

CASE REPORT

MULTIPLE SCLEROSIS WITH LIMITED TREATMENT OPTIONS: A CASE REPORT ON AZATHIOPRINE AS AN ALTERNATIVE THERAPY

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Abstract

Introduction: Multiple sclerosis (MS) is a chronic immune-mediated disease affecting the central nervous system, characterized by demyelination and progressive disability. Estimated prevalence in Indonesia is approximately 0.01 per 100,000 population. Treatment includes managing acute relapses with corticosteroids and DMTs to prevent relapses and further disability. Immunosuppressants such as azathioprine are often used in Indonesia as a more accessible and affordable alternative to standard DMTs.

Case Presentation: A 30-year-old woman presented to the neurology outpatient clinic with a history of progressive bilateral lower-limb weakness since 2019, accompanied by urinary dysfunction and numbness below the abdominal region. Neurological examination revealed paraparesis of the lower limbs, hyperreflexia, positive bilateral Babinski signs, and hypoesthesia below T10. Brain MRI demonstrated demyelinating lesions in the corpus callosum, bilateral periventricular white matter, and subcortical frontal and parietal lobes, forming a Dawson's finger pattern. Spinal MRI revealed a demyelinating lesion at the T11 level. Cerebrospinal fluid (CSF) analysis showed type 2 oligoclonal bands. The patient was diagnosed with multiple sclerosis and treated with intravenous methylprednisolone and azathioprine as maintenance.

Discussion: The clinical presentation, characteristic MRI findings, and positive oligoclonal bands supported the diagnosis of multiple sclerosis. Although azathioprine is not considered a first-line DMT, it remains a practical treatment option where access to approved therapies is limited.

Conclusions: This case highlights the importance of integrating clinical, radiological, and CSF findings in diagnosing multiple sclerosis. Treatment should be individualized according to the patient's clinical condition and available healthcare resources, while improving access to evidence-based DMTs remains an important goal.

Keywords: Azathioprine, Demyelination, Dawson's fingers, Multiple Sclerosis, Oligoclonal bands

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Introduction

Multiple sclerosis (MS) is a chronic immune-mediated demyelinating disorder of the central nervous system

characterized by inflammation, demyelination, and progressive axonal degeneration. It predominantly affects young adults and represents a leading

cause of non-traumatic neurological disability worldwide. Although the prevalence of MS is highest in North America and Europe, increasing recognition in Asian populations suggests that the disease burden in these regions may be underestimated due to limitations in diagnostic resources and reporting systems.^{1,2}

The pathophysiology of MS involves a complex interplay between genetic susceptibility and environmental factors, including viral infections such as Epstein–Barr virus, vitamin D deficiency, and smoking. These factors contribute to dysregulated immune responses, resulting in the activation of autoreactive T and B lymphocytes, disruption of the blood–brain barrier, and formation of focal inflammatory demyelinating lesions within the brain and spinal cord.^{1,4} Magnetic resonance imaging (MRI) plays a central role in diagnosis, typically demonstrating multifocal white matter lesions in the periventricular, juxtacortical, and infratentorial regions, often with the characteristic “Dawson’s fingers” configuration.² Cerebrospinal fluid (CSF) analysis showing oligoclonal IgG bands further supports the diagnosis by indicating intrathecal immunoglobulin synthesis.⁴

The diagnosis of MS is based on the demonstration of dissemination in space and time, as defined by the 2017 revisions of the McDonald criteria, which incorporate clinical, radiological, and laboratory findings to improve diagnostic sensitivity and allow for earlier diagnosis.³ The inclusion of CSF oligoclonal bands as a substitute for dissemination in time has

enhanced diagnostic accuracy, particularly in patients with atypical or early-stage presentations.³

Disease-modifying therapies (DMTs) constitute the cornerstone of MS management, aiming to reduce relapse rates and delay disability progression. Current international guidelines, including those from the European Committee for Treatment and Research in Multiple Sclerosis and the European Academy of Neurology, recommend early initiation of DMTs and individualized treatment strategies based on disease activity, safety considerations, and patient-specific factors.^{1,6} These guidelines emphasize timely treatment escalation in patients with ongoing disease activity to optimize long-term neurological outcomes.

However, in many low- and middle-income countries, access to standard DMTs remains limited due to high costs, restricted availability, and healthcare infrastructure constraints.^{7,10} As a result, conventional immunosuppressive agents such as azathioprine are still utilized as alternative maintenance therapies despite variability in the supporting evidence.^{8,9}

In this report, we present a case of clinically and radiologically confirmed multiple sclerosis managed with azathioprine in a resource-limited setting. Rather than presenting an unusual clinical manifestation, this case highlights the therapeutic challenges encountered when guideline-recommended disease-modifying therapies are inaccessible because of financial and healthcare resource constraints. It illustrates how treatment decisions may need to be individualized while balancing evidence-

based recommendations with local healthcare realities, an issue that remains relevant in many low- and middle-income countries.^{6,11}

Case Presentation

A 30-year-old woman presented to the neurology outpatient clinic with progressive bilateral lower-limb weakness that began in 2019. The weakness initially developed insidiously and gradually worsened over time, leading to difficulty walking without assistance. She also reported numbness below the abdominal region and urinary dysfunction characterized by urgency and incomplete bladder emptying. There was no history of acute visual loss, seizures, head trauma, or previous central nervous system infections. No significant family history of autoimmune or neurological disease was reported.

Neurological examination revealed spastic paraparesis of the lower extremities with Medical Research Council (MRC) muscle strength grading of 4/5 bilaterally. Deep tendon reflexes were brisk in both lower limbs, with positive bilateral Babinski signs. Sensory examination demonstrated hypoesthesia below the T10 dermatome level. Upper extremity strength and cranial nerve examination were unremarkable. Coordination testing of the upper limbs was normal. These findings were consistent with upper motor neuron involvement and suggested thoracic spinal cord pathology.

Magnetic resonance imaging (MRI) of the brain demonstrated multiple hyperintense lesions on T2-weighted and FLAIR sequences located in the corpus

callosum, bilateral periventricular white matter, and subcortical regions of the frontal and parietal lobes. Several lesions were oriented perpendicular to the lateral ventricles, forming a characteristic Dawson's finger pattern. Spinal MRI revealed a focal demyelinating lesion at the T11 vertebral level.



Figure 1. Sagittal brain FLAIR MRI demonstrating multiple periventricular hyperintense lesions oriented perpendicular to the lateral ventricles (Dawson's fingers), characteristic of multiple sclerosis. Sagittal spinal T2-weighted MRI demonstrates a focal hyperintense demyelinating lesion at the T11 level.

Cerebrospinal fluid (CSF) analysis showed type 2 oligoclonal IgG bands, indicating intrathecal immunoglobulin synthesis. Based on the clinical presentation, radiological findings demonstrating dissemination in space, and supportive CSF analysis, a diagnosis of multiple sclerosis was established.

The patient received intravenous methylprednisolone for acute disease control, followed by oral azathioprine as maintenance therapy due to limited access to standard disease-modifying therapies. Regular clinical follow-up was arranged to monitor disease progression and

treatment tolerance. Verbal informed consent for publication of this anonymized case report was obtained from the patient.

Discussion

This case highlights the diagnostic approach and therapeutic challenges in managing multiple sclerosis (MS), particularly in a resource-limited setting. The patient presented with progressive bilateral lower limb weakness, a sensory level below T10, and urinary dysfunction, all of which are characteristic features of spinal cord involvement. The neurological findings of spastic paraparesis, hyperreflexia, and bilateral Babinski signs indicate upper motor neuron pathology, consistent with a thoracic myelopathy.¹

Magnetic resonance imaging (MRI) findings played a pivotal role in establishing the diagnosis. The presence of multiple periventricular and subcortical white matter lesions oriented perpendicular to the lateral ventricles, forming the characteristic “Dawson’s fingers,” is widely recognized as a radiological hallmark of MS and reflects perivenular demyelination.² In addition, the identification of a focal demyelinating lesion at the T11 level on spinal MRI correlates with the patient’s clinical presentation and further supports dissemination in space.³

Importantly, the diagnosis in this patient fulfills the 2017 McDonald criteria for MS. Dissemination in space is demonstrated by lesions in characteristic regions, including periventricular areas (evidenced by Dawson’s fingers) and the spinal cord.³ Although dissemination in time was not demonstrated on serial imaging, the presence of type 2 oligoclonal

IgG bands in cerebrospinal fluid can substitute for dissemination in time under the revised criteria.^{3,4} Thus, the integration of clinical, radiological, and laboratory findings is sufficient to establish the diagnosis.

Important differential diagnoses in patients presenting with myelopathy include neuromyelitis optica spectrum disorder (NMOSD), myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), idiopathic transverse myelitis, and compressive spinal cord lesions. In the present case, the presence of characteristic periventricular lesions with Dawson’s fingers, positive cerebrospinal fluid oligoclonal IgG bands, and multifocal involvement of the brain and spinal cord strongly favored multiple sclerosis. Although AQP4-IgG and MOG-IgG antibody testing were unavailable, the overall clinical, radiological, and cerebrospinal fluid findings were considered more consistent with multiple sclerosis than with these alternative diagnoses.^{2,3,4}

Management of MS involves both treatment of acute relapses and long-term disease modification. High-dose corticosteroids, such as intravenous methylprednisolone, remain the standard therapy for acute exacerbations and function by suppressing inflammatory activity and accelerating neurological recovery, although they do not alter long-term disease progression.¹

A major challenge in this case was the selection of an appropriate maintenance therapy. Current international guidelines recommend early initiation of approved disease-modifying therapies, including interferon beta,

glatiramer acetate, fumarates, sphingosine-1-phosphate receptor modulators, and monoclonal antibodies, according to disease activity and patient characteristics.^{1,6} However, these agents remain unavailable or unaffordable for many patients in low- and middle-income countries because of their high cost and limited reimbursement. Consequently, conventional immunosuppressive agents such as azathioprine continue to be used as alternative maintenance therapies in routine clinical practice.^{6,7,11}

In such settings, conventional immunosuppressive agents such as azathioprine are frequently used as alternative maintenance therapies. Azathioprine, a purine analog that inhibits lymphocyte proliferation, has been studied in MS with variable results. Although azathioprine is no longer recommended as a first-line disease-modifying therapy, several studies have demonstrated that it may reduce relapse frequency and provide modest clinical benefits,

Table 1. 2017 McDonald Criteria for the Diagnosis of Multiple Sclerosis

Clinical Presentation	Additional Data Needed for MS Diagnosis
≥2 attacks and objective clinical evidence of ≥2 lesions	None. Dissemination in space (DIS) and dissemination in time (DIT) are fulfilled
≥2 attacks and objective clinical evidence of 1 lesion	DIS required: • ≥1 T2 lesion in ≥2 of the following CNS regions: – Periventricular – Juxtacortical/cortical – Infratentorial – Spinal cord
1 attack and objective clinical evidence of ≥2 lesions	DIT required (one of the following): • Additional clinical attack • Simultaneous presence of enhancing and non-enhancing MRI lesions • New T2 or enhancing lesion on follow-up MRI • CSF-specific oligoclonal bands
1 attack and objective clinical evidence of 1 lesion (clinically isolated syndrome)	DIS AND DIT required: DIS: ≥1 T2 lesion in ≥2 CNS regions (periventricular, juxtacortical/cortical, infratentorial, spinal cord) DIT (one of the following): • Additional clinical attack • Simultaneous enhancing and non-enhancing lesions • New T2/enhancing lesion on follow-up MRI • CSF-specific oligoclonal bands
Insidious neurological progression suggestive of MS (primary progressive MS)	1 year of disease progression (retrospective or prospective) PLUS 2 of the following: • ≥1 T2 lesion in typical brain regions (periventricular, juxtacortical/cortical, infratentorial) • ≥2 spinal cord lesions • CSF-specific oligoclonal bands

particularly in settings where approved DMTs are inaccessible. Nevertheless, the quality of evidence remains lower than that supporting currently approved DMTs, and treatment selection should therefore be individualized after considering efficacy, safety, availability, and patient-specific socioeconomic factors.^{8,9} Its use is also associated with potential adverse effects, including leukopenia and hepatotoxicity, necessitating regular laboratory monitoring. Because azathioprine is associated with dose-dependent myelosuppression and hepatotoxicity, routine monitoring should include complete blood count and liver function tests every 2 weeks during treatment initiation, followed by periodic monitoring once the maintenance dose is achieved. TPMT or NUDT15 testing should also be considered before treatment initiation, where available.

Despite these limitations, azathioprine remains a pragmatic option in resource-constrained environments, where treatment decisions are often influenced by socioeconomic factors rather than strict adherence to guideline-recommended therapies. Reports from resource-limited settings, including South-West India, have similarly demonstrated that restricted access to specialized neurological care and high-cost disease-modifying therapies substantially influences treatment strategies for patients with multiple sclerosis.¹⁰ Current international guidelines consistently recommend early initiation of approved disease-modifying therapies to reduce relapse rates and delay disability progression. However, in many low- and

middle-income countries, treatment availability and affordability continue to influence therapeutic decisions, leading clinicians to consider alternative immunosuppressive agents such as azathioprine. This case highlights the practical challenges of implementing evidence-based recommendations in resource-limited settings and demonstrates the importance of individualized treatment strategies when standard disease-modifying therapies are not readily accessible.^{6,8,9}

Conclusion

Multiple sclerosis is a chronic demyelinating disease that requires a comprehensive diagnostic approach integrating clinical findings, magnetic resonance imaging, and cerebrospinal fluid analysis. In this case, the presence of characteristic MRI features, including Dawson's fingers, along with type 2 oligoclonal bands and consistent neurological deficits, fulfilled the 2017 McDonald criteria for diagnosis.³

Management of multiple sclerosis involves both acute relapse treatment and long-term disease modification. High-dose corticosteroids remain the standard therapy for acute exacerbations, while disease-modifying therapies are recommended to reduce relapse rates and delay disease progression.^{1,6} However, in resource-limited settings, access to standard disease-modifying therapies is often restricted, necessitating the use of alternative immunosuppressive agents.⁷

Azathioprine, although not considered a first-line therapy in current guidelines, may serve as a practical and

accessible alternative in such contexts. Evidence suggests that it can provide modest benefits in reducing disease activity, although careful monitoring is required due to potential adverse effects.^{8,9}

Conflict of Interest

The authors declared no conflict of interest.

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Consent

Verbal informed consent for publication of this anonymized case report and accompanying images was obtained from the patient.

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