

Leptomeningitis in rheumatoid arthritis

Emmanuel Manolios¹ , Nicholas Manolios^{1,2} , David Spencer^{1,2} 

Abstract

In this case report, we describe the case of a patient given the presumptive diagnosis of rheumatoid leptomeningitis on the basis of clinical findings and clinical response to antirheumatic medications after other causes of meningitis were excluded. Numerous case reports describe rheumatoid meningitis; however, rheumatoid leptomeningitis, in the absence of pachymeningitis, is a rare phenomenon. As such, the literature about it is scant. This unique case provides an opportunity to further characterize the symptoms and radiological findings of leptomeningitis in a patient with rheumatoid arthritis.

Keywords: Arthritis, rheumatoid, meningitis, magnetic resonance imaging, leptomeningitis

Introduction

It is not often that one encounters a rare complication of leptomeningitis in a common disease, such as rheumatoid arthritis (RA).

Case Presentation

Mrs. CJ, a 71-year-old woman, had a long history of erosive seropositive RA, which was well controlled since 1996. She presented with an exacerbation of polyarthritis and right temporomandibular joint pain along with cervical and occipital headache in 2017. There were no behavioral changes or consciousness disturbance. Medications on presentation included methotrexate 5 mg weekly, hydroxychloroquine 200 mg daily, and prednisone 5 mg daily. On examination, there was widespread synovitis involving the hands and pain in the right temporomandibular joint during palpation. The cranial nerve and neurological examination were normal. A computed tomography scan of the cervical spine disclosed age-related spondylosis of the spine with no evidence of atlanto-axial subluxation. Magnetic resonance imaging (MRI) showed leptomeningeal enhancing high T2 fluid-attenuated inversion recovery (FLAIR) signal with diffusion restriction bilaterally superiorly near the falx (Figure 1). Cerebrospinal fluid (CSF) analysis showed no evidence of increased protein or low sugar levels or abnormal cells to implicate neurosarcoid, *Mycobacterium tuberculosis* and other pathogens like enterovirus and herpes simplex virus, and malignancy. Autoantibodies were negative for limbic encephalitis. Antinuclear antibody, extractable nuclear antigen, and anti-neutrophil cytoplasmic antibody serologies were negative. Initially, the methotrexate was increased to 20 mg/week, prednisone increased to 50 mg daily for a short interim, and the patient was commenced on leflunomide 10 mg daily. On follow-up after several months, the patient continued to be symptomatic with poor control of RA and was commenced on adalimumab 40 mg subcutaneously every fortnight. The cervical pain was attributed to cervical spondylosis, and her neck and head pain improved with physiotherapy and low-dose sodium valproate. When last reviewed in March 2020, her headaches had resolved, and her rheumatoid disease was in remission. Repeat MRI in April 2020 showed that the leptomeningeal enhancement in the interhemispheric fissure that was previously noted had substantially improved.

Informed consent was obtained from the patient.

Discussion

The true prevalence of rheumatoid leptomeningitis is unknown and remains rare in clinical practice. The heterogeneous clinical presentations consisting of headache, cranial nerve palsies, altered consciousness, and psychiatric symptoms may reflect the varied underlying histopathology of vasculitis, nonspecific inflammation, or rheumatoid nodules as previously reported (1, 2). MRI findings of diffuse or patchy leptomeningeal enhancement are usually characteristic, albeit nonspecific, given other causes for leptomeningitis. There is a paucity of information on RA leptomeningitis in the literature. RA pachymeningitis is more common than leptomeningitis alone.

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¹ Faculty of Medical and Allied Health, The University of Sydney Northern Clinical School, Sydney, Australia

² Department of Rheumatology, Westmead Hospital, Westmead, Sydney

Address for Correspondence:

Nicholas Manolios; Faculty of Medical and Allied Health, The University of Sydney Northern Clinical School, Sydney, Australia

E-mail: nicholas.manolios@sydney.edu.au

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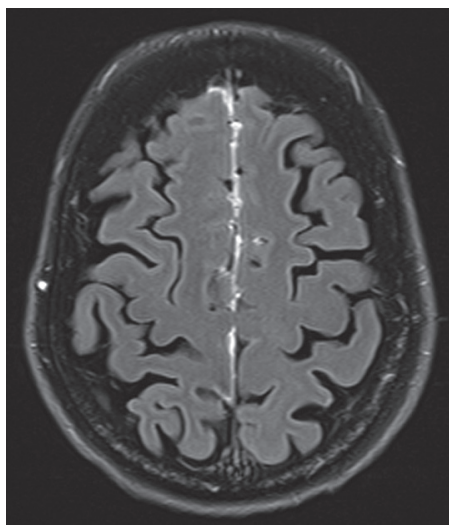


Figure 1. Gadolinium-enhanced axial T1-weighted image showing leptomeningeal enhancement and hyperintense signal in cerebrospinal fluid space, especially over the falx (arrows) and sulci.

Literature review of RA meningitis shows that it is a rare but potentially fatal complication of RA (1, 3) that typically affects patients with seropositive and longstanding RA with a mean duration of RA at the onset of meningitis being 9.9 years (4). The duration of RA is highly variable and is an unreliable predictor of rheumatoid meningeal development (5); case reports show that rheumatoid meningitis can also be the initial presentation of RA (6, 7). Severity of RA is an unreliable predictor of rheumatoid meningitis because less than half of the patients have active synovitis at the time of diagnosis (8). Rheumatoid nodules are the most consistent feature seen in patients with rheumatoid meningitis, with 67% patients having subcutaneous nodules and 47% having visceral nodules (1). Histologically, however, the condition is characterized by an inflammatory infiltrate of the meninges without distinct rheumatoid nodules (1, 2,

8-10). Neurological symptoms are varied and nonspecific. The most common neurological symptoms include altered mental state (confusion, behavioral changes, and loss of consciousness), hemiparesis, headache, and seizures. Other less common symptoms include cranial nerve palsies, unsteady gait, sensorineural hearing loss, and memory loss (1-4, 7-12). These symptoms are largely dependent on the region and the layers of the meninges that are affected. Headaches and cranial nerve palsies are more commonly seen with dural involvement, whereas mental status alterations, hemiparesis, and seizures are more common in leptomeningeal involvement (8). Rheumatoid meningitis is a diagnosis of exclusion that should be considered once the infectious and organic neurological causes are excluded. Other differentials to consider include tuberculous (TB) meningitis, neurosarcoidosis, meningeal metastasis, granulomatosis with polyangiitis, neurosyphilis, and IgG4-related disease (13).

Diagnosis of rheumatoid meningeal involvement is made by a combination of clinical, radiological, and pathological features; however, because the clinical and radiological findings can be nonspecific, histopathological sampling is needed to confirm the diagnosis. Analysis of CSF is highly variable and can range from normal to markedly abnormal. Elevated CSF protein level is the most common abnormality (2). Elevated protein and decreased glucose levels and leukocytosis are often seen; however, they lack sensitivity (12, 13). More novel studies have suggested that elevated anti-cyclic citrullinated peptides, rheumatoid factor, IL-6, and CXCL13 levels in CSF may be useful biomarkers to assist in diagnosis and treatment response (3, 12). Although it is not diagnostic, CSF analysis has its clinical utility in ruling out infective and carcinomatous causes of meningitis. On MRI, characteristic findings on FLAIR images include meningeal thickening and enhancement, with 62% showing unilateral involvement (13-15). Hyperintense signal lesions in the subarachnoid spaces are usually present on FLAIR, and basal cisterns are typically unaffected (unlike in TB meningitis) (16-18). Fluorodeoxyglucose-positron emission tomography can also be performed and has shown increased cerebral glucose metabolism in some cases (12, 19). Diagnosis of rheumatoid meningitis is ultimately confirmed on meningeal biopsy; histopathological findings include diffuse infiltration of lymphocytes, histiocytes, and plasma cells as well as epithelioid granulomas with focal central necrosis (3, 8-12, 16-20). Mild vasculitis and multinucleated giant cell reactions can also be seen (21). Nodules are pres-

ent in 68% of patients, which are mainly confined to the meninges but can be seen in the choroid plexus and rarely in the spinal cord (1).

Given the rarity of the RA meningitis and leptomeningitis, there is little consensus on the most effective treatment. Recent reports show that rheumatoid meningitis can be successfully treated with various combinations of azathioprine, cyclophosphamide, methotrexate, and high-dose corticosteroids (3, 12, 17, 21). Improvement on monotherapy intravenous pulse methylprednisolone after oral prednisone has been well documented (10, 22, 23); however, immunosuppressants may be required while steroids are being weaned. Other case reports show successful treatment with rituximab (24, 25). It is interesting to note that the patients who develop aseptic meningitis while on anti-tumor necrosis factor (TNF) therapy respond well to cessation of anti-TNF treatment and added steroids (26-28).

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Main Points

- The true prevalence of rheumatoid leptomeningitis is unknown and remains rare in clinical practice.
- Clinical presentations vary and may consist of headache, cranial nerve palsies, altered consciousness, or psychiatric symptoms.
- MRI findings of diffuse or patchy leptomeningeal enhancement are usually characteristic.
- Improvement on steroids has been well documented. Immunosuppressants may be required while steroids are being weaned.

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