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Authors

Borad, Amruti

Poa, Hyunah

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CLINICAL VIGNETTE

Polymyalgia Rheumatica versus Late-onset Rheumatoid Arthritis

Amruti Borad, D.O., and Hyunah Poa, M.D.

Introduction

Pain is one of the most common chief complaints. Given there are multiple etiologies, it is often challenging to make the correct diagnosis and provide the most appropriate treatment and to avoid complications of possible underlying disease. Rheumatologic diseases are a common cause of pain, but diagnosis can be difficult as patients do not always meet a specific set of criteria. There are several rheumatologic diseases with overlapping findings. We present with this dilemma, involving an Asian male with likely Polymyalgia Rheumatica (PMR) but with features of Late-onset Rheumatoid Arthritis (LO-RA).

Case Report

The patient is a 72-year-old Asian male with distant history of C6-7 nerve compression, left knee osteoarthritis, and temporomandibular joint dysfunction; he presented to his primary care physician (PCP) with jaw pain and left hand tingling and numbness for one week. The jaw pain was deemed likely secondary to temporomandibular joint (TMJ) dysfunction. The PCP decided to monitor the hand symptoms. One week later, he returned for progressively worsening hand paresthesias, and new onset neck and shoulder stiffness and pain.

The neck pain was felt to be secondary to worsening of known bilateral cervical disc protrusions and moderate nerve compression at C5-6 and C6-7. Thus cervical spine x-rays and MRI were ordered, and he was referred for osteopathic manipulative therapy (OMT). The cervical spine x-rays demonstrated mild degenerative disc disease at C6-7 and multilevel facet arthropathy, but MRI revealed C5-C6 and C6-C7 spinal canal stenosis secondary to disc bulging, left greater than right neuroforaminal narrowing, mild to moderate hypertrophic facet joint degeneration and possible degenerative autofusion at the level C3-4. Shoulder x-rays were completed a week later and were positive for severe AC joint OA. He benefitted significantly from physical therapy (PT), OMT, trigger point injections, acupuncture, and cyclobenzaprine. Approximately one month after symptom onset, he returned with a few days of left hand swelling. He stated that he has had intermittent left hand swelling and weakness since his neck pain had begun, but it would resolve after his home exercises, thus did not find it concerning enough to discuss with his PCP. It was originally thought to be secondary to a questionable NSAID allergy, but it progressed to the point where he was unable to grip with his left hand. He was referred to a Rheumatologist and additional testing including ESR, CRP,

RF, anti-CCP, ANA, and bilateral hand x-rays. The ESR and CRP were significantly elevated, but RF, anti-CCP, and ANA were negative. Bilateral hand x-rays revealed right wrist joint space narrowing and erosions, suggestive of inflammatory arthritis, along with superimposed wrist and hand osteoarthritis. Surprisingly, the left wrist joint was normal and had only mild interphalangeal joint osteoarthritis. The patient deferred Rheumatology consultation until a few weeks later, at which time he was diagnosed with possible Polymyalgia Rheumatica (PMR) versus a seronegative inflammatory arthritis. Prednisone 10 mg orally daily was initiated and given significant symptomatic improvement within a few days, and given he continues to have pain relief months later on low dose prednisone; his most likely diagnosis is PMR.

Discussion

Polymyalgia Rheumatica is an inflammatory rheumatic disease that is characterized by neck, shoulder, and pelvic girdle aching and morning stiffness. It is one of the most common rheumatologic diseases, only second to Rheumatoid Arthritis (RA). It is most likely to occur over the age of 50 with a peak incidence between 70- to 80-years-old. It is two to three times more likely to occur in females versus males.¹ The prevalence is highest in Scandinavian countries, and uncommon in Asians, African Americans, and Latinos, thus suggesting a genetic influence.^{2,3}

There is no single definitive etiology. It is likely a combination of genetic regulation of inflammatory markers, specifically TNF-alpha and IL-6, genetic polymorphisms of IL-1 receptor antagonists, HPA axis suppression, decreased adrenal hormone production, specifically DHEA and cortisol, and environmental factors.^{3,4}

There is no single test or defined criteria to diagnose PMR. The European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) attempted to create guidelines; however, they were significantly less sensitive and specific than for other diseases. Thus, PMR is usually a clinical diagnosis. General criteria include: ≥ 50 years old; abrupt onset proximal, symmetrical, morning aching and stiffness for ≥ 30 minutes, including stiffness after periods of inactivity, in 2 out of 3 regions (neck/torso, shoulder [most commonly, pain with activity and sleep], proximal arm, hip, proximal thigh), over a 2 week period; ESR ≥ 40 ; and rapid resolution with low dose oral steroids, often within three days in 50-70% of patients.⁵⁻⁹

Distal, mild, non-erosive, occasionally asymmetrical synovitis, and bursitis, of which are speculated to be the causes of stiffness, occurs in 50% of patients and may occur in the metacarpophalangeal (MCP) joints, wrists, and knees.¹⁰

Pitting and non-pitting edema and tenosynovitis of the hands, wrists, feet, and ankles may be a presenting sign of PMR, and carpal tunnel syndrome (CTS) occurs in approximately 10-15% of patients.¹⁰ Muscle tenderness itself is usually not prominent. There can be decreased joint range of motion (ROM), especially shoulder abduction. Subjective, but often not objective, weakness exists. Patients may experience systemic, non-specific symptoms, such as fatigue, weight loss, and depression.¹¹ Atypical presentations usually occur in those age 40-50 years old; initial symptoms are asymmetrical; and ESR \leq 40, but an elevated CRP. If ESR and CRP are both low, diagnosis of PMR is less likely.¹² Giant Cell (Temporal) Arteritis (GCA) should always be included in the differential. GCA classically presents as a new onset headache, jaw claudication, scalp tenderness, vision changes, cough, and high fevers.¹³ Exam findings for PMR include limited shoulder abduction, typically not past 90°. Passive ROM is greater than active ROM in the neck, shoulders, hips, and low back; there may be signs of arthritis, tendonitis, bursitis, and muscle strength is preserved. The exam should include evaluation of tender points and temporal artery engorgement and tenderness. Laboratory work up should initially include a complete blood count (CBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP).¹¹ Normocytic anemia and reactive thrombocytosis may be present, but the focus is normally on the ESR and CRP. The ESR is often >100 , but some studies show levels <40 .¹⁴

Studies vary in regards to significantly higher CRP levels in comparison to ESR levels.¹² Serological studies, such as antinuclear antibody (ANA), rheumatoid factor (RF), and cyclic citrullinated peptide antibodies are usually negative. Occasionally, alkaline phosphatase (ALP) levels will be elevated. There is no single diagnostic imaging study but usually begins with x-rays of the suspected joints.¹⁵ They are usually negative, and synovitis is never erosive.¹⁶ Ultrasound (US) or Magnetic Resonance Imaging (MRI) may show extra-articular and synovial inflammation, representing tenosynovitis, and/or bursitis.¹⁶ Despite positron emission tomography (PET) scans having discovered large vessel vasculitis, this is unlikely if there are no symptoms of GCA, and thus there is little current clinical value for PET scan.¹⁷ Mainstay treatment is prednisone 10-20 mg daily with taper based on symptomatic improvement. Approximately 50-70% of patients will improve within 3 days. A lack of response should prompt further investigation into alternative diagnoses.⁸

The differential diagnosis of PMR is extensive; however, the two most important are GCA and RA as these patients often have findings that overlap with and thus are difficult to differentiate from PMR. Thus, the following will be a discussion of similarities and differences between PMR and GCA and RA.

Both PMR and GCA have a similar sequence polymorphism within the HLA-DRB1 gene that is not found in RA.¹⁸ Both are also influenced by environmental factors. PMR is two to three

times more common than the GCA, but ten percent will experience GCA symptoms at any time during the course of PMR, thus it is important to ask about classic GCA symptoms at every follow-up visit (temporal artery tenderness, jaw claudication, etc).^{2,19} In GCA, patients can develop high fevers and significantly elevated ALP levels. Classic GCA symptoms are normally lacking in a true diagnosis of PMR, thus if there are no such signs or symptoms present, a temporal artery biopsy is usually not performed.²⁰ If a patient has true PMR, symptoms will drastically improve within three days to a month of initiating high dose prednisone. If this does not occur, and high fevers or significantly elevated ESR levels persist, consider possible diagnosis of GCA. If a large artery is involved, a biopsy, which is not affected by prednisone use, may be negative; if suspicion for GCA is still high, vascular imaging may be necessary.²¹

In terms of PMR and RA, there are no consistent differences in alleles. If there is symmetric synovitis in an elderly patient, it is often difficult to distinguish between the two diagnoses (specifically seronegative RA) and can be considered a diagnoses of late-onset RA (LO-RA) or elderly onset RA (EO-RA).²² In comparing PMR to RA, PMR patients are usually younger, present more commonly with myalgias and less often PIP, MCP, and wrist joint arthritis. PMR usually presents with significantly higher levels of inflammatory markers (ESR, CRP, IL-6) and greater reduction in symptoms with prednisone (usually 15 mg daily, followed by a taper), usually within 1 month.³ Prednisone and methotrexate versus prednisone alone results in a greater response. However, prednisone and TNF-alpha inhibitors versus prednisone alone results in no significant difference in response or side effects.³ RA usually presents with symmetric, polyarthritis of the small joints, especially hands and feet, but also may present with many other extra-articular manifestations.^{3,23} RF and anti-CCP markers are usually positive, and joint erosions are often seen on x-rays. It is usually partially responsive to low-dose steroids and methotrexate is a common treatment. LO-RA normally presents as symmetrical mild synovitis, is non-erosive or less erosive given higher levels of IL-6, which protects bone. However, as in PMR, it has rapid and/or complete response to prednisone.³ Overall, there is significant overlap between PMR and RA. One study documented changing diagnosis of PMR to RA after 1 year. Another study showed inflammatory markers higher in PMR, while others report no difference. A physician may be able to differentiate between both by observing the rapidity of improvement of symptoms after initiating PMR-dose steroids, followed by a taper. A trial of RA treatments, such as methotrexate, may be useful if arthritis is not improving or evolves into RA. However, it may still take months to differentiate between both diagnoses.^{22,24,25}

Conclusion

The differential diagnosis of pain is broad and challenging, especially in the elderly. Overlap of symptoms, laboratory and imaging findings, and treatment responses are all confounding factors. As for PMR, further analysis of symptoms and certain lab values (specifically acute phase reactants and cytokines), especially in the elderly population with symmetrical inflammatory and musculoskeletal complaints, would assist in

differentiating between PMR and other conditions, and may provide for more appropriate treatment.³

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