Myalgia with Elevated Inflammatory Markers in an Obese Young Female: Fibromyalgia or Polymyalgia Rheumatica?

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Conflict of interest: None declared

Patient: Female, 38
Final Diagnosis: Fibromyalgia
Symptoms: Myalgia • pain
Medication: —
Clinical Procedure: —
Specialty: Rheumatology

Objective: Mistake in diagnosis
Background: Fibromyalgia (FM) is a common disorder of diffuse musculoskeletal pain. It is distinctly different from polymyalgia rheumatica (PMR), a disease seen in people over the age of 50 years. Hallmark features of PMR are the presence of elevated erythrocytes sedimentation rate (ESR) and/or C-reactive protein (CRP). These markers are normal in FM. Obesity in itself can be associated with elevated CRP and ESR, and when obese patients present with myalgia and elevated inflammatory markers, diagnostic confusion can ensue.

Case Report: We describe a case of 38-year-old female with diffuse musculoskeletal pain and elevated ESR and CRP who was initially misdiagnosed with PMR and responded partially to steroids. She developed severe adverse effects from chronic steroid use. She was ultimately diagnosed with FM.

Conclusions: We highlight features to help clinicians avoid the pitfall of diagnosing PMR in young obese patients with FM and elevated inflammatory markers. In this case report, we discuss the features of FM, PMR, PMR-like symptoms presentation, and the association of obesity with elevated inflammatory markers.

MeSH Keywords: C-Reactive Protein • Fibromyalgia • Obesity • Polymyalgia Rheumatica

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Background

Polymyalgia rheumatica (PMR) is characterized by pain and stiffness, primarily in the shoulder and hip girdles. An age of 50 years or above is required for classifying a patient with PMR [1]. PMR is common in those with northern European ancestry and is accompanied by significantly elevated inflammatory markers. It is extremely rare in African-Americans [2]. Fibromyalgia (FM) is a common condition seen in 2–4% of the general population [3], manifested by chronic widespread musculoskeletal pain, and often accompanied by fatigue, cognitive disturbance, psychiatric symptoms, and multiple somatic symptoms. It can occur at any age but is most common in middle-aged females.

One of the features distinguishing FM from inflammatory conditions is the absence of elevated inflammatory markers in FM [4]. More recently, inflammatory fibromyalgia has also been described, although the subjects’ body mass index (BMI) was not reported [5]. Obesity has been independently linked to elevated inflammatory markers [6–8]. About 39.6% of the US population is obese [9]. Since obesity and FM are common, providers will likely encounter patients with FM who are obese and have elevated inflammatory markers. These patients can present a diagnostic dilemma and may receive unnecessary treatment. We describe a case of a 30-year-old obese female with FM who had elevated inflammatory markers and was initially diagnosed with PMR. She received prolonged treatment with steroids and then methotrexate. She developed significant adverse effects from the prednisone and came to our clinic for a second opinion, where she was diagnosed with FM. We aim to highlight the association of obesity and inflammation and discuss how it can confound the diagnosis of FM. This case emphasizes the importance of treating the patient and not focusing exclusively on abnormal lab test results.

Case Report

A 30-year-old African-American woman with a past medial history of hypertension, asthma, gastroesophageal reflux disease, migraines, obesity (BMI of 41), and obstructive sleep apnea presented for evaluation of myalgia with elevated inflammatory markers. Her symptoms started the previous year with sudden onset of dysphagia, generalized muscle tenderness, and tender neck lymphadenopathy. Her primary care physician treated her with antibiotics and a prednisone taper. It is unclear why the prednisone was given initially. She responded fairly well, but the muscle symptoms recurred when the prednisone was stopped. She was placed back on prednisone (average dose of 25–35 mg daily) while awaiting a rheumatology consultation. Over this time, her myalgia became more widespread. Three months into the course of her disease, she was seen by a rheumatologist and an extensive autoimmune work up was negative except for an elevated ESR (100 mm/h, normal <29) and CRP (35 mg/L, normal <8.0). A magnetic resonance imaging (MRI) scan of the neck showed mild degenerative disk disease. A presumptive diagnosis of PMR was made and methotrexate was added to allow tapering of prednisone. The minimal effective prednisone dose that kept her functional was 20 mg daily. Higher doses provided more relief but not resolution of her symptoms. A malignancy evaluation by an oncologist, including computed tomography (CT) scan of the chest, abdomen, and pelvis, was reportedly negative. She also reported orthostatic symptoms, and evaluation by a neurologist, including tilt-table testing, was unremarkable. During this treatment period, she developed steroid-induced hypertension, steroid-induced diabetes, steroid-induced peripheral edema, and a 30-pound weight gain.

At our rheumatology clinic, she reported a history of diffuse muscle pain and said that she hurt all over and had exquisite tenderness to touch. At one time, her pain was so severe that she could not get out of the bed. She endorsed muscle pain and denied joint pain. She described extreme fatigue; her sleep apnea was untreated. She denied any fever, rashes, bowel symptoms, claudication, or giant cell arteritis symptoms. She did not smoke or drink alcohol. She was a mechanical engineer by profession. Her younger sister had complex regional pain syndrome that developed after a foot surgery.

At the time of her evaluation, she had been tapered off the prednisone for 3 weeks. She reported feeling achier. An examination revealed a cushingoid female with generalized tenderness to touch in multiple areas. She had full range of motion of her joints and had no difficulty in getting up from a sitting position. A joint exam revealed no synovitis. Muscle strength was intact. Her peripheral pulses were strong and symmetrical. Extensive autoimmune testing, including a myomarker panel, and serum protein electrophoresis were negative. ESR at our visit was 53 (normal less than 20 mm/h) and CRP was 27 (normal less than 8 mg/L).

Due to her protracted history, significant adverse effects from her current treatment, and elevated inflammatory markers, further evaluations were pursued while she remained off immunosuppressive therapy. She was referred to neurology, where an underlying muscle disease was ruled out. An electromyography of the left upper extremity was negative. A positron emission tomography (PET)/CT scan was unremarkable for any areas of inflammation or malignancy.

She was given a diagnosis of fibromyalgia. She was advised to stop the methotrexate and not to resume the prednisone. Fibromyalgia management principles were discussed and she was advised to treat her sleep apnea. She was also started on...
muscle relaxants, dietary modifications, and physical activity. On verbal follow-up several weeks later, she remained off immunosuppressive agents. She felt somewhat better and was relieved to no longer take prednisone. Her inflammatory markers continued to remain variably high.

Discussion

This case highlights the confounding influence of elevated CRP/ESR on medical decision-making. A young African-American female was diagnosed with PMR and treated with prednisone for several months. She developed significant adverse effects and her condition did not improve. This patient was a 30-year-old African-American, obese, had diffuse muscle pain rather than shoulder and hip girdle stiffness and pain, and she had not responded significantly to prednisone. All these features make the diagnosis of PMR unlikely. In this review, we briefly discuss features of PMR and FM and the influence of elevated inflammatory markers and obesity on clinical decision-making.

FM is the most common cause of generalized musculoskeletal pain in women between the ages of 20 and 55 years. FM is characterized by widespread musculoskeletal pain and fatigue, often accompanied by other somatic symptoms, as well as cognitive and psychiatric disturbance. FM is usually a diagnosis of exclusion in patients who present with chronic myalgias. Rendering a diagnosis of FM requires a careful clinical evaluation for any underlying condition that may be responsible for the FM. Clinical exam is negative for any synovitis and characterized by muscle tenderness. Laboratory testing is usually carried out to exclude other conditions such as spondyloarthritis, systemic autoimmune disorders, polymyalgia rheumatica, inflammatory myopathy, and hypothyroidism.

The annual incidence of PMR is up to 50/100 000 population starting from age 50 years, with peak above age 70 years [10]. Age above 50 years is a required criterion for PMR classification [1]. A diagnosis of PMR is extremely rare in young patients, especially at the age of 30, as in our patient. PMR in 40-year-old patients has been reported. These cases were confirmed to have PMR by PET imaging [11]. PET scanning has very good accuracy in diagnosing PMR [12]. Uptake at the ischial tuberosity, lumbar spinous process, and greater trochanter provide a high yield for diagnosing PMR [13]. Our patient had a negative PET scan.

Another distinct characteristic of PMR is a rapid and effective therapeutic response to low-dose glucocorticoids. A 75% improvement in clinical and laboratory parameters within 7 days of treatment with 15 mg of prednisone equivalent is consistent with PMR [14]. Our patient required high doses of prednisone, which were only marginally effective. She did initially get some symptomatic relief from the prednisone. Steroids are not effective in fibromyalgia management [15]. It is not entirely clear why she responded partially to the prednisone. Inflammatory foci have been found in the skin of a subset of FM patients and it is postulated that this may account for the response to non-steroidal anti-inflammatory drugs in some FM patients [16]. It is unclear if steroids have any role in pain modulation in FM patients with obesity-related inflammation. Inflammatory FM remains an open area for further research [17]. Steroids are used as adjuvants in many pain conditions [18]. Some of the response in this case could also have been a placebo effect.

There is increasing evidence that obesity is characterized by chronic and low-grade systemic inflammatory response. An association between abdominal obesity and increased levels of inflammatory markers such as CRP has been noted [6,7,19]. Abdominal adipose tissue is a major source of cytokines, including tumor necrosis factor-alpha and interleukin-6, which in turn increase hepatic CRP production [20,21]. An association between CRP and the presence of obesity and comorbidity has been reported in FM as well [22]. Careful interpretation of clinical data is necessary in obese patients, as elevated CRP and ESR may be a non-specific finding and not necessarily reflective of any underlying disease process.

Elevated inflammatory markers in an obese patient, however, should not be automatically attributed to obesity. An appropriate workup should be pursued based on clinical evaluation. More common rheumatologic disorders such as rheumatoid arthritis, spondyloarthritis, or connective tissue diseases can present with symptoms compatible with FM and must be ruled out. Sometimes, PMR-like symptoms in young females can be the initial manifestation of rare disorders such as Takayasu arteritis [23]. In patients younger than age 50, typical PMR is an uncommon diagnosis and should be distinguished from what has been described as atypical PMR, which can be a manifestation of occult malignancy [24]. We refer to atypical PMR as PMR-like presentation. Features of PMR-like symptoms include age under 50 years, absence of prolonged morning stiffness, involvement of only 1 site, ESR <40 or >100 mm/h, peripheral arthritis, asymmetric involvement at atypical sites, and partial or delayed response to steroids. Patients with such presentation should be investigated for disseminated cancer, connective tissue disease, or other vasculitic disorders [25]. Our patient did not have any of these conditions. PMR is very unlikely in young patients; therefore, a careful evaluation for conditions presenting with PMR-like symptoms should be pursued.

The high CRP and ESR in our patient likely prompted a diagnosis of PMR but was emanating from the underlying obesity. The classic teaching is that CRP and ESR are not elevated in FM. However, as our case illustrates, an exception is the patient
with FM who is obese. Our patient’s history was typical for fibromyalgia. Her symptoms responded more favorably with fibromyalgia treatment and without the prednisone. Table 1 provides comparative features of FM, PMR, PMR-like symptoms, and FM with elevated inflammatory markers.

### Table 1. Comparative features of fibromyalgia, polymyalgia rheumatica, and their variants.

|                           | Fibromyalgia (FM) | Polymyalgia rheumatic (PMR) | Polymyalgia rheumatic like presentation | Fibromyalgia in obese patient |
|---------------------------|-------------------|-----------------------------|----------------------------------------|--------------------------------|
| Common age (years)        | 30–50             | >50                         | <50                                    | <50                           |
| Sex                       | Females>Males     | Females>Males               | Variable                               | Females>Males                 |
| Race                      | Variable          | Caucasian                   | Variable                               | Variable                      |
| Anatomic areas            | Diffuse           | Shoulder and hip girdle     | Variable                               | Diffuse                       |
| Somatic symptoms          | Dominant          | Minimal                     | Minimal to variable                    | Dominant                      |
| Peripheral synovitis      | Absent            | May be present              | May be present                         | Absent                        |
| Inflammatory markers      | Normal            | Elevated                    | Variable                               | Elevated                      |
| Response to 15 mg prednisone | Usually none | Excellent                   | Partial                                | None to partial                |

### Conclusions

PMR is almost exclusively a diagnosis made in patients over 50 years old. FM and PMR can have some similarities but they are distinct disorders. Obesity and FM are common conditions and obese patients with FM may present with elevated inflammatory markers. It is important for the treating provider to understand the association between obesity and elevated CRP and ESR. However, before labelling obese patients presenting with elevated inflammatory markers as having FM, appropriate clinical workup should be pursued to exclude alternate diagnoses.

### Department and Institution where work was done

Division of Rheumatology, Mayo Clinic, Scottsdale, AZ, U.S.A.

### Conflicts of interest

None.

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