

When the plot thickens: a rare complication of rheumatoid arthritis

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a common illness with many extraarticular manifestations. Rheumatoid pachymeningitis is a rare neurologic complication of this common disease. Here in we present a patient with longstanding RA who developed this uncommon complication.

Case description: A 75-year-old woman with longstanding RA presented to the clinic with multiple seizure-like spells per day. Upon admission to the hospital, brain MRI showed enhancement of the meninges. After an extensive workup for possible other infectious or inflammatory causes, the patient was diagnosed with rheumatoid pachymeningitis.

Conclusion: Rheumatoid pachymeningitis is a rare complication of RA that usually occurs late in the disease course. It may have many neurologic manifestations include mimicking seizure or stroke and must be considered in patients with RA presenting with neurologic symptoms. Pachymeningitis is treated distinctly from articular RA, so early recognition can lead to appropriate treatment.

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1. Introduction

Rheumatoid arthritis (RA) is a common disease which affects around 1% of the adult population and is more common in women [1]. While RA predominantly causes joint disease, there are significant extraarticular manifestations. These include neurologic manifestations like central nervous system vasculitis or meningitis. The meningitis associated with RA is sometimes called pachymeningitis and is a rare manifestation of this common disease [2]. We present a case of a patient with longstanding rheumatoid arthritis initially presenting with a focal seizure who was found to have RA pachymeningitis.

2. Case description

A 75-year-old woman with a nine year history of RA presented with a three week history of worsening right upper extremity paresthesias and weakness accompanied by a frontal headache. She reported having difficulty with her right hand as if it 'wouldn't go where I want it to go.' She also reported feeling facial jerks and sometimes having uncontrollable rhythmic movements of her right hand and leg. During these episodes, which lasted about 20 minutes, she had difficulty talking without loss of consciousness or confusion. She had no bladder or bowel


incontinence during the episodes and did not bite her tongue. The episodes started gradually but at the time of presentation they were occurring multiple times per day. Along with the spells, she reported nausea and dizziness. She denied any history of fever or chills, neck pain, shortness of breath or chest pain. She had no increase in baseline joint pain.

Her medical history was significant for RA, controlled hypertension, and hip osteoarthritis. She was taking leflunomide, hydroxychloroquine, and low dose prednisone (7.5 mg per day). She did not smoke cigarettes or drink alcohol.

On exam, her blood pressure was 144/84 mm Hg and other vital signs were normal. On neurologic exam, she was oriented to person, place and time. Cranial nerve exam was normal. On motor exam, she had 4/5 symmetric strength in her upper and lower extremities without fasciculations. Her reflexes were 2/4 in upper and lower extremities. Her sensation was intact.

She underwent evaluation for an acute stroke including a non-contrast head CT head and a brain MRI. MRI showed no acute stroke, but did show diffuse pachymeningeal enhancement in the supratentorial pachymeninges and scattered additional infratentorial enhancement. (Figures 1 and 2)

Chest x-ray, complete metabolic panel (CMP), complete blood count (CBC), and urinalysis (UA)

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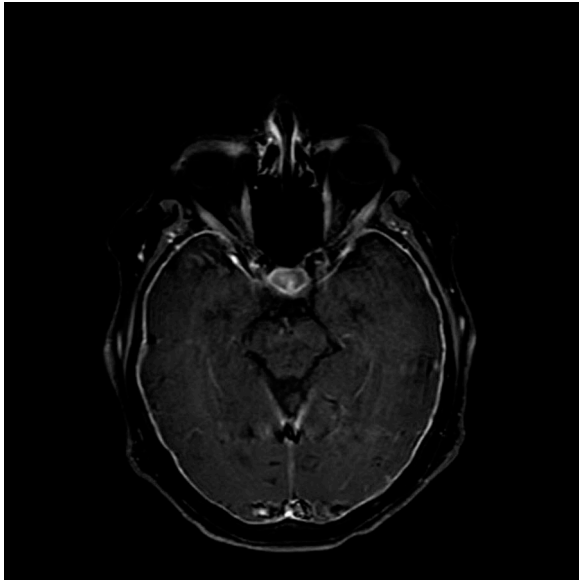


Figure 1. MRI showing diffuse T2 hypertensity of meninges.

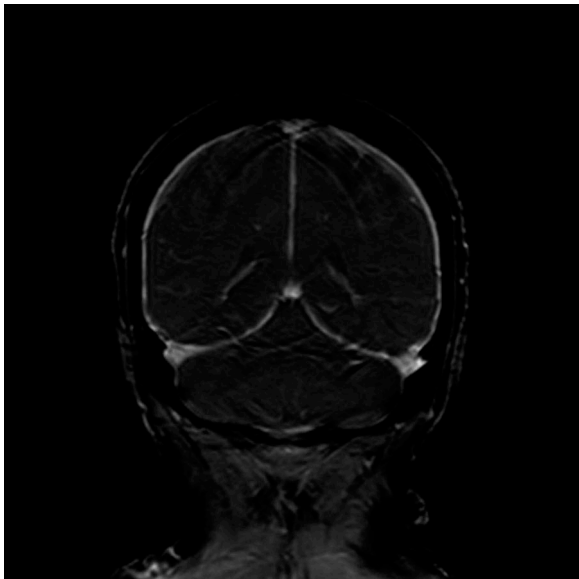


Figure 2. MRI showing diffuse T2 hyperintensity of meninges.

were unremarkable. The patient was admitted for further work-up.

Shortly after admission, the patient had an episode of involuntary muscle contraction of her right extremity and right facial twitching lasting 20 seconds without loss of consciousness. Following the event, the patient had residual right arm weakness. The episode was thought to be a simple, partial seizure. The patient had multiple similar episodes during her admission, some of which had associated aphasia and involvement of the left lower extremity. She underwent further evaluation with an EEG, lumbar puncture, and additional blood testing. Patient had one spell on video EEG with no electrographic correlate.

CSF analysis did not suggest an infectious or malignant etiology with a mildly elevated white blood cell count of 14 cells per microliter (reference

range 0–5 cells per microliter), mildly elevated total protein of 69 mg/dL (reference range 15–45 mg/dL), and negative culture, negative viral PCR's, and negative cryptococcal antigen. Flow cytometry did not show a clonal B or T cell population. CSF angiotensin-converting enzyme (ACE) was elevated at 3.8 U/L (reference range 0–2.5 U/L), but serum ACE levels were normal.

Additional lab testing demonstrated an elevated erythrocyte sedimentation rate of 92 mm/hour (reference range 0–30 mm/hour). Her rheumatologic serologies included a highly elevated rheumatoid factor and anti-CCP. Anti-nuclear cytoplasmic antibody testing was negative and IgG sub-fractions did not show an elevation in IgG4 levels. Interferon gamma release assay was negative. Chest CT did not show any evidence of pulmonary sarcoidosis.

The primary team discussed a confirmatory brain biopsy with neurology, neurosurgery, and neuropathology, but because the significant history of RA, the significant risks of a biopsy, combined with no other features of an alternative systemic diagnosis (like isolated neurosarcoidosis or

IgG4-related disease) she was started on empiric treatment for RA-associated pachymeningitis. After starting prednisone 60 mg daily, her symptoms improved over several days. Her symptoms recurred when prednisone was tapered and she was later treated with rituximab. 3 months after initial presentation, her symptoms had resolved with these therapies.

3. Discussion

Rheumatoid arthritis had been estimated to affect around 1% of the population with an approximately two to three times as many women as men affected [1]. Though primarily an autoimmune disease attacking the synovium, rheumatoid arthritis has numerous extraarticular manifestations including rheumatoid nodules, pericarditis, interstitial lung disease, and neurologic diseases. A retrospective study on a population of patients with RA in Olmsted county from 1995–2007 estimated that 6.7% develop severe extraarticular manifestations [2,3].

Extraarticular manifestations of rheumatoid arthritis affecting the central nervous system (CNS) are rare. The most well-known CNS involvement is C1-C2 atlantoaxial subluxation resulting in cervical myelopathy. Other rare manifestations include vasculitis, compressive rheumatoid nodule formation, and pachymeningitis [3].

Pachymeningitis is inflammation of the dura mater, the most superficial layer of the meninges. Patients may present with headache, focal neurologic deficits, seizure, confusion or ataxia [4]. Pachymeningitis has a broad differential of infectious, malignant, and autoimmune etiologies, including IgG4-related disease [5]. There are 51 case reports

of rheumatoid pachymeningitis in the medical literature on Embase. Most reported cases of rheumatoid pachymeningitis have occurred in patients with advanced longstanding seropositive disease. However, there have been several reports of vague neurologic symptoms as the presenting symptom of rheumatoid arthritis before the onset of joint inflammation [4].

Diagnosis of pachymeningitis may be suggested by hypertrophic thickening of meninges with contrast enhancement on MRI. Serology, imaging, and CSF analysis may highly suggest rheumatoid pachymeningitis though definitive diagnosis requires biopsy [6]. Serologically, the diagnosis of RA is suggested with a positive rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP). Though non-specific, an inflammatory process is also suggested by an elevation in erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). In pachymeningitis, CSF fluid typically shows pleiocytosis, elevation in protein, and either a normal or slightly low glucose. MRI findings can greatly increase suspicion of pachymeningitis with a classic but not-specific meningeal thickening with contrast enhancement [5]. Sarcoidosis and IgG4-related disease may both cause meningeal enhancement and may be difficult to distinguish from RA pachymeningitis. Neurosarcoidosis is suggested by increased CSF angiotensin-converting enzyme level but this is a non-specific finding [7]. In our patient's case, neurosarcoidosis was thought less likely as the patient had no evidence of systemic sarcoid disease such as hypercalcemia and hilar adenopathy. IgG4-related disease may cause meningeal enhancement, but most patients with this disease would have elevated serum IgG4 levels, which were normal in our patient's case [8]. She also had no other associated signs or symptoms of IgG4-related disease such as lymphadenopathy or other organ infiltration.

In our patient's case, she had a history of RA for many years and her serologic testing showed a markedly elevated RF and anti-CCP to support RA as an accurate pre-existent diagnosis [9]. In the current case, no biopsy was performed to confirm diagnosis because of the high clinical suspicion of RA pachymeningitis and risks outweighed the benefits in a clinically improving patient. Neuropathology also felt that given the similarly granulomatous nature in manifestations, a biopsy would not differentiate between neurosarcoidosis and rheumatoid meningitis.

Given the low incidence of the disease, there is no standardized treatment for rheumatoid pachymeningitis. Historically, morbidity and mortality was high at 60% but this percentage has been improved with earlier diagnosis from improvements in imaging

modalities as well as improving therapies. Based off the 50 case reports compiled from Magaki in 2015, 20 cases used corticosteroids alone with a 60% survival. More recent case reports have also used induction doses of steroids with the addition of methotrexate, cyclophosphamide, or rituximab as adjunctive maintenance therapies [5]. Interestingly, there are multiple cases that have reported the onset of pachymeningitis within months of initiating TNF-inhibitor therapy for RA [10]. These patients with RA pachymeningitis are often atypical as their duration of disease is much less than the previously described cohort. As such, TNF-inhibitor therapy is thought to be contraindicated in cases of RA with known pachymeningitis.

4. Conclusion

Rheumatoid arthritis may present with extraarticular manifestations even when patients are already on stable regimens for their articular disease. Neurologic complications can include pachymeningitis which is diagnosed by brain biopsy or by characteristic imaging findings in a patient with known longstanding rheumatoid arthritis. Early recognition is key to initiation of aggressive therapy and improving outcomes and providers should be aware of prior history of pachymeningitis when selecting treatments for RA.

Authors' Disclaimer

The views expressed in this article are the authors' own and do not reflect an official position of Hennepin County Medical Center or the University of Minnesota.

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none

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