EJCRIM
European Journal
of Case Reports
in Internal Medicine

RHEUMATOID ARTHRITIS: A RARE CAUSE OF PACHYMENINGITIS AND OPTIC NEURITIS

Muhammad Umer Riaz Gondal[1], Josette Graves[2], Haider Khan[1], Mohammad Baig[1], Toqeer Khan[3], Fatima Khalid[1], Pavani Pagolu[1]

[1] Department of Internal Medicine, Tower Health, Reading Hospital, West Reading, USA
[2] Department of Internal Medicine, Drexel University, West Reading, USA
[3] Department of Internal Medicine, University of New Mexico, Albuquerque, USA

Corresponding author's e-mail: umer_rz@hotmail.com

Received: 16/10/2024
Accepted: 22/10/2024
Published: 11/11/2024

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Patient consent has been obtained.
Acknowledgements: The authors acknowledge and thank Dr. Gregory Emkey, MD for his collaboration in the realization of this work.

How to cite this article: Gondal MUR, Graves J, Khan H, Baig M, Khan T, Khalid F, Pagolu P. Rheumatoid arthritis: a rare cause of pachymeningitis and optic neuritis. *EJCRIM* 2024;**11**:doi:10.12890/2024_004964

ABSTRACT

Introduction: Rheumatoid pachymeningitis and optic neuritis are rare complications of rheumatoid arthritis (RA) and are a diagnosis of exclusion.

Case description: A 75-year-old male with a history of seronegative RA presented to the emergency department with left eye pain and blurry vision lasting two days. He had been diagnosed with seronegative RA around nine months previously. His blood pressure was elevated at 204/75 mmHg upon arrival. Physical examination revealed left conjunctival injection, mild ptosis, painful extraocular movements and tenderness over the orbit and sinuses. Initial treatments included painkillers and intravenous labetalol, which alleviated his symptoms and decreased his blood pressure. Laboratory tests showed a C-reactive protein of 2.5 mg/dl and an erythrocyte sedimentation rate of 32 mm/h, with other blood work unremarkable. A computed tomography (CT) angiogram of the head and neck showed no high-grade stenosis. Given his RA history, initial concerns included scleritis. A magnetic resonance imaging (MRI) of the brain and orbit revealed inflammation around the left optic nerve, and pachymeningitis at the left cerebral convexity and interhemispheric fissure, suggesting hypertrophic pachymeningitis. An ophthalmologic examination was unremarkable. Treatment was adjusted to include pulse doses of intravenous methylprednisolone for optic neuritis, resulting in significant pain relief. Though inadequate for complete testing, a lumbar puncture indicated an inflammatory disorder with elevated glucose (199 mg/dl), protein (109 mg/dl), and unremarkable WBC/RBC and Gram staining. Cytology and culture were unremarkable. The most likely diagnosis at this point was rheumatological meningitis and rheumatological optic neuritis. The patient improved markedly with high-dose steroids over four days and was discharged on prednisone.

Conclusion: In cases of optic neuritis and pachymeningitis, RA should remain on the differential in patients with or without a prior diagnosis.

KEYWORDS

Rheumatoid arthritis, pachymeningitis, optic neuritis

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

LEARNING POINTS

- Rheumatoid arthritis (RA) is a systemic disease but can rarely cause neurological involvement.
- Pachymeningitis is an inflammation of the dura mater, rarely caused by RA.
- Optic neuritis can also rarely be caused by RA and responds to steroids.

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic disease but can rarely cause neurological involvement. Rheumatoid pachymeningitis and optic neuritis are rare complications of RA and are a diagnosis of exclusion.

CASE DESCRIPTION

A 75-year-old male with a history of seronegative RA and hypertension presented to the emergency department with left eye pain and blurry vision lasting two days. He had been diagnosed with seronegative RA around nine months previously, starting with the abrupt symptoms of hand and knee swelling and pain. He had positive antinuclear antibody titres (1:100) with negative rheumatoid factor and cyclic citrullinated peptide. He had been on a steroid taper and had methotrexate added three months previously. For the past two days, eye movements exacerbated the pain and were unrelieved by painkillers. He had no symptoms of photophobia, neck stiffness, vomiting, weakness, balance issues or speech disturbances. His blood pressure was elevated at 204/75 mmHg upon arrival. Physical examination revealed left conjunctival injection, mild ptosis, painful extraocular movements and tenderness over the orbit and sinuses, but no temporal artery tenderness. Muscle strength and reflexes were normal.

Initial treatments included a migraine cocktail and intravenous labetalol, which alleviated his symptoms and decreased his blood pressure. Laboratory tests showed a C-reactive protein (CRP) of 2.5 mg/dl and an erythrocyte sedimentation rate (ESR) of 32 mm/h, with other blood work unremarkable. A computed tomography (CT) angiogram of the head and neck showed no high-grade stenosis. Given his RA history, initial concerns included scleritis. A magnetic resonance imaging (MRI) of the brain and orbit revealed inflammation around the left optic nerve and pachymeningitis at the left cerebral convexity and interhemispheric fissure, suggesting hypertrophic pachymeningitis *(Fig. 1)*. An ophthalmologic examination was unremarkable.

Treatment was adjusted to include pulse doses of intravenous methylprednisolone for optic neuritis, resulting in significant pain relief. Neurology consultation considered various differentials for pachymeningitis including infectious, autoimmune (RA, sarcoidosis, Sjögren's, neuromyelitis optica, myelin oligodendrocyte glycoprotein antibody disease, IgG4-related disease), and less likely causes such as paraneoplastic syndrome, vaccine-related issues or multiple sclerosis (given the patient's advanced age). Though inadequate for complete testing, a lumbar puncture indicated an inflammatory disorder with elevated glucose (199 mg/dl), protein (109 mg/dl), unremarkable white and red blood counts (WBC/RBC) and Gram staining. Cytology was negative, as were cerebrospinal fluid mycobacterial, spirochaetal and other bacterial, fungal and viral studies. The most likely diagnosis at this point was rheumatological meningitis and rheumatological optic neuritis. The patient improved markedly with high-dose intravenous steroids over four days and was discharged on a tapering oral prednisone regimen. Follow-up with rheumatology led to a change from methotrexate to azathioprine.

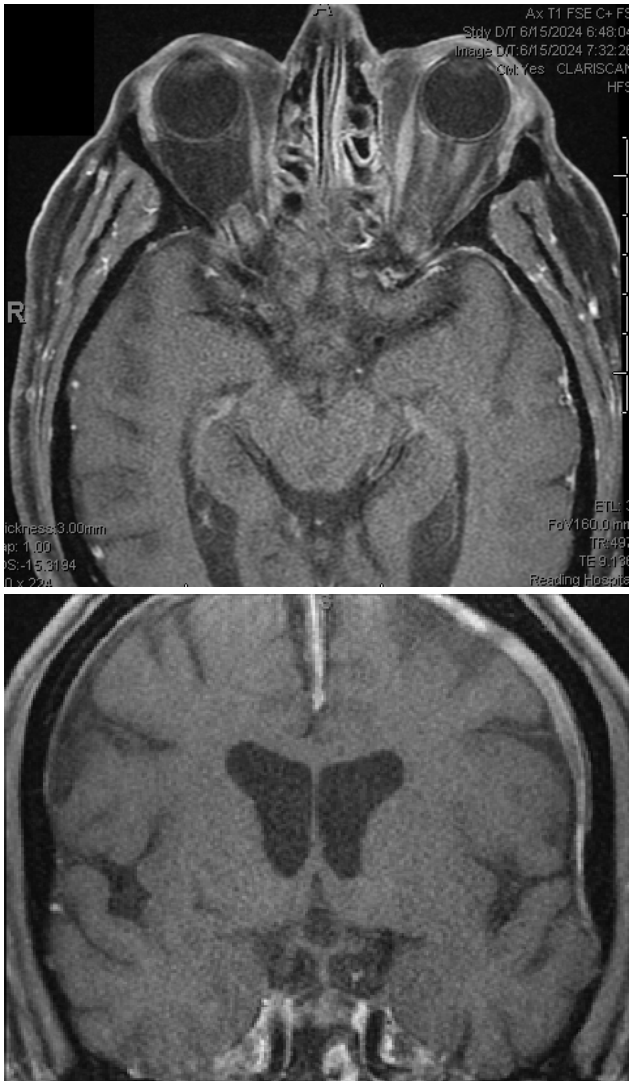

Figure 1. A magnetic resonance imaging (MRI) scan of the brain and orbit showed inflammation surrounding the left optic nerve, as well as pachymeningitis along the left cerebral convexity and in the interhemispheric fissure, indicating the presence of hypertrophic pachymeningitis.

DISCUSSION

RA is an autoimmune disease characterised by polyarthritis, although extra-articular involvement can occur[1]. Women are more commonly affected, with an incidence peak between 30 and 55 years of age. Neurologic symptoms frequently occur in patients with RA. Peripheral manifestations include carpal tunnel syndrome, mononeuritis multiplex and distal symmetric polyneuropathy. Central involvement is associated with mood disorders. However, worrisome pathologies include inflammatory processes such as central nervous system vasculitis, rheumatoid nodules and rheumatoid meningitis. Inflammatory central nervous system involvement is rarer and in the case of this patient, rheumatoid pachymeningitis was a diagnosis of exclusion among the amalgam of pathologies.

Pachymeningitis is a rare inflammatory process of the dura mater in the brain or spinal cord[1]. Hypertrophic pachymeningitis occurs when there is a thickening of the dura that becomes adherent to the leptomeninges (subarachnoid space and pia mater)[2]. Involvement may be focal or diffuse, affecting the parasellar and cavernous regions more anteriorly and the posterior third of the falx, tentorial and clival dura mater posteriorly[2]. As the dura encases the proximal portion of cranial nerves, optic nerve sheath and cavernous sinus, pachymeningitis often compromises the function of these structures[2]. Areas of inflammatory involvement usually inform neurologic manifestations[3]. In this case, the patient presented with blurry vision and progressive eye pain with extraocular movement, suggesting the involvement of cranial nerves II, III, IV and VI. Other symptoms associated with pachymeningitis, informed by case studies, include headaches (which occur almost in all patients), seizures, dizziness, gait ataxia, hearing loss and stroke-like symptoms[3,4]. Causes of pachymeningitis previously mentioned include infectious (viral, fungal and bacterial), paraneoplastic, autoimmune (RA, multiple sclerosis, sarcoidosis, Sjögren's, neuromyelitis optica, myelin oligodendrocyte glycoprotein antibody disease, IgG4-related disease, Behçet's syndrome, relapsing polychondritis and giant cell arteritis), vaccine-related and idiopathic sources[1-6]. In the setting of previously diagnosed seronegative RA the patient, in this case, was found to have rheumatoid pachymeningitis with optic neuritis. Rheumatoid meningitis is rare and includes both pachymeningitis (inflammation of the dura mater) and, more commonly, leptomeningitis (inflammation of the subarachnoid space and pia mater)[1]. In a systematic review conducted in 2021 following PRISMA guidelines, Villa et al. evaluated 103 studies with 130 cases of rheumatoid pachymeningitis, and 83% of patients were previously diagnosed with RA with a mean disease duration of 11 years. The mean age was 62 (range 32–89), and 53.85% were female[3]. Focal neurologic signs were the most common symptom, followed by systemic and neuropsychiatric symptoms[3]. Compared to this systematic review, the patient in this case had a much shorter disease duration (nine months) and was on the higher end of the age range. A brain MRI is the modality of choice as the next step to evaluate a patient with known RA and neurologic-presenting symptoms[3,5]. Hyperintense foci in the frontal and parietal lobes on T2-weighted images were the most common locations affected in this systematic review, comprising about 80% of cases[3]. Other areas included the falx, tentorium, posterior fossa or brainstem[3]; this case found hyperintensities in the left cerebral convexity and interhemispheric fissure, consistent with the literature[3,6].

In terms of laboratory tests, while serum studies demonstrated elevated levels of CRP and ESR, positive rheumatoid factor and positive anti-cyclic citrullinated peptide (anti-CCP) titres in about 89% of patients, this case was negative for rheumatoid factor and anti-CCP[3]. Cerebrospinal fluid demonstrated elevated levels of WBC with mononuclear predominance in more than 85% of cases, along with elevated proteins in 76% of cases[3]. This contrasts with our case, in which WBC was normal with negative Gram stain, and there were elevated glucose levels (a finding only present in 20% of cases in the systematic review).

Since the clinical suspicion was low for a neoplastic process, the patient did not undergo a biopsy. In the systematic review, a biopsy was performed in 75% of patients, with rheumatoid meningitis occurring in 95% of cases[3]. Treatment involves early initiation of corticosteroid therapy for 3–5 days with induction of immunomodulator maintenance therapy (such as methotrexate), which our patient received[1-6]. There is some debate over waiting for a confirmatory biopsy before administering corticosteroids[6]. Unless there is a neoplastic concern that would preclude using corticosteroids (potential for masked biopsy findings in lymphoma), the benefits of initiating corticosteroids before biopsy results likely outweigh the risks of disease progression[6]. In patients with seronegative RA, such as the patient in this case, a biopsy for confirmatory diagnosis may be more helpful than in someone with confirmed serologic findings[6]. Outpatient management with rheumatology is recommended as relapse rates may be as high as 30%, although about 55% of patients may demonstrate complete remission of the disease[3].

Ophthalmologic symptoms only occur in about 25% of the patients with RA[7]. Keratoconjunctivitis occurs in 10–35% of patients but accounts for 85% of the ocular conditions seen in RA[7]. Other conditions include scleritis, peripheral ulcerative keratitis and retinal vasculitis[7]. Our patient's ophthalmological examination was unremarkable, ruling out these conditions.

Optic neuritis is an optic nerve inflammation; RA is a rare cause of optic neuritis. There have been case reports of RA causing pachymeningitis and optic neuritis, similar to our case[8]. An MRI of the orbits is the modality of choice for diagnosis, and optic neuritis is most easily identified on imaging as a unilateral optic nerve swelling with high T2 signal and contrast enhancement. Optic neuropathy was first reported in RA in 1980[9]. An autopsy showed necrotising vasculitis of the right posterior ciliary artery,

lymphocytic vasculitis and perivasculitis of the left posterior ciliary artery[9]. Approximately 25% of patients with RA have vasculitis, with involvement in all sizes of veins and arteries on post-mortem examination[9]. Occluding one of the posterior ciliary arteries or its branches produces ischaemic optic neuropathy with a spectrum of changes that result in complete blindness or variable visual field defects[9]. As with any case of optic neuritis, patients respond well to high-dose steroids, such as in our case.

CONCLUSION

Neurological or ophthalmic symptoms in a patient with RA require a thorough evaluation to determine whether they are related to RA itself or another aetiology. In cases of optic neuritis and pachymeningitis, RA should remain on the differential in patients with or without prior diagnosis. Workup consisting of neuroimaging with MRI brain, lumbar puncture, laboratory testing (CRP, ESR, antinuclear antibody and anti-CCP) and biopsy can inform clinical decision-making[3,5]. Early initiation of corticosteroids and maintenance therapy is necessary for treatment and is associated with a good prognosis.

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