>1,3</sup>, Zainab Alshareef<sup>2</sup> and Ghassan Wali<sup>1,2</sup>

<sup>1</sup>Department of Medicine, Medical College, Umm Alqura University, Saudia Arabia

<sup>2</sup>Department of Medicine, King Faisal Specialist Hospital and Research Center, Saudia Arabia

<sup>3</sup>Alzaidi Chair of Research in Rheumatic Diseases, Umm Alqura University, Saudia Arabia

**Abstract:** In this report, we introduce a case of erosive polyarthriti s in a 55-year-old female diagnosed with *Mycobacterium abscessus* pulmonary infection. Her arthritis has been worsened after use of DMARDs. The patient demonstrated a significant response to the antimicrobial regimen that was administered. We call special attention to the possibility of *Mycobacterium abscessus* being a cause of reactive polyarthriti s, particularly if symptoms worsened after use of disease-modifying antirheumatic drugs (DMARDs), but further studies are necessary for clarification.

**Keywords:** *Mycobacterium abscessus*, rheumatoid arthritis, polyarthriti s.

### INTRODUCTION

*Mycobacterium abscessus* (*M. abscessus*) is a non-tuberculous mycobacterium (NTM) and an emerging pathogen causing skin, soft tissue and pulmonary infections [1]. *M. abscessus* is the third most frequently recovered NTM respiratory pathogen in the United States and accounts for approximately 80% of NTM respiratory disease isolates [2]. Conditions such as rheumatoid arthritis and other chronic diseases with pulmonary manifestations can predispose a person to NTM pulmonary disease [3].

Atypical mycobacteria can affect soft tissues and joints directly [4, 5] or indirectly through suspected immunological mechanisms in a reactive way [4,6]. The latter form was described thoroughly recently as reactive arthritis associated with TB or (Poncet's disease) [7]. However, the risk of infections with mycobacteria in general increases in patients with rheumatic diseases [8] and particularly with the use of disease-modifying antirheumatic drugs (DMARDs) and biological therapies [4].

Precise data on the incidence and prevalence of NTM lung disease is limited by the fact that unlike tuberculosis, these infections are generally not reportable to public health authorities [9]. In Saudi Arabia, there is no reliable estimates of incidence or prevalence of NTM infection. Though there is only one case series of chronic lung disease caused by *M. abscessus*, in two immunocompetent patients [10].

In this article, we report a case of seronegative erosive polyarthriti s in an elderly female patient who has been discovered to have *M. abscessus* pulmonary infection. This case is an example of the possibility of *M. abscessus* being a

cause of reactive polyarthriti s, particularly if symptoms worsened after the use of DMARDs.

### CASE REPORT

A 55- year old Saudi female patient newly diagnosed as a case of osteoporosis and polymyalgia rheumatic was presented to the outpatient rheumatology clinic in December 2011 at King Faisal Specialist Hospital and Research Center, in Jeddah, with a month-long history of bilateral hand joints pain and morning stiffness lasting for 1 hour. She had no other joints involvement or any systemic symptoms.

Hand examination revealed tenderness over the metacarpophalangeal (MCPs), proximal interphalangeal (PIPs) and wrists joints but there was no swelling. Laboratory studies showed that WBCs=  $12.8 \times 10^9/L$  (4.00-11.0 x 10<sup>9</sup>/L) erythrocyte sedimentation rate (ESR) =15 mm/hr (<30 mm/hr), C-reactive protein (CRP) = 0.459 mg/dl (0-5mg/dl). Antinuclear antibodies, rheumatoid factor & anti-citrullinated protein peptide antibody (ACPA) were negative. Ultrasound exam of hands showed erosions in the right second MCP and effusion in both second MCPs and wrists joints. At that time she was diagnosed as inflammatory arthritis. Methotrexate 12.5 mg/week, folic acid 5mg/week and 10 mg prednisolone once daily were initiated.

In April 2012, she was still complaining of hand joints pain and morning stiffness. Arthritis remained active despite the treatment with methotrexate. A biological treatment was considered. The PPD skin test showed 15 mm reaction and CXR showed left lower lobe nodule. She denied any symptoms suggestive of tuberculosis (TB). Patient was referred to the Infectious Diseases (ID) and Isoniazid (INH) with pyridoxine were initiated. Two weeks later she developed a productive cough, an intermittent fever and a night sweat. A sputum culture and Computed tomography (CT) scans of the chest were arranged.

\*Address correspondence to this author at the Department of Medicine, Medical College, Umm Alqura University, Saudia Arabia; Tel: 00966505703935; Fax: 0096625501000, Ext. 4652; E-mail: HaniAlmoallim@hotmail.com

In her follow up in June 2012 with ID service, only one culture showed acid-fast bacilli of atypical mycobacterium further identification grew *M. abscessus*. Polymerase chain reaction (PCR) for mycobacterium was negative. The patient did not meet the American Thoracic Society (ATS) criteria for NTM [11]. The sputum culture was repeated. She was maintained on INH. Meanwhile, it was considered that probably she had transient infectious process. In July 2012, a biological treatment was initiated, Etanercept; which is a TNF blocker (Enbrel) administered at a dose of 50 mg subcutaneous every one week.

On her follow up in September 2012, she demonstrated improvement in her arthritis but still had nonspecific symptoms with vague history of productive cough, intermittent undocumented fever, weight loss (4 kg) and the new development of chest pain. The decision was made to continue on Enbrel while she was being worked up for the presence of NTM.

By the end of September 2012 the repeated culture grew Mycobacterium Avium Complex (MAC) isolation. CT-chest showed left pleural-based granuloma. The ID service evaluation considered *M. abscessus* as the likely atypical mycobacterium causing the symptoms and MAC was considered as a contamination. Azithromax, ciprofloxacin and doxycycline were initiated as a treatment for *M. abscessus*. The biological therapy was discontinued.

In November 2012, she had the same non-specific complaints of productive cough and intermittent undocumented fever with no improvement on the antibiotic regimen that was given. Ethambutol was added to add further coverage to include MAC but it was discontinued after one month. The subsequent culture was negative.

In December 2012, she newly developed azithromax allergic reaction in form of gastrointestinal upset. The first culture and sensitivity showed intermediate resistant to Azithromax. Therefore, linezolid was initiated and Azithromax was discontinued.

In January 2013 with her follow up in rheumatology clinic, her symptoms improved. She gained 2Kg and her appetite was back to normal. She demonstrated significant improvement in her joint symptoms. The ultrasound exam of hands showed mild effusion in her joints. She remained off Enbrel and we decided to continue on the same treatment with follow up.

## DISCUSSION

It was a challenge to diagnose an infection caused by NTM as it requires a high index of suspicion. Acid-fast stains are often negative. Thus the organism is not typically detected in routine bacterial culture [12]. A single positive sputum culture, especially with a small number of organisms, is generally regarded as an indeterminate diagnosis of NTM lung disease. Patients should have at least three sputum specimens collected on separate days and analyzed for AFB to optimize positive predictive value of sputum analysis [2]. In the patient reported here there was only one positive culture while the diagnostic criteria established by the ATS in 1997 required 2 or more cultures that were positive for the pathogen [11].

The chest radiograph from patients with *M. abscessus* lung disease usually shows multilobar, patchy, reticulonodular, or mixed interstitial-alveolar opacities with upper lobe

predominance. Cavitation occurs in only approximately 15% of cases [2]. HRCT of the lung frequently shows associated cylindrical bronchiectasis and multiple small (<5 mm) nodules. Overall, the radiographic pattern is similar to the nodular bronchiectatic form of MAC lung disease [2]. However, the chest radiograph of our patient here demonstrated tiny opacities at the left lower lung and a pleural based nodule of the same side in the chest high-resolution computed tomography (HRCT) scan. The classical radiological findings of NTM infections in the HRCT are cylindrical bronchiectasis and multiple small (<5 mm) nodules with upper lobe predominance [2]. Recently, two cases from Saudi Arabia about a NTM lung infection without arthritis showed fibronodular infiltration in the radiological imaging [10]. There is a single pleural base nodule with erosive polyarthritis in the case presented here. We could not find a similar presentation following a thorough literature search.

Inflammatory markers such as ESR or CRP are normal in about 60% of patients with early RA [13]. In the case presented here, CRP level was normal based on the value of our laboratories (0-5mg/L). Despite this normal level, the patient had erosive polyarthritis and was suspected to have a NTM infection. Nevertheless, the CRP level may be used as a marker of significant bacterial infection [14].

Macrolides, such as clarithromycin and azithromycin (AZM), are frequently the only oral antibiotics that are active against *M. abscessus* [15]. *M. abscessus* isolates are uniformly resistant to the standard anti-tuberculous agents [2]. Treatment for *M. abscessus* was initiated for the patient reported here with azithromax, ciprofloxacin and doxycycline. The second positive culture that isolated MAC was considered as a contamination as supported by other reports [16]. MAC is a co-infection in approximately 15% of patients with *M. abscessus* lung disease [9]. This is the explanation of Ethambutol trial in this case report. The patient showed no improvement so she was retained back to cover only *M. abscessus* that were effective in improving her condition. It was concluded that the treatment should be based on *M. abscessus* despite the lack of definitive diagnosis as suggested by ATS [11]. It was planned to continue minimum of 2-4 months on a combination antibiotic therapy as recommended [9, 17] hoping to reach 80.5% successful treatment outcome as reported [17].

The relationship between rheumatic diseases and infectious etiologies has been an area for extensive research. In a study where joint tissue of RA patients was screened for bacteria using sensitive pan-bacteria PCR, no bacterial DNA was found [18]. However, a bacterial cell wall component, muramic acid, was detectable in few RA and OA patients in the same cohort [19]. Several studies have implicated bacterial cell wall components as having multiple immunologic activities that may contribute to joint inflammation [20]. We did not perform a bacterial cell wall study in the presented case. However, the association between bacterial cell wall components and reactive arthritis could be a form of type III hypersensitivity reaction.

On the one hand, *M. abscessus* in the case presented here may have played a triggering role in inducing erosive polyarthritis through possibly breaking tolerance to self-antigens. This might be through nonspecific mechanisms not related to the classical molecular mimicry [20]. On the other hand, polyarthritis in the patient presented here had been present for a long time and resulted in development of erosions. RA is a likely diagnosis with this possibility and serves simply as a risk

factor for *M. abscessus*. It was suggested in several reports that RA would be associated with *M. abscessus* and NTM pulmonary disease in general even in the absence of treatment with immunosuppressant [11,21]. It is possible that the short use of methotrexate might have triggered this *M. abscessus* infection as it a rapidly growing opportunistic mycobacterial pathogen. The use of DMARDs and biological therapies represent risk factors for acquiring *M. abscessus* [5, 22]. However, the case presented here had long lasting history of non-specific complaints that labeled here as fibromyalgia. These symptoms could be retrospectively had been attributed to *M. abscessus* infection.

Another explanation for polyarthritis presented in the case reported here can be based on the concept of reactive arthritis in response to *M. abscessus* infection. The majority of clinical presentation of arthritis associated with TB (Poncet's disease) was at time of initial presentation of TB [7]. However, this concept should be expanded as some cases may present during or after treatment of TB [7]. *M. abscessus* was reported to be complicated with RA [11]. The presence of erosions in the case reported here may not support the possibility of this arthritis being a reactive one to *M. abscessus*. Another possibility is that *M. abscessus* might cause erosions and this case is just an example.

## CONCLUSION

We report a case of *M. abscessus* pulmonary infection associated with seronegative erosive polyarthritis. The explanation of polyarthritis could be that it is either a reactive arthritis associated with *M. abscessus* or seronegative RA induced by *M. abscessus*. We recommend that *M. abscessus* should be included in the differential diagnosis of polyarthritis in any patient in an endemic area with a thorough search for primary site of infection particularly if symptoms worsened after use of DMARDs [4] as was observed in our case. In *M. abscessus* infection a routine bacterial culture will not detect the organism and acid-fast stains are often negative [12]. After identification of *M. abscessus* a long-term treatment with a combination antibiotic therapy consisting of macrolides should be initiated.

## CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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