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Differential Diagnosis of Multiple Sclerosis Among Patients Presenting with Headache

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ABSTRACT

Multiple sclerosis (MS) and migraine are both socially significant neurological disorders that may present with overlapping clinical and radiological features, particularly in young women. This report presents a challenging case in which the differential diagnosis required careful integration of clinical findings, neuroimaging, cerebrospinal fluid (CSF) analysis, and immunological markers. The importance of dynamic MRI monitoring and multidisciplinary evaluation is emphasized.

Abbreviations: MS: Multiple Sclerosis; CSF: Cerebrospinal Fluid; IgG: Immunoglobulin G; OCBs: Oligoclonal Bands; SLE: Systemic Lupus Erythematosus; CGRP: Calcitonin Gene-Related Peptide

Introduction

Multiple sclerosis (MS) is a chronic, disabling autoimmune disease that primarily affects young adults. Diagnosis is based on a combination of clinical, radiological, and laboratory evidence. Despite significant advances, no single diagnostic biomarker has been definitively validated. The most widely used laboratory marker remains the detection of immunoglobulin G (IgG) oligoclonal bands (OCBs) in the cerebrospinal fluid (CSF). Migraine is also a socially significant disorder, characterized by recurrent unilateral headache attacks, often accompanied by nausea, vomiting, photophobia, and phonophobia. Migraine triggers vary and include stress, hormonal changes, certain foods, and environmental factors. The most common form, migraine without aura, accounts for approximately 75% of cases. Structural MRI studies in migraine patients have identified parenchymal changes, including white matter lesions, volumetric alterations, and iron deposition, which may overlap with findings in MS. This complicates the differential diagnosis, especially in young female patients.

Case Presentation

We present the case of a 28-year-old woman with recurrent episodes of left arm numbness and weakness, accompanied by speech disturbances lasting with duration more than 24 hours. The episodes were followed by severe right-sided headache associated with nausea and vomiting. She had experienced three similar attacks in total. Her medical history included intracranial hypertension since childhood, for which she was treated with acetazolamide. On this occasion, MRI of the head and neck with contrast demonstrated supratentorial demyelinating lesions suspicious for MS. No active disease was observed, and repeat MRI was recommended after 6–12 months (Figures 1-3). The patient was admitted to the neurology clinic for further evaluation. Additional studies included lumbar puncture, testing for aquaporin-4 and anti-MOG antibodies, ANA profile, Lyme disease serology, and genetic testing for thrombophilia. CSF analysis revealed elevated leukocytes (mainly lymphocytes, 184 x10^6/L), erythrocytes (300 x10^6/L), and total protein (723 mg/L), with negative oligoclonal bands. Antibodies for NMOSD and Lyme disease were negative. Thrombophilia screening showed no pathogenic mutations (Factor V Leiden – normal; Prothrombin mutation G20210A – normal; PAI-1 4G/5G – heterozygous). The ANA profile showed increased titers of AMA-M2, Ro-52, and SS-A antibodies, raising suspicion for systemic autoimmune diseases such as Sjögren's syndrome or systemic lupus erythematosus (SLE). AMA-M2 is a specific marker for primary biliary cholangitis, while anti-Ro-52 and anti-SS-A are linked to Sjögren's syndrome [1-5].

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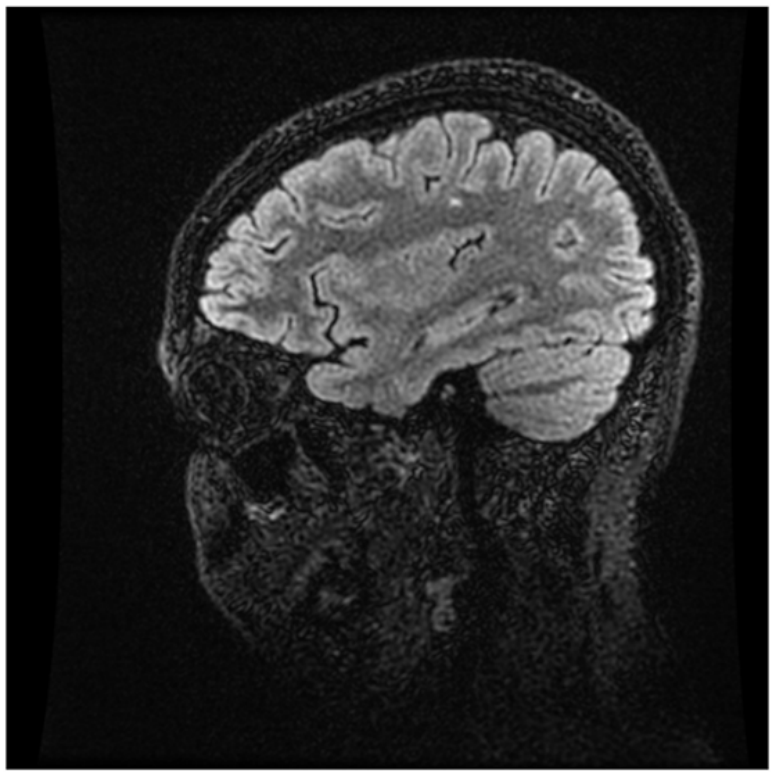

Figure 1: MRI head and neck with contrast showing supratentorial demyelinating lesions.

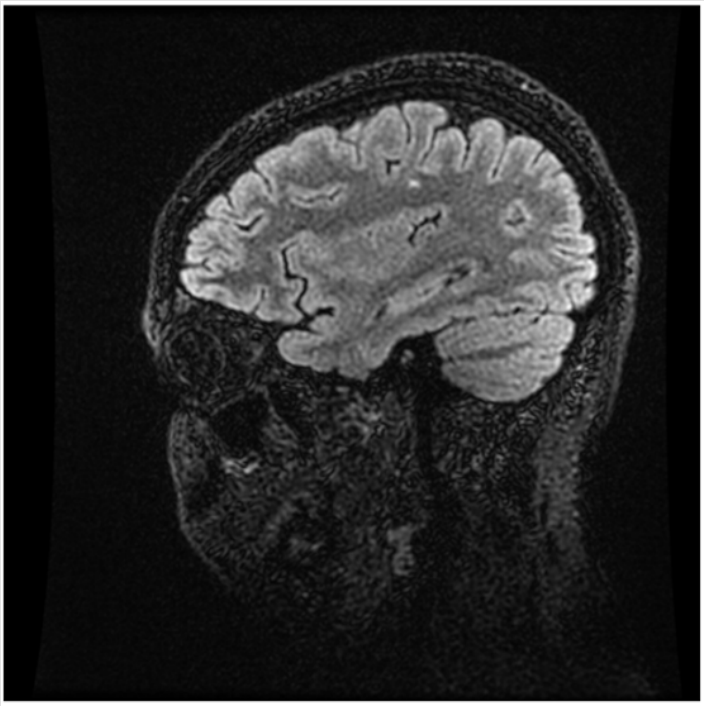

Figure 2: Axial MRI demonstrating periventricular white matter hyperintensities.

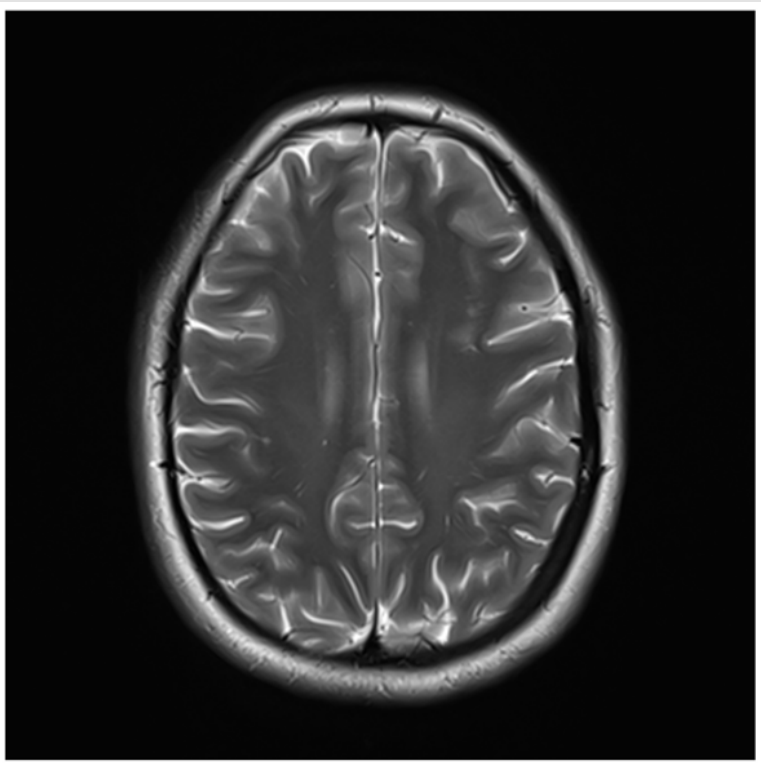

Figure 3: Follow-up MRI revealing a lesion with the central vein sign.

However, the patient lacked the common sicca symptoms (ocular, oral, or vaginal dryness). Brain MRI in Sjögren's syndrome may demonstrate white matter hyperintensities, but these findings were nonspecific. The patient was therefore monitored by a rheumatologist. A follow-up contrast-enhanced brain MRI performed six months later revealed one lesion with the characteristic central vein sign, a strong biomarker supporting MS diagnosis. The patient was treated with steroids and topiramate, which alleviated headaches and left-hand numbness. Topiramate was selected for its dual efficacy in migraine prophylaxis and reduction of intracranial pressure, due to its carbonic anhydrase inhibition. It also reduces calcitonin gene-related peptide (CGRP) and glutamate release from trigeminal neurovascular nerve endings, thereby disrupting cortical spreading depression. This mechanism supports its role in both epilepsy and migraine management.

Discussion

The differential diagnosis between MS and migraine can be particularly challenging, as both conditions share overlapping clinical and radiological features. Migraines with transient neurological deficits may mimic MS relapses. Conversely, early MS symptoms may be dismissed as atypical migraine. Careful evaluation is therefore essential. Migraine-associated MRI findings typically include supratentorial white matter hyperintensities, especially in the frontal lobes and periventricular regions. These can resemble demyelinating plaques but usually lack the central vein sign seen in MS. Regular MRI monitoring and integration of clinical findings, CSF analysis, and serological testing are critical for accurate diagnosis. This case highlights the need for interdisciplinary evaluation involving neurologists, radiologists, and rheumatologists. Although the ANA profile raised suspicion for systemic autoimmune involvement, the absence of systemic symptoms reduced the likelihood of Sjögren's syndrome. Dynamic MRI follow-up ultimately confirmed the MS diagnosis.

Conclusion

MS should be considered in the differential diagnosis of young women presenting with migraine-like headaches and transient focal neurological deficits, particularly when imaging reveals white matter lesions. Early identification and treatment are essential to prevent irreversible disability. Comprehensive diagnostic evaluation, including MRI with advanced markers, CSF analysis, and autoimmune testing, remains the cornerstone of diagnosis. Ongoing follow-up with repeat imaging is mandatory to monitor disease evolution.

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