CME/CE ACTIVITY

Case Studies in Multiple Sclerosis and Aging

Case Focus: Memory, Aging, and MS

Case 1

Case Focus: What If It Is Not Normal Pressure Hydrocephalus?

Case 2

Case Focus: To Treat or Not to Treat?

Case 3

Jointly Provided by

AACME® AMERICAN ACADEMY OF CME, INC.

CAN DO MULTIPLE SCLEROSIS

This program is supported in part by an independent medical educational grant from Mylan Specialty L.P., a Viatris Company.

Release date: May 15, 2024
Expiration date: May 15, 2025
Estimated time to complete: 1.0 hours

See last page for How to Claim CME/CE credit

Faculty Educators

Kalina Sanders, MD, MHA
Neurologist
Baptist Neurology Group
Jacksonville, FL

Megan Weigel, DNP, APRN-c
Nurse Practitioner
Baptist Neurology Group.
Jacksonville, FL

Learning Objectives: After participating in the activity, learners should be better able to:

- Identify the clinical difference between age-related/neurodegenerative cognitive decline and MS-related cognitive impairment.
- Discuss the role of potential biomarkers in identifying coexisting neurodegenerative disorders.
- Explain why it is important for the care team to address comorbid vascular risk factors for cognitive decline, including lifestyle modification and healthy behaviors

Target Audience: This activity has been designed to meet the educational needs of clinicians caring for patients with MS (MDs, NPs, PAs, RNs). Other healthcare providers may also participate.

Accreditation and Credit: In support of improving patient care, this activity has been planned and implemented by American Academy of CME, Inc. and Can Do Multiple Sclerosis. American Academy of CME, Inc. is Jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

JOINTLY ACCREDITED PROVIDER™ INTERPROFESSIONAL CONTINUING EDUCATION

Physicians: American Academy of CME, Inc., designates this enduring material for a maximum of 1.0 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurse Practitioners and Nurses: American Academy of CME, Inc., designates this educational activity for 1.0 ANCC contact hours (0.6 pharmacotherapeutic contact hours. California: Provider approved by the California Board of Registered Nursing, Provider Number CEP16993 for 1.0 contact hours.

PAs: Per the American Academy of PAs, PAs attending an educational activity that has been designated for *AMA PRA Category 1 Credit™* may claim up to the maximum number of credits designated.

Other HCPs: Other members of the care team will receive a certificate of participation.

Method of Participation: There are no fees to participate in the activity. Participants must review the activity information including the learning objectives and disclosure statements, as well as the content of the activity. To receive CME/CNE credit for your participation, please complete the post-test (achieving a passing grade of 70% or greater), and program evaluation. Your certificate can be printed immediately. For any questions, please contact: CEServices@academycme.org

Disclosures: According to the disclosure policy of the Academy, all faculty, planning committee members, editors, managers and other individuals who are in a position to control content are required to disclose any relationships with any ineligible company(ies). The existence of these relationships is not viewed as implying bias or decreasing the value of the activity. Clinical content has been reviewed for fair balance and scientific objectivity, and all of the relevant financial relationships listed for these individuals have been mitigated. Disclosure of relevant financial relationships are as follows:

Faculty Educators and Planners: Kalina Sanders, MD, MHA, discloses the following relationships: Advisory Board/Consultant: Genentech, Octave; Grant/Research Support: Genentech; Speaker's Bureau: Biogen Idec, Bristol Myers Squibb, EMD Serano, Genentech

Megan Weigel, DNP, APRN-c, discloses the following relationships: Advisory Board/Consultant—Horizon, TG therapeutics, Cycle Pharma, Octave; Speakers Bureau: Horizon, Sanofi, TG Therapeutics, Bristol Myers Squibb

Planning Committee: John JD Juchniewicz, MCIS, CHCP, FACEHP, Natalie Kirkwood, RN, BSN, JD, American Academy of CME: Nothing to disclose. Kathleen Costello, CRNP, MSCN, Can Do Multiple Sclerosis, discloses the following relationships: Amgen, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Novartis, Sandoz, Sanofi and Viatris.

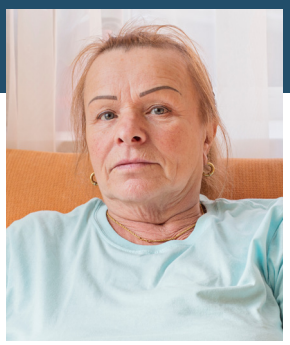
This activity will review off-label or investigational information.

The opinions expressed in this accredited continuing education activity are those of the faculty, and do not represent those of the Academy or Can Do Multiple Sclerosis. This educational activity is intended as a supplement to existing knowledge, published information, and practice guidelines. Learners should appraise the information presented critically, and draw conclusions only after careful consideration of all available scientific information.

CME/CE information continued on last page of monograph

CASE 1

Case Focus: Memory, Aging, and MS



Case Learning Outcomes

- Identify the clinical difference between age related/ neurodegenerative cognitive decline and MS related cognitive impairment.
- Discuss the role of potential biomarkers in identifying coexisting neurodegenerative disorders.
- Describe the importance of addressing comorbid vascular risk factors for cognitive decline, including lifestyle modification and healthy behaviors

Chief Complaint

Short-term memory loss and word-finding issues following TIA

Presentation

Mrs. Williams is a 69-year-old Caucasian female with multiple sclerosis (MS). She was diagnosed with MS in 1990 (at age 32) after an episode of right optic neuritis. She has been on disease modifying therapy (DMT) since 1996 after having a spinal cord relapse. Five years ago, she was diagnosed with hypertension and placed on hydrochlorothiazide. Her blood pressure has been poorly controlled for the past 1 year. She was admitted to the hospital for a transient ischemic attack (TIA) 6 months ago.

At her yearly appointment with her MS care team, she complains of increased forgetfulness. She notes difficulty with short-term memory. She is having trouble with keeping details straight about recent conversations and events. She also reports some word-finding issues. She remains independent in her activities of daily living. She reports that her mother was diagnosed with Alzheimer's disease at age 75 and is concerned that she may be in the beginning stage of dementia.

Past Medical History

MS, hypertension, TIA

Medications

hydrochlorothiazide 25mg PO daily; dimethyl fumarate 240mg PO BID; aspirin 81mg daily; atorvastatin 40mg PO daily

Family History

Alzheimer's disease (mother); hypertension, hyperlipidemia, coronary artery disease (father); systemic lupus erythematosus (sister)

Social History

Non-smoker; 1-2 glasses of wine per week; no recreational drug use; married; retired

Physical Examination

Temperature: 98.6°F
Height: 5' 4"
Blood pressure: 122/78 mmHg
Weight: 170 lbs
Heart rate: 76 beats per minute
BMI: 29.2 kg/m^2

General

69-year-old, overweight female in no acute distress. Physical exam is normal, including the absence of carotid bruits. Neurological exam is positive for R>LLE spasticity and hip hike on R with mild foot drop. Mini-Mental State Examination (MMSE) score is 29/30.

Laboratory Studies

MRI Brain, Cervical and Thoracic show no new or enhancing lesions and brain shows atrophy consistent for age; CBC w/ diff and CMP are normal; Hgb A1c is 5.6%; lipid profile is normal with LDL 68; B12 348; folate 15; TSH 2.5

Preventative Health History

The addition of atorvastatin to her medication regimen after TIA decreased LDL from 110 to 68; she has lost 15 pounds with diet changes (reduction of processed foods including sugars and following a plant-based diet) and increased exercise (she does online exercises for MS 5 times per week and rides a stationary bicycle, total of 200 min/week).

Additional Important Information:

Neuropsychometric testing has been ordered after today's visit due to the age of the patient, vascular risk factors, and family history that may impact cognitive function differently than MS. The Symbol Digit Modalities Test (SDMT) is the gold standard for baseline and regular monitoring of cognitive function in MS, however, it is expensive for clinics to use; similarly, use of free electronic versions is limited because of the need for iPad or computer access by the patient during the clinic visit. If these tests are not available to a clinic, repeating the same cognitive screen with additional comprehensive testing (neuropsychometric testing) when indicated should be the approach used (Kalb, 2018).

Although she reports restorative sleep and minimal fatigue, a polysomnogram has been ordered due to sleep apnea as a risk factor for cerebrovascular disease and association with memory issues. In addition, although she does not report any changes in mood, a depression screening test is administered as depression can impact cognitive function (Kalb, 2018).

She was advised to start oral B12 supplementation, 1000mcg daily, at today's visit.

continued on next page

Case Focus: Memory, Aging, and MS

Learner Reflection Question #1
What are the key differences between amnestic Mild Cognitive Impairment and MS-related cognitive impairment?

Clinical Commentary

The profile of cognitive deficits is the key difference between amnestic mild cognitive impairment (MCI) and MS-related cognitive impairment. MS is not associated with impairment of memory consolidation (Shumita, 2018). The cognitive profile of patients with MS includes deficits in information processing speed, verbal learning, executive function, and visuospatial learning (Branco, 2019). Retention deficit is not seen in MS, whereas poor retention, and rapid forgetting, are hallmark features of Alzheimer's disease (Shumita, 2018).

Learner Reflection Question #2
When evaluating cognitive decline, is there a role for biomarkers in identifying a coexisting neurodegenerative disorder?

Clinical Commentary

Screening assessments should be concise, straightforward, and highly accurate. Common assessments for multiple sclerosis include the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ), Paced Auditory Serial Addition Task with a 3-second interval (PASAT 3), and Symbol Digit Modality Test (SDMT) (Meca-Lallana, 2021). Neuropsychological testing can be conducted for a more comprehensive evaluation. However, it can be difficult distinguishing the two with neuropsychological testing only (Londoño, 2022).

Screening for depression should be conducted regularly and if cognitive symptoms are reported. Depression is known to negatively impact cognition (Kalb, 2018).

CSF Biomarkers and neuroimaging can potentially distinguish coexistent neurodegenerative dementia subtypes in people with MS (Meca-Lallana, 2021). Decreased thalamic volume, for example, is associated with cognitive impairment in MS (Amin, 2021). While both cerebro-spinal fluid (CSF) total tau, phosphorylated tau, and amyloid-beta proteins have been implicated in cognitive impairment in Alzheimer's disease, their roles in MS cognitive impairment are less clear and somewhat controversial.(Londoño, 2022; Esmaeili 2023). PET hypometabolism patterns may be useful in determining if an additional neurodegenerative cognitive disorder exists (Londoño, 2022).

Learner Reflection Question #3
Does addressing comorbid vascular risk factors help?

Clinical Commentary

Vascular risk factors such as hypertension and hyperlipidemia are two of the most prevalent comorbidities in patients with MS (Magyari, 2020). They are also independent risk factors for cognitive decline. Therefore, lifestyle and pharmacological interventions for cardiovascular risk factors should be considered carefully in the management of MS (Reia, 2021; Brandstadter, 2016; Sand, 2023; Li, 2023; Braley, 2023).

Working Together as a Team
What interdisciplinary referrals could make the most difference for him?

A referral to neuropsychology for formal cognitive testing is indicated in this case. Further referrals would include cognitive rehabilitation and/or investigation for other causes of memory problems. Cognitive rehabilitation has been shown to improve motor tasks and working memory (though not visual spatial skills) in patients with MS-related cognitive impairment, and may also improve quality of life in this population (Vaughn, 2019).

Patient education would also be important. For example, the MS nurse could explain to the patient the differences between memory problems in MS and Alzheimer's disease, as well as strategies to improve brain health including healthy diet, exercise, sleep hygiene, stress reduction, and improved mental health (Brandstadter, 2016; Sand, 2023; Li, 2023; Braley, 2023).

The team might also consider B12 and/or folate supplementation if the patient has an insufficient or deficient level of either vitamin. Adding donepezil and memantine (which are indicated for the treatment of dementia associated with Alzheimer disease) has not been shown to be effective in memory issues related to MS (Vaughn, 2019).

continued on next page

Closing Commentary

Understanding the differences between amnestic MCI and MS-related cognitive impairment is crucial, with MS primarily affecting processing speed, verbal learning, and executive function, while amnestic MCI focuses on memory consolidation deficits. Biomarkers like CSF analysis and neuroimaging can aid in identifying coexisting neurodegenerative disorders in patients with MS, while addressing vascular risk factors is essential for managing cognitive decline. Collaboration among the MS care team, including referrals to neuropsychology and cognitive rehabilitation, can optimize care and outcomes for patients with MS who have cognitive challenges. This case poses a unique opportunity to empower someone living with MS to continue healthy lifestyle changes to improve overall brain health and deter cognitive loss.

References

Amin M, Ontaneda D. Thalamic injury and cognition in multiple sclerosis. *Frontiers in Neurology*. 2021;11, 623914. https://doi-org.proxy1.library.jhu.edu/10.3389/fneur.2020.623914.

Braley T, Shieu M, et al. Pathways between multiple sclerosis, sleep disorders, and cognitive function: longitudinal findings from The Nurses' Health Study. *Multiple Sclerosis.* 2023;29(3), 436-446. doi: 10.1177/13524585221144215.

Brandstadter R, Sand IK, Sumowki JF. Beyond rehabilitation: a prevention model of reserve and brain maintenance in multiple sclerosis. *Multiple Sclerosis,* 2019;25(10):1372-1378.

Branco M, Ruano L, Portaccio E, et al. Aging with multiple sclerosis: prevalence and profile of cognitive impairment. *Neurol Sci.* 2019;Aug;40(8): 1651-1657. doi: 10.1007/s10072-019-03875-7. Epub 2019 Apr 23. *Erratum in: Neurol Sci.* 2020;Jan;41(1):243. PMID: 31011932.

Esmaeili S, Obeidat AZ, Zabeti A. Molecular biomarkers and cognitive impairment in multiple sclerosis: A Review. *Biomarkers in Neuropsychiatry.* 2023;9:100077. doi:10.1016/j.bionps.2023.100077.

Kalb R, Beier M, Benedict RH, Charvet L, et al. Recommendations for cognitive screening and management in multiple sclerosis care. *Mult Scler.* 2018 Nov;24(13):1665-1680. doi: 10.1177/1352458518803785. Epub 2018 Oct 10. PMID: 30303036; PMCID: PMC6238181.

Li G, You Q, Hou X, et al. The effect of exercise on cognitive function in people with multiple sclerosis: a systematic review and meta-analysis of randomized controlled trials. *Journal of Neurology.* 2023;270(6), 29088-2923. doi: 10.1007/s00415-023-11649-7.

Londoño DP, Arumaithurai K, Constantopoulos E, et al. Diagnosis of coexistent neurodegenerative dementias in multiple sclerosis. *Brain Communications.* 2022;4(4):fcac167.

Magyari M, Sorensen PS. Comorbidity in Multiple Sclerosis. *Front Neurol.* 2020;11:851. doi: 10.3389/fneur.2020.00851.

Meca-Lallana V, Gascón-Giménez F., Ginestal-López RC, et al. Cognitive impairment in multiple sclerosis: diagnosis and monitoring. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*. 2021;42(12):5183–5193. https://doi.org/10.1007/s10072-021-05165-7.

Reia A. Petruzzo M. Falco F, et al. A Retrospective Exploratory Analysis on Cardiovascular Risk and Cognitive Dysfunction in Multiple Sclerosis. *Brain Sci.* 2021;11:502. https://doi.org/10.3390/ brainsci11040502.

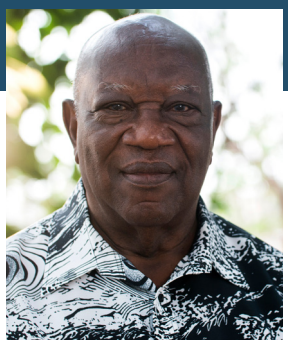
Sand IK, Levy S, Fitzgerald K, et al. Mediterranean diet is linked to less objective disability in multiple sclerosis. *Mult Scler.* 2023;Feb 29(2):248-260. doi: 10.1177/13524585221127414. Epub 2022 Oct 13. PMID: 36226971; PMCID: PMC9918647.

Shumita R, Drake A, Snyder S, et al. Preliminary investigation of cognitive function in aged multiple sclerosis patients: Challenges in detecting comorbid Alzheimer's disease, *Multiple Sclerosis and Related Disorders*. 2018;22:52-56. https://doi.org/10.1016/j.msard.2018.03.008.

continued on next page

CASE 2

Case Focus: What If It Is Not Normal Pressure Hydrocephalus?



Case Learning Outcomes

- Effectively describe the effects of immunosenescence in MS
- Develop decision making strategies the care team can use to provide safe MS care to an older patient
- Define the use of common and less commonly used forms of rehabilitative therapies to improve quality of life

Chief Complaint

Progressive gait issues and neurogenic bladder

Presentation

Mr. Smith is a 72-year-old African American male with at least a 10-year history of gait spasticity. He was evaluated for and diagnosed with normal pressure hydrocephalus (NPH) because of gait ataxia, urinary frequency/urgency, difficulty with hand dexterity, and paresthesias. His MRI Brain showed ventriculomegaly consistent with NPH, and cisternogram was positive. He underwent VP shunt placement, but his symptoms were unchanged. During that time, he had an MRI Brain that showed an enhancing lesion in the corona radiata. Once he "failed" his procedure, he and his wife sought a second opinion. Further imaging was completed. He was found to have nonenhancing spinal cord lesions in addition to the enhancing brain lesion. Lumbar puncture revealed unique oligoclonal bands. Review of history was notable for two episodes of "uveitis" in his 20s.

Past Medical History

as above; hypertension, T2DM, chronic pain related to degenerative disc disease

Past Surgical History

lumbar laminectomy,
VP shunt placement

Medications

lisinopril 10mg PO daily; metformin 1000mg PO BID; pregabalin 550mg PO TID; mirabegron 25mg PO daily

Family History

T2DM (mother, father, brothers)

Physical Examination

Temperature: 98.2°F
Height: 6' 2"
Blood pressure: 148/90 mmHg
Heart rate: 80 beats per minute
Weight: 250 lbs
BMI: 31.1 kg/m^2

General

Tall, obese African American male in no acute distress. Neurological examination notable for 4/5 left upper extremity strength, 4/5 bilateral lower extremity hip flexion, 5-/5 left dorsiflexion; diminished sensation in stocking distribution to pin; brisk lower extremity reflexes with left upgoing toe. Clasp-knife rigidity noted in the BLE. Walks with walker; gait is slow with a broad base and left foot drop.

Laboratory Studies

MRI Brain showed enhancing lesion in corona radiata with multiple short segment non-enhancing lesions in the cervical and thoracic spinal cord regions. CSF + for 6 oligoclonal bands that were unique to the CSF. Labs for MS mimics were unremarkable.

Preventative Health History

Mr. Smith complained of weakness that limits his ability to exercise. He prefers a diet of convenience. He receives regular medical care for his other medical conditions and assumed that walking issues were related to Lumbar disc disease and diabetes.

Additional Important Information:

No history of cognitive complaints; reports decreased sense of well-being because of limitations from his symptoms, as well as disappointment because shunt placement did not help him.

Learner Reflection Question #1
What leads to the misdiagnosis of multiple sclerosis in the older population?

Clinical Commentary

Late Onset Multiple Sclerosis (LOMS) has symptom onset at ages above 50. Very Late Onset Multiple Sclerosis (VLOMS) is defined as symptom onset above the age of 60. LOMS and VLOMS are relatively uncommon, representing about 5% and 3.6% of the MS population, respectively (Naseri, 2021). Due to the lower prevalence, healthcare providers might not consider it as a differential diagnosis initially, especially if the patient doesn't fit the typical demographic for MS. Diagnostic uncertainty can pose a problem in a patient at older age of diagnosis. There may be atypical presentations including progressive gait dysfunction, which can be

continued on next page

misdiagnosed as cervical myelopathy or NPH. Additionally, older individuals often have other comorbidities that can mask or mimic symptoms of MS, such as stroke history, degenerative disc disease, peripheral neuropathy. The clinician should become comfortable with evaluating lesion characteristics on MRI and CSF evaluation in the older patient with possible MS.

Learner Reflection Question #2
What role does immunosenescence play in multiple sclerosis in the aging population?

Clinical Commentary

Both chronological age and biological age play important roles in the aging process in MS. Chronological age refers to the actual number of years a person has lived since birth. Chronological age is associated with faster decline in relapse rates, and increased accumulation of disability (Graves, 2023). There is a significant age-related change in central nervous system (CNS) pathology between relapsing and progressive forms of MS. Immunosenescence, which increases with age, is marked by age-dependent decreases in the proportions of B cells and CD8+ T cells (Buscarinu, 2023). Additionally, in older patients with progressive disease, inflammation primarily affects CNS border regions, causing damage to deeper CNS cells via released soluble factors or activation of microglia and astrocytes (Graves, 2023).

Biological age represents the physiological age of an individual's body, which may differ from their chronological age. Biological age can be expressed by telomere length. A shorter length of leukocyte telomeres has been linked to increased disability scores and reduced brain volume, regardless of the individual's chronological age (Graves, 2023). Patients with MS may be at risk for accelerated biological aging (Miner, 2023). Biological aging is characterized by chronic low-grade inflammation and age-related increases in gastrointestinal permeability that contribute to immune dysregulation in MS (Graves, 2023). This process leads to the activation of microglia in the CNS and promotes pathogenic changes in chronic active lesions (Graves, 2023). Furthermore, immunosenescence-related alterations in lymphocytes may exacerbate MS pathology and hinder repair mechanisms. Immunosenescence may also impact the efficacy of MS disease modifying therapies, increase the risk of infections and may dampen immunization response–all necessitating consideration when treating an older individual with an MS DMT (Thakolwiboon, 2023).

Understanding the interplay between these factors can help the care team to tailor treatment approaches and interventions to address the unique needs of older individuals with MS and optimize their quality of life as they age.

Learner Reflection Question #3
What decision making strategies should the healthcare team consider when caring for older patients with MS?

Clinical Commentary

The care team should adopt a comprehensive approach to the older patient with MS. Through multidisciplinary collaboration, including neurologists, nurses, therapists, and social workers, the team assesses the patient's medical history, disease severity, cognitive status, functional abilities, and psychosocial factors. Based on this assessment, an individualized treatment plan is developed, considering the person's age, comorbidities, treatment preferences, and goals of care. This treatment plan should consider immunosenescence, which may cause the patient to have fewer relapses but more disability acquisition. Changes in the immune system as a result of aging may also put the patient at greater risk for infectious side effects of disease modifying therapies (Graves, 2023; Buscarinu, 2022; Thakolwiboon, 2023).

Before initiating or adjusting DMTs, a thorough risk-benefit assessment is conducted by the team to evaluate efficacy, safety profile, potential adverse effects, and impact on quality of life. Fall prevention strategies, cognitive screening, medication management, and regular monitoring are integrated into the care plan of the individual patient to address specific needs and mitigate risks associated with aging and MS progression. Regular access to rehabilitation services can enhance physical function, minimize fall risks, preserve upper limb capabilities, and instruct on energy conservation and cognitive compensation techniques (Buscarinu, 2023). Additionally, advance care planning discussions are initiated to ensure alignment with the patient's preferences for end-of-life care.

By implementing these strategies, the care team optimizes safety, quality of care, and overall outcomes for older patients with MS.

continued on next page

Case Focus: What If It Is Not Normal Pressure Hydrocephalus?

Working Together as a Team

What interdisciplinary referrals could make the most difference for him?

Referrals to PT, OT, ST and music therapy, if indicated, could improve symptomatology and quality of life; referral to a mental health counselor could help with adjustment and/or mood disorder; referrals for MS education could help patient/family make sense of "what is/isn't MS". Referral also placed to urology for assistance with neurogenic bladder.

Closing Commentary

In addressing the complexities of MS in the older population, it becomes evident that misdiagnosis and treatment challenges arise due to the nuanced nature of symptom presentation and the influence of aging on disease pathology. Understanding the interplay between immunosenescence, biological aging, and chronological age is crucial in tailoring effective treatment strategies. By adopting a comprehensive approach that includes multidisciplinary collaboration, individualized treatment plans, and proactive risk assessment, healthcare teams can optimize care for older patients with MS.

References

Buscarinu MC, Reniè R, Morena E, et al. Late-onset MS: Disease course and safety-efficacy of DMTS. *Frontiers in Neurology.* 2022;13. doi:10.3389/fneur.2022.829331.

Graves JS, Krysko KM, Hua LH, et al. Ageing and multiple sclerosis. *The Lancet Neurology.* 2023;22(1):66-77. doi:10.1016/s1474-4422(22)00184-3.

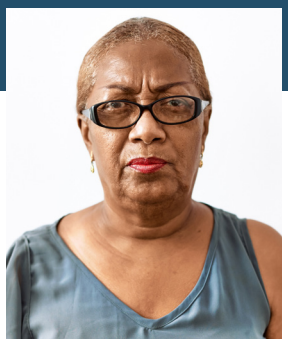
Miner AE, Yang JH, Kinkel RP, Graves JS. The NHANES Biological age index demonstrates accelerated aging in MS patients. *Multiple Sclerosis and Related Disorders.* 2023;77:104859. doi:10.1016/j.msard.2023.104859.

Naseri A, Nasiri E, Sahraian MA, et al. Clinical features of late-onset multiple sclerosis: A systematic review and meta-analysis. *Multiple Sclerosis and Related Disorders*. 2021;50:102816. doi:10.1016/j.msard.2021.102816.

Thakolwiboon S, Mills EA, Yang J, Doty J, Belkin MI, Cho T, Schultz C, Mao-Draayer Y. Immunosenescence and multiple sclerosis: inflammaging for prognosis and therapeutic consideration. *Front Aging*. 2023 Oct 13;4.

continued on next page ▸

Case Focus: To Treat or Not to Treat?



Case Learning Outcomes

- Discuss best practices for the choosing DMT in the older adult with active MS
- Review key points related to initiation, continuation, or discontinuation of DMTs in the older adult
- Discuss the importance of comprehensive care management in the older adult with MS, including primary, specialty, and mental health care

Chief Complaint

"I was in a car accident, and my neck pain and headaches aren't getting better. They said my MRIs were abnormal."

Presentation

Ms. Jules is a 60-year-old African American female who was involved in a motor vehicle accident 2 years ago. She had neck pain and headaches that did not resolve with conservative treatment. MRIs without contrast of brain and cervical spine were ordered and revealed multiple lesions consistent with MS. Contrast scans were ordered that showed enhancing lesions in both the brain and cervical spine; lumbar puncture revealed oligoclonal bands. She is intermittently hypertensive in the office; depressed; has chronic pain; and is risk averse.

Past Medical History

hypertension, depression, chronic pain

Past Surgical History

none

Medications

tramadol 50mg PO TID as needed for pain;
tizanidine 2mg PO at bedtime as needed

Family History

Parental history unknown; sister has depression/anxiety, breast cancer survivor

Social History

non-smoker; drinks 1-2 drinks on Friday night; works as RN on psychiatric floor of local hospital; divorced

Physical Examination

Temperature: 97.9°F
Blood pressure: 160/90 mmHg
Height: 5'7"
Weight: 150 lbs
BMI: 23.5 kg/m^2
Heart rate: 85 beats per minute

General

Tall, thin African American female in no acute distress with flat affect, depressed mood, and normal thought processes. Mild tenderness and moderate spasm noted in the trapezii and cervical paraspinous muscles and occipital notches bilaterally with normal cervical ROM; nontender temporal arteries with normal pulsations; neck flexion elicits Lhermitte's sign. Normal cranial nerves. Motor strength is 5/5 all extremities. Sensation is diminished distal hands and feet. Reflexes are symmetrically brisk in the UE/LEs and toes are down-going.

Laboratory Studies

MRI Brain revealed enhancing lesion in left periventricular region perpendicular to the ventricle with 2 other non-enhancing ovoid white matter lesions; MRI cervical spine revealed enhancing short segment lesion at C3-4. LP positive for elevated CSF IgG synthesis and 3 oligoclonal bands. Labs for MS workup notable for TSH of 0.4 mIU/L; JCV antibody positive with index of 3.6; Vitamin D 25OH 12 nmol/L.

Preventative Health History

Ms. Jules is up to date on preventive screenings including mammogram, Pap smear, and colonoscopy. She has never seen a dermatologist. Her TSH was high with her annual labs last year, and her primary care provider told her she would "watch it." She walked for exercise prior to her car accident but has not been able to do anything other than her PT exercises, which she sometimes avoids due to pain. She has a low appetite.

Additional Important Information:

She has a history of multiple drug allergies and prefers to treat issues naturally.

continued on next page ▸

Case Focus: To Treat or Not to Treat?

Learner Reflection Question #1
What DMTs might be presented to a risk averse older person with MS?

Clinical Commentary

When presenting choices to patients, factors the care team should consider include comorbidities, degree of monitoring required, and adverse events. It is also important to consider whether or not aging patients were included in clinical trials for suggested DMTs. (Graves 2023; Siddiqui 2024)

DMT Class	Comorbidities to Consider	Other Safety Concerns
Beta Interferons	None	Ability to administer injection
Glatiramer acetate	None	Ability to administer injection, lipoatrophy risk
Sphingosine-1-phosphate modulators	Diabetes, cardiovascular disease, cerebrovascular disease that cause contraindication or cautious use	Infection risk increases with age; drug interactions with medications that prolong the QT interval
Fumarates	None	Grade 3 lymphopenia risk increases with age, and thus, risk for PML
Teriflunomide	Hypertension, diabetes	None
Natalizumab	Prior immunosuppressant exposure, length of time on natalizumab	Risks of more severe PML increase at higher ages
Anti-CD20 therapy	Frequent infections prior to starting therapy	Risks of malignancy and infection increase with age
Cladribine	History of malignancy, frequent infections prior to starting therapy	Risks of malignancy and infection increase with age
Alemtuzumab	History of malignancy, frequent injections prior to starting therapy	Risks of malignancy and infection increase with age

(Table Ref: Graves, 2003; Vaughn, 2019)

Learner Reflection Question #2
Why might the care team not feel comfortable initiating a DMT in her case?

Clinical Commentary

MTs should be used with caution in aging people with an increased risk for adverse events, contraindications to their use due to medical comorbidities, and/or concern about patient follow-through with monitoring trajectory. However, certain cases require initiation of a DMT because of active inflammation as evidenced by MRI change and relapse that cause risk of disability. In those cases, the DMT with the best risk to benefit ratio should be chosen (see above table) (Siddiqui, 2024). In addition, knowledge of any evidence of how DMTs performed in an older population is critical information when making treatment decisions. For example, in the CLARITY clinical trial of oral cladribine and a post-hoc analysis *suggested* its efficacy is similar in people both above and below those aged 45 years (Vaughn, 2019).

continued on next page ▸

Learner Reflection Question #3

What strategies might the care team use to encourage her to quickly initiate and stay on DMT?

Clinical Commentary

If the patient agrees, share images with them so disease process is understood.

Another strategy would be to discuss the findings of DISCO-MS (Corboy, 2023). Specifically, the study was unable to prove whether discontinuation of DMT was non-inferior to continuation in people 55 years and over without recent relapse or new MRI activity. The authors concluded that discontinuation may be a reasonable option in people similar to the study population, however, findings also suggested there might be a small increased risk of MRI activity with discontinuation.

A third strategy might be to discuss the importance of general health and comorbidities management, as well as lifestyle changes to support health (Vaughn, 2019). Healthy lifestyle changes empower patients to be a part of their disease management. In MS, vascular comorbidities, including obesity, are associated with worse MS. One vascular comorbidity increases the likelihood of reaching an EDSS of 6 by 6 years (Marrie, 2010). Small vessel disease caused by vascular comorbidities and risks is independently associated with memory and gait dysfunction, compounding the risk for disability in those of older age (Sharma 2023; Jimenez-Balado, 2019).

Since our patient is of older age, she is less likely to completely recover from relapses and more likely to develop disability, so decreasing relapse rate with initiation of DMT is important to her health trajectory (Siddiqui, 2024).

Working Together as a Team

This case presents a great opportunity for conversation between the MS provider and nurse to develop a strategy to provide comprehensive education and engage in shared decision making with the patient regarding the decision to use DMT. It also presents an opportunity to make sure Ms. Jules is getting age-appropriate primary care and any referrals to specialists for conditions that may affect MS symptomatology, in this case: thyroid disease and fatigue, hypertension, chronic pain, and depression. The MS care team might also discuss rehabilitation strategies, which may benefit her painful conditions.

Closing Commentary

The diagnosis of MS at an older age is associated with increased disability. It is therefore important for the MS care team to discuss risks and possible benefits of DMT with patients and engaging them in shared decision making to determine the best plan of care.

References

Corboy JR, Fox RJ, Kister I, et al. Risk of new disease activity in patients with multiple sclerosis who continue or discontinue disease-modifying therapies (DISCOMS): a multicentre, randomized, single-blind, phase 4, non-inferiority trial. *Lancet Neurology.* 2023;22(7):568-577.

Graves J, Krysko K, Hua L, et al. Ageing and multiple sclerosis. *Lancet Neurology*. 2023;22:66-77.

Jimenez-Balado J, Riba-Llena I, Abril O, et al. Cognitive impact of cerebral small vessel disease changes in patients with hypertension. *Hypertension*. 2019;73(2):342-349.

Marrie RA, Rudick R, Horwitz R, et al. Vascular comorbidity is associated with more rapid disability progression in multiple sclerosis. *Neurology*. 2010;30(74):1041-1047.

Sharma B, Wang M, McCreary CR, et al. Gait and falls in cerebral small vessel disease: a systematic review and meta-analysis. *Age and Ageing*. 2023;52(3):afad011. doi: 10.1093/ageing/afad011.

Siddiqui A, Yang J, Hua Le, et al. Clinical and treatment considerations for the pediatric and aging patients with Multiple Sclerosis. *Neurological Clinics*. 2024;42:255-274.

Vaughn CB, Jakimovski D, Kavak K, et al. Epidemiology and treatment of multiple sclerosis in elderly populations. *Nature Reviews Neurology*. 2019;15:329-342.

CME/CE information continued from page 1

Implicit Bias: Implicit bias refers to unconscious attitudes and stereotypes that influence our thoughts, judgements, decisions, and actions without our awareness. Everyone is susceptible to implicit bias, even clinicians. In healthcare, implicit biases can have a significant impact on the quality of care an individual receives. These biases can be both favorable and unfavorable, and are activated involuntarily without an individual's awareness or intentional control.

Studies have indicated that healthcare providers' incorrect perceptions can impact providers' communications and clinical decision-making contributing to disparities in clinical outcomes. Addressing implicit biases in healthcare is critical to improving health outcomes and promoting health equity for all patients. Patient-centered care can reduce the impact of implicit bias, by treating each patient as a unique individual who may or may not hold beliefs associated with their backgrounds and circumstances. In addition, recognizing implicit bias in one's own practice using techniques such as self-reflection and mindful clinical decision-making can ensure more equitable and effective care for all patients.

Over the past several decades, cognitive science research has demonstrated human behavior, beliefs and attitudes are shaped by automatic and unconscious cognitive processes. The healthcare profession is devoting greater attention to how these automatic and unconscious processes impact care including: (1) preferential treatment toward or against specific patient populations causing healthcare inequities, (2) influence patient-provider communications leading to misunderstandings and mistrust, and (3) impact access to healthcare and affect treatment decisions resulting in misdiagnosis, delays in treatment and specialty referrals and poor pain management. Considering one might have unconscious biases and exploring them may be uncomfortable because the very idea that they exist may conflict with how clinicians perceive themselves. It is only by becoming aware of one's unconscious biases that members of the healthcare team can take steps to mitigate them to ensure all their patients receive quality healthcare.

Hardware/Software Requirements: Adobe Reader

Questions: For any questions about this CME/CE activity contact: CEServices@academycme.org

Privacy: For more information about the American Academy of CME privacy policy, please access academycme.org/privacy.htm

Faculty Educator Biographies

Kalina Sanders, MD, MHA
Neurologist
Baptist Neurology Group
Jacksonville, FL

Kalina Sanders, MD, MHA, is a board-certified neurologist with Baptist Neurology in Jacksonville Beach, FL. She received her Doctor of Medicine degree from the University of Texas HSC – San Antonio. She completed her Internal Medicine Internship and Neurology Residency at the University of Florida – Jacksonville. She subsequently completed a Master of Health Administration at the University of North Florida. She is currently the Director of the Comprehensive Multiple Sclerosis Center at Baptist Health. She serves on a number of executive committees for her practice and the hospital. She is also the chair of the Florida Healthcare Provider Council with the National MS Society. She has a passion for clinical care, medical research, and patient education.

Megan Weigel, DNP, APRN-c
Nurse Practitioner
Baptist Neurology Group.
Jacksonville, FL

Dr. Megan Weigel is a nurse practitioner specializing in neurological care in Jacksonville Beach, FL. She has been a Multiple Sclerosis (MS) certified nurse since 2005, and an NP for over 20 years. She is also a board-certified Advanced Practice Holistic Nurse. She earned her doctorate of nursing practice from the University of Florida, where her research emphasis was on preventive healthcare. She completed a fellowship in Integrative Medicine at the University of Arizona in the Fall of 2018 which complements her practice focus on wellness and holistic care. She is the past-president of the International Organization of MS Nurses and the co-founder of oMS Yoga, a non-profit organization that brings free yoga classes to people living with MS.

CLAIM CME/CE CREDIT

Scan the QR Code or click Here to claim CME/CE credit.
https://form.jotform.com/AcademyCME/23CD2W