

CASE REPORT

An Unusual Course of PMR

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A 75-year-old woman presented to rheumatology for an evaluation polymyalgia rheumatica (PMR). The patient had acute onset of severe neck and bilateral shoulder pain to the point where she was unable to lift her arms. She had no lower extremity pain or weakness. She presented initially to an outside emergency room where she was noted to have an elevated ESR and diagnosed with presumed PMR. She was started on prednisone 40mg daily with rapid improvement of her symptoms and then tapered to prednisone 20mg daily when she was seen in rheumatology. On initial visit, she had minimal pain and stiffness. She had no headaches, no jaw claudication or vision changes. Her only concern was that she was experiencing mood changes on the prednisone and was eager to taper her dose further.

Her past medical history was significant for having granuloma annulare of the skin for over 30 years. Topical treatments were ineffective and the patient continued to have chronic, persistent skin lesions. The rashes, though, did not bother her so she never sought out systemic treatment. She also had cervical disc disease, osteoporosis with history of a compression fracture, hyperlipidemia, esophageal reflux and basal cell skin cancer. Her medications included prednisone 20mg daily, atorvastatin, alendronate, calcium and vitamin D, ranitidine, tacrolimus ointment and fish oil. Past surgical history was significant for a splenectomy and right arm fracture repair after a motor vehicle accident. She was a prior smoker who quit at the age of 40. She drinks a few glasses of wine a week and has no history of prior drug use. She has no known family history of autoimmune disease.

On physical exam she was a well appearing woman in no apparent distress. Her heart and lung exams were normal. She had no myofascial pain. Her joints were non-tender, non-swollen and with normal range of motion. The only significant finding was a large granuloma annulare skin lesion that spanned the length of her back. Her initial labs showed a normal CBC, normal chemistry, normal TSH, normal CK and a mildly elevated ESR of 30 (normal <25). She also had negative ANCA, rheumatoid factor and anti-CCP serologies. Her ANA was positive 1:160 speckled, thought to be due to her granuloma annulare. Her autoimmune panel was otherwise negative including dsDNA, SSA, SSB, Smith, RNP, centromere, Scl-70 and TPO serologies. There were no contributing imaging studies.

Clinical course: The patient was initiated on a prednisone taper but was unable to taper below 12.5mg daily without recurrence of her pain and stiffness. Follow-up labs were remarkable for an elevation of her liver enzymes AST 65 (normal 13-47), and ALT 100 (normal 8-64). The patient stopped drinking alcohol and her statin was held. She was negative for hepatitis B and hepatitis C. Her anti-mitochondrial antibody serology was normal and her anti-smooth muscle antibody was borderline positive at 1:20 (normal <1:20). Abdominal ultrasound showed no evidence of fatty liver. Repeat liver tests showed rising levels; AST 154 (normal 13-47), and ALT 245 (normal 8-64). She was to hepatology for further evaluation. Additional labs included hepatitis E IgM positive, suggestive of an acute hepatitis E infection. A confirmatory hepatitis E viral DNA was sent to the CDC, but would not return for one month.

Since an acute viral infection with hepatitis E was a concern, another prednisone taper was tried, in hopes to help her clear the infection. On repeat labs, her liver function tests continued to rise to AST 207 (normal 13-47), and ALT 388 (normal 8-64). The patient's pain and stiffness also returned and the prednisone dose had to be increased back to 15mg daily in order to alleviate her pain. The CDC results eventually returned showing a negative hepatitis E viral load. A liver biopsy showed findings consistent with autoimmune hepatitis. The patient was started on azathioprine but was unable to tolerate the medication due to severe nausea, vomiting and abdominal pain. She was switched to mycophenolate which was well tolerated. She had improvement of her liver tests, improvement of her granuloma annulare and increased success in tapering her steroids.

Discussion

This patient had a classic presentation of polymyalgia rheumatica (PMR). The diagnosis of PMR is a clinical diagnosis typically in patients over 50 years old that present with new bilateral shoulder and/or hip pain in the presence of morning stiffness of >45 minutes and elevated inflammatory markers (ESR/CRP).¹ Rapid resolution of symptoms with low dose corticosteroids as seen in this case is also suggestive of the diagnosis.² The typical management of PMR begins with prednisone treatment in low to moderate doses between 10-25mg daily. The prednisone regimen is then slowly tapered every 2-4 weeks while monitoring symptoms of disease activity, inflammatory markers and adverse events to find the lowest effective steroid dose.³ In most patients, PMR runs a

self-limited course, and glucocorticoid therapy can eventually be discontinued after one to two years. However, some patients have persistent or relapsing disease that requires a longer treatment.²

This patient's clinical course became more complex after developing abnormal liver tests, thought to be initially due to hepatitis E when her Hepatitis IgE IgM level returned positive. There is no known association between Hepatitis E and PMR but general arthralgias and myalgias have been reported with an acute infection. Other extra-hepatic manifestations reported with hepatitis E infection include neuralgic amyotrophy, Guillain Barre syndrome, cryoglobulinemia, glomerulonephritis, pancreatitis, meningitis, thyroiditis, myocarditis and hematologic abnormalities.⁴ A higher rate of anti-hepatitis E virus seroprevalence has been reported in patients with autoimmune hepatitis when compared to healthy controls, patients with RA as well as patients with hepatitis B or C.⁵ It is unclear if the hepatitis E infection is a trigger for the development of autoimmune hepatitis or if there are higher false positive lab results due to other elevated circulating autoimmune antibodies.⁴

The patient's liver abnormalities were concluded to be due to autoimmune hepatitis based on her liver biopsy, borderline positive smooth antibody level, negative PCR IgE viral levels and positive response to steroid treatment. Concurrent autoimmune diseases are common in patients with autoimmune hepatitis and mirror the full range of known autoimmune diseases. In a study of 278 patients with autoimmune hepatitis, 111 (40%) were found to have concurrent autoimmune disease. Besides overlap syndromes for primary biliary sclerosis, autoimmune thyroiditis was the most common concurrent disease (28 patients, 10%). Other concurrent autoimmune diseases comprised of vitiligo (5 patients), rheumatoid arthritis (5 patients), Sjogren syndrome (4 patients), ulcerative colitis (4 patients), celiac disease (3 patients), systemic lupus (2 patients), type I diabetes (2 patients), multiple sclerosis (2 patients), and polymyalgia rheumatica (2 patients).⁶

Furthermore, the patient had long-standing granuloma annulare. Granuloma annulare is a benign granulomatous inflammatory skin condition of unknown cause. There have been many proposed disease associations and triggers. The most common disease associations reported have been with insulin-dependent diabetes and dyslipidemia. Other reported associations include thyroid disease, uveitis, HIV and hepatitis B and C. Many triggers have also been reported that include tattoos, lightening, bee stings, vaccines to Hepatitis B, tetanus and BCG, as well as medications such as allopurinol, and topiramate. Medications with anti-TNF therapy and interferon have shown to help in some cases and be a triggers in others.⁷ Treatment is not always needed as spontaneous resolution of granuloma annulare is frequently observed, especially in localized forms. Disseminated manifestations as seen in this patient tend to persist longer. Treatment options include topical steroids, tacrolimus ointment or systemic treatments with dapsone, hydroxychloroquine, retinoids, fumaric acid, cyclosporine, and anti-TNF α .⁸

It is unusual to have a combination of granuloma annulare, PMR and autoimmune hepatitis in the same patient. The patient's symptoms did not improve until all components of her autoimmunity were addressed with both prednisone and mycophenolate. This case highlights the need to monitor for overlaps of autoimmune diseases that can be contributing to the overall clinical picture.

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