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Case Report

New-onset seizures: an unusual neurologic manifestation of rheumatoid arthritis

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Abstract

Rheumatoid arthritis (RA) is a chronic inflammatory condition primarily affecting the musculoskeletal system but can often involve other organ systems as well. Rheumatoid meningitis is a rare central nervous system (CNS) manifestation of RA characterized by pachymeningeal and leptomeningeal enhancement. Herein, we present a case of a 64-year-old male who presented with left lower extremity weakness and witnessed seizures. The diagnostic work-up, including lumbar puncture, brain MRI and meningeal biopsy ruled out malignancy and were consistent with the diagnosis of rheumatoid meningitis. The patient was discharged on high-dose steroids along with anti-seizure medications. On subsequent follow-up visits, the patient remained seizure-free.

INTRODUCTION

Neurological involvement in rheumatoid arthritis is uncommon, but when it happens, it can present in various forms, including cervical myelopathy, rheumatoid nodules within the central nervous system (CNS), compression and non-compression neuropathies, behavioral changes, CNS vasculitis and stroke [1]. Aseptic or rheumatoid meningitis (RM) is a rare manifestation of rheumatoid arthritis with an unknown frequency. In literature, it has been reported to present with symptoms including headache, fever, and sometimes focal seizures [2]. We are reporting this unique case of rheumatoid meningitis in a 64-year-old male with quiescent RA.

CASE PRESENTATION

A 64-year-old male with a medical history of RA, hypertension, lung nodules, and ischemic stroke without any residual deficits was brought to the emergency department (ED) after experiencing multiple episodes of witnessed seizures. The seizures began in the morning upon awakening from sleep, accompanied by a headache. Subsequently, he developed multiple seizure episodes characterized by predominant shaking of his left arm and leg. These episodes occurred every few minutes, each lasting less than one minute, with preserved awareness. No aura, urinary incontinence, tongue bite, or postictal confusion were noted. The patient did report tingling and numbness in his left upper and lower extremities. He denied any vision, speech, or mental status changes, as well as dizziness, current headache, swallowing difficulty, or hearing loss.

Notably, the patient was admitted to another hospital a month ago due to left-sided weakness, where he was diagnosed with a right thalamic stroke and received thrombolytic therapy. Following the thrombolytic treatment, he experienced one episode of seizure, which led to the initiation of Keppra. An EEG at that time showed no seizure activity, and the patient reported compliance with his medications, with no further seizures until the day of presentation. He also reported good compliance with methotrexate for his quiescent RA over the years.

Upon arrival at the ED, the patient was hemodynamically stable. On examination, he exhibited repeated episodes of left-side shaking involving the left neck, left upper, and lower extremities with preserved awareness. Pronator drift was positive in the left upper extremity, and power was 3/5 in the left lower extremity. The rest of his neurological exam was intact. The patient received Lorazepam and a loading dose of Levetiracetam, which helped to control the seizures. Initial CT head revealed sulcal effacement with isodense material, raising concerns for a leptomeningeal process (Fig. 1). EEG showed cortical hyperexcitability with focal seizure activity in the right frontocentral and parasagittal area. MRI of the brain ruled out ischemic stroke but indicated focal right frontal pachymeningeal and leptomeningeal enhancement with concerns for possible malignancy (Fig. 2). He was subsequently admitted to the general neurology service, and seizures

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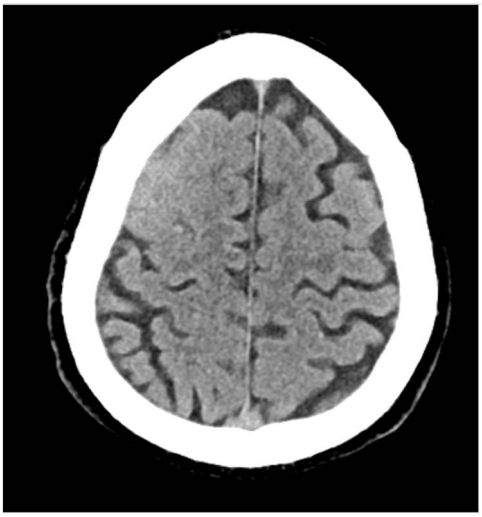

Figure 1. CT head demonstrates increased density in the sulci of the right frontal lobe which are isodense to gray matter suggesting leptomeningeal process.

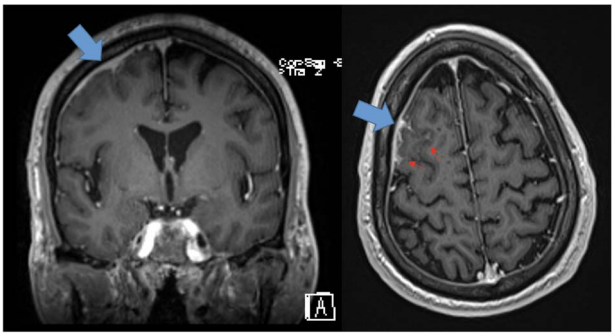

Figure 2. Initial MRI brain, blue arrows demonstrate Pachymeningeal enhancement along the right frontal lobe and red arrows demonstrate leptomeningeal enhancement.

were eventually controlled with Levetiracetam, Lacosamide, and Clobazam. His initial left-sided weakness resolved in a few days, indicating Todd's paralysis.

Baseline laboratory tests, including complete blood cell count, electrolyte panel, liver function, hepatitis B, hepatitis C, vitamin D, HIV, angiotensin-converting enzyme, proteinase 3, C3, C4, extractable nuclear antibodies, immunoglobulin G4 (IgG4), myeloperoxidase, rapid plasma reagin, and anti-dsDNA, were all negative. His rheumatoid factor (RF) was mildly elevated. Anti-cyclic citrullinated peptide (Anti-CCP antibody) was > 250 U/ml. Subsequently, a lumbar puncture was performed, and the CSF analysis showed normal cell count, protein, and glucose levels. Other CSF studies, including rheumatoid factor, angiotensin-converting enzyme, Lyme disease, syphilis, *Mycobacterium tuberculosis* polymerase chain reaction, adenosine deaminase, cytology, and flow cytometry, yielded negative results. CSF bacterial, fungal, and mycobacterial cultures also showed no growth. CT scan of the chest/abdomen/pelvis revealed only small pulmonary nodules unchanged from last year, and MRI of the spine was unremarkable.

Due to the suspicion of rheumatoid meningitis, the patient underwent a right frontal dural and brain biopsy, which revealed mixed lymphoplasmacytic inflammation and aggregates of macrophages, leading to the diagnosis of rheumatoid meningitis (Fig. 3). The patient was subsequently started on prednisone 60 mg. Upon discharge, he was continued on anti-epileptics and prednisone, while methotrexate was discontinued. During subsequent follow-up visits with his rheumatologist, he remained seizure-free.

Given the patient's underlying lung disease (COPD and long-standing benign lung nodules), Abatacept was administered instead of Rituximab to mitigate the risk of infection, particularly COVID-19. A repeat MRI brain after 8 weeks showed resolution of the pachymeningeal and leptomeningeal enhancement (Fig. 4).

DISCUSSION

Rheumatoid meningitis (RM) is a rare condition mediated by an inflammatory infiltrate of the meninges [2]. It is rare but a potentially fatal complication of RA [3, 4]. Because of its rarity, no specific estimated frequency has been reported in literature. It typically affects patients with seropositive and longstanding RA, with a mean duration of RA at the onset of meningitis being 9.9 years [5]. Its symptoms can mimic those of infectious etiology or CNS malignancy. Other differentials include tuberculous (TB) meningitis, neurosarcoidosis, meningeal metastasis, granulomatosis with polyangiitis, neurosyphilis, and IgG4-related disease [6]. Rheumatoid meningitis is a diagnosis of exclusion; therefore, it is crucial to rule out these differentials before diagnosing rheumatoid meningitis [5].

The variability in clinical presentations consisting of headaches, cranial nerve palsies, altered consciousness, and psychiatric symptoms may be due to the varied underlying histopathology of vasculitis, nonspecific inflammation, and rheumatoid nodules [2]. Most patients have longstanding seropositive disease [7]; however, in one case report the patient did not have previously known systemic disease but presented with rheumatoid meningitis as the first sign of their RA [8]. A recent systematic review and meta-analysis of 103 studies by Villa et al showed that 35% of patients with RM had active and uncontrolled RA. They also found that about 60% of patients presented with focal neurological signs [9]. Pellerin et al. reported a case of RM in which the patient presented with non-convulsive seizures and features of parkinsonism [10]. In a case series of 6 patients with RM, 5 out of 6 patients presented with stroke like symptoms and only one patient presented with seizures [11]. All of these patients had pachymeningeal and/or leptomeningeal enhancement on MRI. Our patient had quiescent RA and presented with both weakness and multiple seizures. Even though stroke was initially among the differential, it was later ruled out based on characteristic findings for RM on MRI and brain biopsy.

After a thorough history and physical examination, the mainstay of diagnostic work-up includes an MRI of the brain and spine, CSF studies, and meningeal biopsy. Brain imaging with contrast-enhanced MRI is the most critical noninvasive study to rule-in the diagnosis of rheumatoid meningitis in a patient with suspected rheumatoid meningitis. Contrast MRI findings include meningeal thickening and/or enhancement. The enhancement may be restricted to only the pachymeninges. Other characteristic findings on FLAIR images include meningeal thickening and enhancement, with 62% showing unilateral involvement [4, 12]. Hyperintense signal lesions in the subarachnoid spaces are usually present on FLAIR, and basal cisterns are typically unaffected, in contrast with TB meningitis [13]. CSF analysis is the next best tool to rule out the main differentials of infectious and carcinomatous meningitis. CSF protein elevation is the most common abnormality, but pleocytosis and depressed glucose have also been described. Confirmatory diagnosis relies on the examination

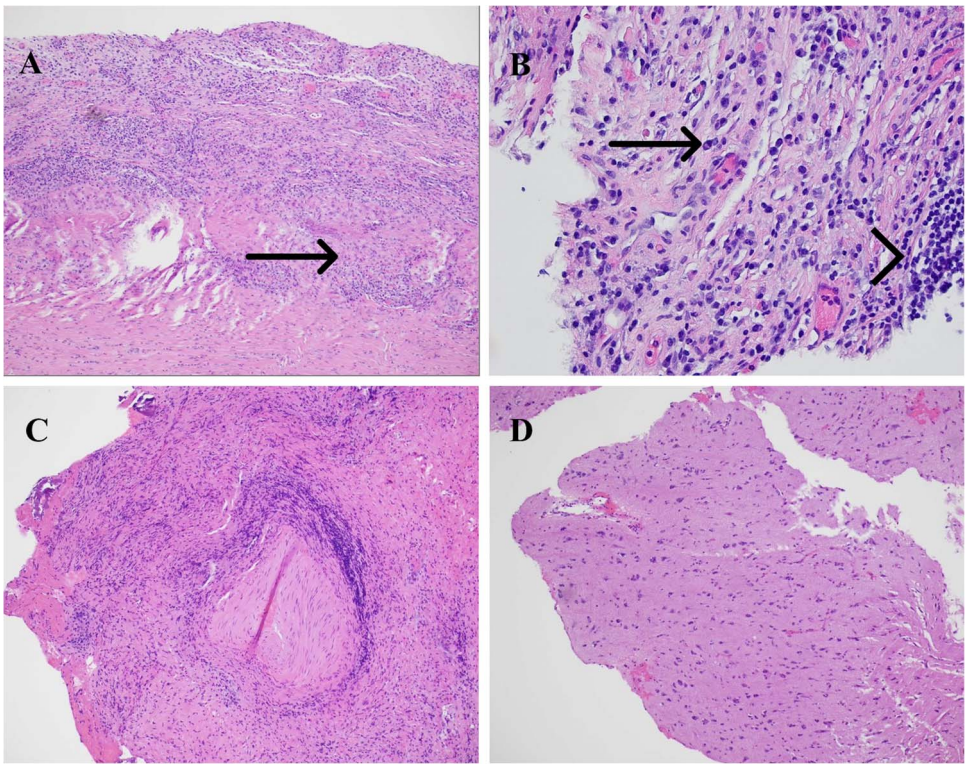

Figure 3. Dura biopsy (**A** and **B**) shows vague granuloma formation (**A**, arrow) and prominent inflammatory infiltrates of the dura which are composed of mixed lymphocytes (**B**, arrows), plasma cells (**B**, arrowhead), few neutrophils and rare eosinophils. (**C**) Leptomeninges also shows similar mixed lymphoplasmacytic inflammation and aggregates of macrophages. (**D**) The adjacent brain tissue shows mild reactive gliosis.

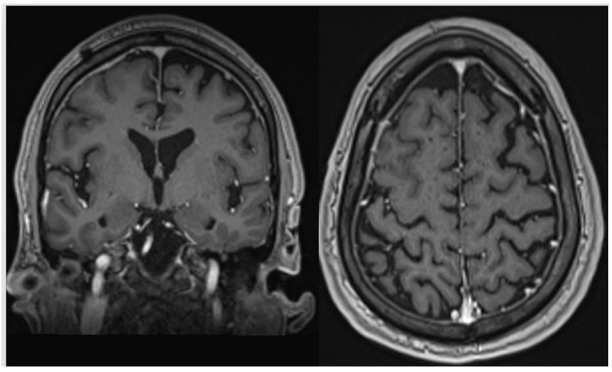

Figure 4. MRI brain after 8 weeks demonstrates marked improvement/resolution of pachymeningeal and leptomeningeal enhancement.

of a meningeal biopsy, with the presence of plasma cells and rheumatoid nodules. Rheumatoid factor and anti-citrullinated peptide antibodies have been detected in the CSF in a few cases but are not very common [14].

The mainstay of treatment for RM is steroids. A review of the available literature shows improvement on monotherapy with intravenous pulse methylprednisolone followed by oral prednisone. In one retrospective study, patients with high clinical probability without meningeal biopsy were treated empirically and they showed clinical improvement [7]. Immunosuppressants may be required while steroids are being weaned off. Rheumatoid meningitis occurring in patients treated with Tumor Necrosis Factor (TNF) inhibitors has also been reported to respond well to glucocorticoid treatment after stopping further TNF inhibitors [15]. In rare cases, rituximab has been successfully used in combination with steroids to treat RM. However, due to the overall low frequency of RM further clinical data and treatment guidelines are needed to standardize care for this rare disease entity.

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CONFLICT OF INTEREST STATEMENT

We report no conflict of interest.

FUNDING

Not applicable.

CONSENT

The patients provided written, informed consent for the publication of this report.

GUARANTOR

Dr. Omair Khan MBBS.

PRIOR PRESENTATION

None.

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