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Polymyalgia Rheumatica-Like Onset of, and a Flare-up Pattern in Seropositive Rheumatoid Arthritis - 2 Cases and a Review: An Uncommon Face of a 'Not so Uncommon' Disease

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ABSTRACT

Rheumatoid arthritis (RA) and polymyalgia rheumatica (PMR) are inflammatory rheumatic diseases, each with its own characteristic features and typical presentation. However, diseases do not always present similar to the way they are outlined in the textbook. This article examines the cases of two American Indian patients who had a PMR-like presentation of RA. The first patient was vastly seronegative except for 14.3.3 ETA, a dynamic biomarker with high specificity for RA. This appears to be a novel presentation, as there have not been prior documented cases of PMR-like onset of isolated 14.3.3 ETA+ RA. The second patient was noted to have an atypical PMR-like exacerbation of strongly triple seropositive RA. Intense lifestyle treatment combined with standard/conventional therapy led to a significant resolution of symptoms in both cases.

Keywords

Rheumatoid arthritis, Autoimmune diseases, Polymyalgia rheumatica, Biomarker.

Introduction

Rheumatoid arthritis (RA) is an autoimmune rheumatic condition, i.e. immune mediated disease, characterized by a constellation of articular and extra-articular manifestations that is present in about 0.5-1.0% of the general population [1]. It can occur at any age, but the incidence is greatest in 20-50 years of age, and the disease is 2–3 times more common in women than in men [1]. It primarily presents as symmetric, polyarticular arthralgia, swelling, and stiffness [1], and can affect any peripheral joint, but classically involves the metacarpophalangeal (MCP), proximal interphalangeal (PIP), second through fifth metatarsophalangeal (MTP), wrist, and knee joints [2]. Morning stiffness that is located in the affected joints lasting greater than 1 hour is a typical feature of inflammatory rheumatic diseases including RA [2]. Extra-articular manifestations of RA include constitutional symptoms (fatigue, fever, weight loss, and malaise), subcutaneous rheumatoid nodules, rheumatoid vasculitis, muscular weakness and atrophy, pleuropulmonary involvement etc. [2]. The nature of the course of this disease is progressive, and it has the potential to cause significant disability and decline in functional status of affected individuals. This disease exhibits an increased prevalence in individuals of American Indian/Native American (AI/NA) descent [3]. Additionally, those of AI/NA descent often see earlier onset and increased severity of RA [3]. Multiple modalities of treatment

for this condition exist, and with proper management including an intense lifestyle treatment strategy + disease modifying anti-rheumatic drug (DMARD) therapy, RA can have a favorable outcome.

Polymyalgia rheumatica (PMR) is the most common inflammatory rheumatic disease of the elderly [4]. It is an autoimmune condition of unclear etiology that presents after the age of 50, more common in women than men [4] predominantly as symmetric, bilateral aching of the shoulder and pelvic girdle [4]. It can be associated with giant cell arteritis in a significant proportion of cases. PMR symptom onset can be acute or gradual. About one-third of PMR patients have systemic manifestations such as anorexia, malaise, and low-grade fever. Clinical features of PMR include the previously described symptoms, as well as bilateral upper arm tenderness, neck pain, distal musculoskeletal manifestations such as arthritis/arthralgia of the hands, pitting edema of the hands, and carpal tunnel syndrome [4]. One of the most characteristic features of PMR is its relatively rapid response to glucocorticoid administration. Patients may need to take glucocorticoids daily for multiple months and occasionally up to one or several years in order to achieve sufficient control of their symptoms [4]. Glucocorticoids are the treatment of choice for PMR, and the starting dose is 15-20 mg daily [4]. Prognosis of PMR is favorable and survival is similar to survival of the general population with early diagnosis and treatment [4]. Given the increased prevalence of rheumatoid arthritis, systemic lupus erythematosus, connective tissue diseases, and spondyloarthropathies in the AI/NA population, it is likely the prevalence of PMR in this population is increased as well [5]. There has yet to be a definitive study regarding this phenomenon with PMR and the AI/NA population specifically.

Case 1

A 59-year-old AI/NA male presented with diffuse periarticular achiness and stiffness that had started rather abruptly without any obvious inciting factors about 3 months ago. The periarticular muscle stiffness made it somewhat difficult to turn his head or move his joints. It was present near his bilateral shoulders and hips extending down to his knees. He had to seek an emergency department evaluation and was started on oral prednisone with a miraculous relief. However, as the dose of prednisone was decreased, the symptoms came back with a vengeance. He was referred to Rheumatology. On physical examination, the patient had mild Cushingoid swelling of his face, mild tenderness to palpation of periarticular muscles located near bilateral shoulders, elbows, and knees. A detailed rheumatologic workup was requested, and he was counseled to taper down his prednisone dose in a much gentler fashion and to start hydroxychloroquine 200 mg twice daily to serve as a DMARD as well as a steroid sparing agent. Over a period of 1 month, the patient stated his symptoms were markedly improved, and he denied any joint swelling or pain on the follow-up visit. The laboratory results showed a normalization of the acute phase reactants, a negative rheumatoid factor (RF), and negative anti-cyclic citrullinated peptide antibodies (CCP). However, he tested positive for the 14.3.3 ETA protein marker. With a diagnosis of an unusual PMR-like onset of seropositive RA, the patient was counseled to continue hydroxychloroquine along with a tapering schedule of prednisone and of course, adhering to a low-fat, whole food, plant-based anti-inflammatory diet.

Case 2

A 51-year-old AI/NA female who presented to the rheumatology clinic for follow-up of rheumatoid arthritis. At her prior visit about 6 months ago, it was decided to discontinue methotrexate due to transaminitis. It was also decided that the patient would continue taking etanercept 50 mg subcutaneously weekly and hydroxychloroquine 200 mg orally daily. Due to insurance/reimbursement constraints, the patient was not able to get the etanercept for about 1 month. The patient started experiencing significant achiness and stiffness in and around the pectoral and pelvic girdles requiring a visit to the Indian Health Services emergency department. The cardiac work-up including electrocardiogram, chest radiograph, and laboratory studies including high-sensitivity troponin were negative. The patient saw her primary care provider and was started on a tapering schedule of oral prednisone, which resolved the previously described shoulder joint and scapular region stiffness and pain. On the physical examination after the prednisone taper, the patient was free of active synovitis in peripheral and axial joints. Acute phase reactants had normalized. This patient had a flare-up of her strongly RF and CCP positive RA that was PMR-like in nature. This was quite remarkable especially given her miraculous and completely positive response to glucocorticoid administration. The patient continues to do well on a regimen of low-fat whole-food plant-based nutrition, etanercept, and hydroxychloroquine.

Discussion

The unique presentation of the two previously described cases has profoundly humbling implications. An article published in 1979 described elderly patients that presented with PMR-like symptoms of generalized aches and pains particularly in the shoulders and the pelvic girdle that 2.5 months later developed pain, swelling, and signs of synovitis in several joints in a symmetrical pattern, when a diagnosis of rheumatoid arthritis was made [6]. In a prospective study of patients with PMR-like onset of symptoms published in 2001, the authors studied a cohort of 116 patients where multiple patients presented with PMR-like onset of RA [7]. These patients were diagnosed with RA according to the 1987 ACR criteria, which did not utilize the newer and more specific markers, CCP and 14.3.3 ETA protein. Our first patient presented with classic PMR-like features but tested positive for 14.3.3 ETA protein, which is 91-93% specific for RA and can help diagnose early

RA in 20% cases negative for RF and CCP . The second patient presented with a flare-up of her established seropositive RA in a PMR-like fashion highlighting the significant overlap between the two immune-mediated rheumatic conditions.

Conclusion

The rather uncommon PMR-like presentation of these two patients (1 at the onset, 1 on follow-up) of a not so uncommon condition, i.e. RA, emphasizes the need for the clinician to astutely and diligently seek out unusual presentations of not so unusual diseases in Medicine. To the best of our knowledge, this is the first observation of seropositive RA presenting or flaring-up in a PMR-like fashion in the AI/NA population. Larger studies need to be done.

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