A Veteran With Fibromyalgia Presenting With Dyspnea

Lakshmana Swamy, MD; Paul Monach, MD; Alan Fine, MD; and Anthony C. Breu, MD

Case Presentation. A 64-year-old US Army veteran with a history of colorectal cancer, melanoma, and fibrinolytic presented with dyspnea to VA Boston Healthcare System (VABHS). Seven years prior to the current presentation, at the time of her diagnosis of colorectal cancer, the patient was found to be HIV negative but to have a positive purified protein derivative (PPD) test. She was treated with isoniazid (INH) therapy for 9 months. Sputum cultures collected prior to initiation of therapy grew Mycobacterium avium complex (MAC) in 1 of 3 samples, with these results reported several months after initiation of therapy. She was a never smoker with no known travel or exposure. At the time of the current presentation, her medications included bupropion, levothyroxine, capsaicin, cyclobenzaprine, ibuprofen, and acetaminophen.

Dr. Breu

Dr. Breu is a Hospitalist and the Director of Resident Education at VA Boston Healthcare System and an Associate Professor of Medicine at Harvard University in Massachusetts and supervises the VA Boston Medical Forum Chief Resident case conferences. All patients or their surrogate decision makers understand and have signed appropriate patient release forms. This article has received an abreviated peer review. Correspondence: Dr. Breu (anthony.breu@va.gov)

Lakshmana Swamy, MD, Chief Medical Resident, VABHS and Boston Medical Center. Dr. Monach, this patient is on a variety of pain medications and has a diagnosis of fibromyalgia. This diagnosis often frustrates doctors and patients alike. Can you tell us about fibromyalgia from the rheumatologist's perspective and what you think of her current treatment regimen?

Paul A. Monach, MD, PhD, Chief, Section of Rheumatology, VABHS and Associate Professor of Medicine, Boston University School of Medicine. Fibromyalgia is a syndrome of chronic widespread pain without known pathology in the musculoskeletal system. It is thought to be caused by chronic dysfunction of pain-processing pathways in the central nervous system (CNS). It is often accompanied by other somatic symptoms such as chronic fatigue, irritable bowel syndrome, and bladder pain. It is a common condition, affecting up to 5% of otherwise healthy women. It is particularly common in persons with chronic nonrestorative sleep or posttraumatic stress disorder from a wide range of causes. However, it also is more common in persons with autoimmune inflammatory diseases, such as lupus, Sjögren syndrome, or rheumatoid arthritis. Concern for one of these diseases is the main reason to consider referring a patient for evaluation by a rheumatologist. Often rheumatologists participate in the management of fibromyalgia. A patient should be given appropriate expectations by the referring physician.

Effectiveness of treatment varies widely among patients. Nonpharmacologic approaches such as aerobic exercise, cognitive behavioral therapy, and tai chi have support from clinical trials, and yoga and aquatherapy also are widely used. The classes of drugs used are the same as for neuropathic pain: tricyclics, including cyclobenzaprine; serotonin and noradrenaline reuptake inhibitors (SNRIs); and gabapentinoids. In contrast, nonsteroidal anti-inflammatory drugs and opioids are ineffective unless there is a superimposed mechanical or inflammatory cause in the periphery. The key point is that continuation of any treatment should be based entirely on the patient's own assessment of benefit.

Dr. Swamy. Seven years later, the patient returned to her primary care provider, reporting increased dyspnea on exertion as well as significant fatigue. She was referred to the pulmonary department and had repeat computed tomography (CT) scans of the chest, which indicated persistent right middle lobe (RML) bronchiectasis. She then underwent bronchoscopy with a subsequent bronchoalveolar lavage (BAL) culture growing MAC. Dr. Fine, please interpret the baseline and follow-up CT scans and help us understand the significance of the MAC on sputum and BAL cultures.
Prior to this presentation, the patient had a pleural-based area of fibrosis with possible associated RML bronchiectasis. This appears to be a postinflammatory process without classic features of malignant or metastatic disease. She then had a sputum, which grew MAC in only 1 of 3 samples and in liquid media only. Importantly, the sputum was not smear positive. All of this suggests a low organism burden. One possibility is that this could reflect colonization with MAC; it is not uncommon for patients with underlying chronic changes in their lung to grow MAC, and it is often difficult to tell whether it is indicative of active disease. Structural lung disease, such as bronchiectasis, predisposes a patient to MAC, but chronic MAC also may cause bronchiectasis. This chicken-and-egg scenario comes up frequently. She may have had a MAC infection, but as she is HIV negative and asymptomatic, there is no urgent indication to treat, especially as the burden of therapy is not insignificant.

Dr. Swamy. Do we need to worry about **Mycobacterium tuberculosis** (MTB)?

Dr. Fine. Although she was previously PPD positive, she had already completed 1 year of isoniazid (INH) therapy, making active MTB less likely. From an infection control standpoint, it is important to distinguish MAC from MTB. The former is not contagious, and there is no need for airborne isolation.

Dr. Swamy. Dr. Fine, where does MAC come from? Does it commonly cause disease?

Dr. Fine. In the environment, MAC is nearly ubiquitous, especially in water and soil. In one study, 20% of showerheads were positive for MAC; when patients are infected, we may suggest changing/bleaching the showerhead, but there are no definitive recommendations. Because MAC is so common in the environment, it is unlikely that measures to target MAC colonization will be clinically meaningful. On the other hand, the incidence of nontuberculous mycobacterial infections is increasing across the US, and it may be a common and frequently underdiagnosed cause of chronic cough, especially in postmenopausal women.

Dr. Swamy. Given her ongoing fatigue and systemic symptoms (morning

Clinical Takeaways

- Fibromyalgia is a syndrome of chronic widespread pain without known pathology. Nonpharmacologic approaches including aerobic exercise, cognitive behavioral therapy, and tai chi, have support from clinical trials. The continuation of any treatment, pharmacologic or otherwise, should be based entirely on the patient's own assessment of benefit.
- The history and physical exam can help differentiate inflammatory disease from fibromyalgia. The most common joints affected in rheumatoid arthritis and lupus are the wrists, hands, ankles, and feet. Rheumatoid arthritis can have atypical presentations in the elderly, including symptoms resembling polymyalgia rheumatica.
- **Mycobacterium avium** complex (MAC) is nearly ubiquitous in the environment, especially in water and soil. Diagnosing an infection with MAC requires a combination of symptoms, imaging, and microbiologic data. It is not contagious.
- Nontuberculous mycobacterial infections often present in patients with chronic lung disease or in elderly women without preexisting lung disease.
- Treatment for MAC involves a prolonged multiple drug regimen. The decision to treat depends on multiple factors. As MAC rarely is the cause of debilitating disease, the decision to treat should not be taken lightly.

Dr. Swamy. Four years prior to the current presentation, the patient developed a cough after an upper respiratory tract infection that persisted for more than 2 weeks. Given her history, she underwent a repeat chest CT, which noted a slight increase in nodularity and ground-glass opacity restricted to the RML. She also reported dyspnea on exertion and was referred to the pulmonary medicine department. By the time she arrived, her dyspnea had largely resolved, but she reported persistent fatigue without other systemic symptoms, such as fevers or chills. Dr. Fine, does MAC explain this patient's dyspnea?

Dr. Fine. As her pulmonary symptoms resolved in a short period of time with only azithromycin, it is very unlikely that her symptoms were related to her prior disease. The MAC infection is not likely to cause dyspnea on exertion and fatigue and should be worked up more broadly before attributing it to MAC. In view of this, it would not be unreasonable to follow her clinically and see her again in 6 to 8 weeks. In this context, we also should consider the untoward impact of repeated radiation exposure derived from multiple CT scans. When a patient has an abnormality on CT scan, it often leads to further scans even if the symptoms do not match the previous findings, as in this case.
stiffness of the shoulders, legs, and thighs, and leg cramps), she was referred to the rheumatology department where the physical examination revealed muscle tenderness in her proximal arms and legs with normal strength, tender points at the elbows and medial side of the bilateral knees, significant tenderness of lower legs, and no synovitis.

Dr. Monach, can you walk us through your approach to this patient? Are we seeing manifestations of fibromyalgia? What diagnoses concerns you and how would you proceed?

Dr. Monach. The history and exam are most helpful in raising or reducing suspicion for an underlying inflammatory disease. Areas of tenderness described in her case are typical of fibromyalgia, although it can be difficult to interpret symptoms in the hip girdle and shoulder girdle because objective findings are often absent on exam in patients with inflammatory arthritis or bursitis. Similarly, tenderness at sites of tendon insertion ( enthuses) without objective abnormalities is common in different forms of spondyloarthritis, so tenderness at the elbow, knee, lateral hip, and low back can be difficult to interpret. What this patient is lacking is prominent subjective or objective findings in the joints most commonly affected in rheumatoid arthritis and lupus: wrists, hands, ankles, and feet.

Dr. Swamy. Initial laboratory data include an erythrocyte sedimentation rate of 79 with a normal C-reactive protein. A tentative diagnosis of polymyalgia rheumatica is made with consideration of a trial treatment of prednisone. Dr. Monach, can you explain why RA comes up now on serology but was not considered initially? Why does this presentation fit RA, and was her response to treatment typical? How does this fit in with her previous diagnosis of fibromyalgia? Was that just an atypical, indolent presentation of RA?

Dr. Monach. Though her presentation is atypical for RA, in elderly patients, RA can present with symptoms resembling polymyalgia rheumatica. The question is whether she had RA all along (in which case “elderly onset” would not apply) or had fibromyalgia and developed RA more recently. The response to empiric glucocorticoid therapy is helpful, since fibromyalgia should not improve with prednisone even in a patient with RA unless treatment of RA would allow better sleep and ability to exercise. Rheumatoid arthritis typically responds very well to prednisone in the 5-mg to 15-mg range.

Dr. Swamy. Given the new diagnosis of an inflammatory arthritis requiring immunosuppression, bronchoscopy with BAL is performed to evaluate for the presence of MAC. These cultures were positive for MAC. Dr. Fine, does the positive BAL culture indicate an active MAC infection?

Dr. Fine. Yes, based on these updated data, the patient has an active MAC infection. Active infection is defined as symptoms or imaging consistent with the diagnosis, supporting microbiology data (either 2 sputum or 1 BAL sample growing MAC) and the exclusion of other causes. Previously, this patient grew MAC in just one expectorated sputum; this did not meet the microbiologic criteria. Now sputum has grown in the BAL.
sample; along with the CT imaging, this is enough to diagnosis active MAC infection.

Treatment for MAC must consider the details of each case. First, this is not an emergency; treatment decisions should be made with the rheumatologist to consider the planned immunosuppression. For example, we must consider potential drug interactions. A specific point should be made of the use of tumor necrosis factor (TNF)-α inhibition, which data indicate can reactivate TB and may inhibit mechanisms that restrain mycobacterial disease. Serious cases of MAC infection have been reported in the literature in the setting of TNF-α inhibition.\(^5,6\) Despite these concerns, there is not a contraindication to using these therapies from the perspective of the active MAC disease. All of these decisions will impact the need to commit the patient to MAC therapy.

> **Dr. Swamy.** Dr. Fine, what do you consider prior to initiating MAC therapy?

> **Dr. Fine.** The decision to pursue MAC therapy should not be taken lightly. Therapy often entails prolonged multidrug regimens, usually spanning more than a year, with frequent adverse effects. Outside of very specific cases, such as TNF-β inhibition, MAC is rarely a life-threatening disease, so the benefit may be limited. Treatment for MAC is certainly unlikely to be fruitful without a diligent and motivated patient able to handle the high and prolonged pill burden. Of note, it is also important to keep this patient up-to-date with influenza and pneumonia vaccination given her structural lung disease.

> **Dr. Swamy.** The decision is made to treat MAC with azithromycin, rifampin, and ethambutol. The disease is noted to be nonfibrocavitary. The patient underwent monthly liver function test monitoring and visual acuity testing, which were unremarkable. Dr. Fine, can you describe the phenotypes of nontuberculous mycobacterial (NTM) disease?

> **Dr. Fine.** There are 3 main phenotypes of NTM.\(^3\) First, we see the elderly man with preexisting lung disease—usually chronic obstructive pulmonary disease—with fibrocavitary and/or reticulonodular appearance. Second, we see the slim, elderly woman often without any preexisting lung disease presenting with focal bronchiectasis and nodular lesions in right middle lobe and lingula—the Lady Windermere syndrome. This eponym is derived from Oscar Wilde’s play “Lady Windermere’s Fan, a Play About a Good Woman,” and was first associated with this disease in 1992.\(^7\) At the time, it was thought that the voluntary suppression of cough led to poorly draining lung regions, vulnerable to engraftment by atypical mycobacteria. Infection with atypical mycobacteria is associated with this population; however, it is no longer thought to be due to the voluntary suppression of cough.\(^7,8\) Third, we do occasionally see atypical presentations, such as focal masses and solitary nodules.

> **Dr. Swamy.** At 1-year follow-up she successfully completed MAC therapy and noted ongoing control of rheumatoid symptoms.

**Author disclosures**

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**References**


