The Differential Diagnosis of ADEM vs MS: A Case Report

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The Differential Diagnosis of ADEM vs MS: A Case Report

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ABSTRACT

Background: Multiple sclerosis (MS) and acute disseminated encephalomyelitis (ADEM) are both inflammatory demyelinating diseases that affect the central nervous system (CNS). Unlike MS, the diagnosis of ADEM is rare and remains primarily clinical without an identifiable biomarker to distinguish it. Furthermore, misdiagnoses can occur between ADEM and MS because they have similar presentations at onset. As part of the healthcare team, physical therapists may be the first to notice the subtle clinical differences between these similar disease states. Thus, the purpose of this case is to compare and contrast the clinical presentation, pathogenesis, and diagnostic criteria of MS and ADEM, in order to better understand how to differentiate these two inflammatory demyelinating diseases of the CNS. Case Description: The patient was a 35-year-old woman hospitalized for dizziness, nausea, unsteady gait, and slurred speech that started initially as intermittent vertigo, but progressed over a 1-month period. The patient was transferred to the neurology unit and diagnostic testing was performed in order to determine potential diagnoses. Assessments: Due to the presentation of symptoms at onset, the patient received a computerized tomography angiography (CTA) of the head, magnetic resonance imaging (MRI) of the brain and cervical spine, and a lumbar puncture to retrieve cerebrospinal fluid (CSF) for analysis. Discussion: This case report represents the initial episode of symptom onset in an individual suffering from an inflammatory demyelinating disease of the CNS. Although this patient presented to the Emergency Department (ED) for worsening symptoms, her initial symptoms began one-month prior with intermittent vertigo. Physical therapists often evaluate and treat this diagnosis; therefore, it is vital to have an evolving knowledge of different diagnoses in order to identify the subtle signs of systemic involvement of disease and be a potential referral source to provide the highest quality care.

Key Words: Multiple sclerosis; acute disseminated encephalomyelitis; neurology; differential diagnosis; physical therapy; rehabilitation
Background and Purpose

Primary demyelination of the central nervous system (CNS) results from damage to the myelin sheath or oligodendroglias, which can be produced by metabolic disturbances, toxicities, infection, and autoimmunity. One of the primary demyelinating diseases of the CNS is multiple sclerosis (MS), a chronic immune-mediated, demyelinating disease that can present with a myriad of symptoms such as changes in sensation, mobility, balance, sphincter control, vision, and cognition. MS is on the spectrum of idiopathic inflammatory demyelinating diseases (IIDD). This spectrum represents CNS disorders that cannot be differentiated entirely based on clinical course, lesion distribution, and laboratory findings according to Lu et al. Acute disseminated encephalomyelitis (ADEM), a monophasic demyelinating disorder with multifocal and aggressive neurological deficits and correlated with a viral infection or immunization, is also classified under this spectrum of diseases. ADEM and MS are both classified as demyelinating inflammatory diseases that affect the CNS and it can be challenging to differentiate upon initial clinical presentation. Although treatment for the initial presentation of MS or ADEM may appear similar, as they will likely reflect the use of corticosteroids due to their anti-inflammatory and immunomodulatory effects, this is simply the acute stages of treatment. The prognosis of these two diseases can take very different courses. Although there is not one standard form of treatment for ADEM, the currently available treatment regimens appear to have positive outcomes for patients, with some achieving full neurological recovery. However, the course of MS can be more unpredictable due to the various categories of the disease. While the initial onset of symptoms may present and be treated similarly to suppress the inflammatory immune response, the therapeutic interventions following this acute management will be heavily influenced by the prognosis of the diagnosis and therefore, impact the overall plan of care of that individual.

MS is an inflammatory demyelinating disease that remains complex and not fully understood in terms of pathogenesis, but is thought to have a genetic and environmental influence. There are currently 5 classifications of MS and these include: relapsing-remitting (RRMS), clinically isolated syndrome (CIS), radiologically isolated syndrome (RIS), primary-progressive (PPMS), and secondary-progressive multiple sclerosis (SPMS). Each of these classifications has its own criteria that need to be met; however, relapsing-remitting and primary progressive MS are diagnosed based on formal guidelines provided by the McDonald 2010 diagnostic criteria. Based on the high prevalence of relapsing-remitting and primary progressive, these two classifications will be the primary focus of this paper. RRMS is the most common classification and represents about 85-90% of patients diagnosed with MS. This form of MS is characterized by 'relapses' or episodes of neurological dysfunction that last a minimum of 24 hours without signs of fever or an infection, followed by periods of 'remission' or absence of these neurological deficits. Some typical symptom presentations include acute unilateral optic neuritis, double vision, cerebellar ataxia and nystagmus, partial myelopathy, sensory symptoms, Lhermitte’s symptom, asymmetric limb weakness, and urge incontinence or erectile dysfunction. Relapsing-remitting MS tends to affect young adults, with the average age onset being 30-years-old, and women are three times more likely than men to be affected. Primary progressive MS affects around 10-15% of patients with this disease and presents as a progressive loss of neurological function and increase in disability over time, typically without any relapses. Some clinical symptoms include an asymmetric paraparesis that develops over months to years, occasionally progressive hemiparesis or cerebellar ataxia, and very rarely an occurrence of visual failure or dementia. Patients with this diagnosis present around 40-years-old and there is an equal prevalence in males and females. Overall, the clinical presentation will vary depending upon the location of lesions and the symptom onset to distinguish between RRMS and PPMS.

Aside from clinical presentation supporting a demyelinating disease, the diagnosis must also be represented objectively through diagnostic imaging. Magnetic resonance imaging (MRI) is utilized to identify abnormal brain and spinal cord lesions as well as to help exclude other diagnoses.
be identified as RRMS and PPMS, there must be demonstration of dissemination in space (DIS) and dissemination in time (DIT) through MRI.\(^8\) DIS requires that lesions affect at least two areas of the CNS that are commonly affected in MS, which would include the periventricular, juxtacortical, infratentorial, and spinal cord.\(^8\) To illustrate this clinically, a patient may have a history of optic neuritis and now presents with a brainstem syndrome.\(^8\) This would satisfy DIS because there is objective clinical evidence of two separate lesions involving the CNS. The diagnostic criteria also requires the demonstration of dissemination in time (DIT) which involves the CNS lesions developed over time to prevent misdiagnosis of a monophasic illness.\(^8\) For example, there must be record of two clinical attacks with objective data to support both, or at least a credible historical account of the other.\(^8\) When the clinical presentation and diagnostic imaging criteria are met, then there is no need to pursue further testing. However, not all initial episodes of symptom onset meet the diagnostic criteria, which typically results in the use of cerebrospinal fluid (CSF) to be examined for further clarification.\(^6\) Currently, the examination of CSF is not required for diagnosis by the McDonald 2010 criteria.\(^2\) In general, MS is not a ‘diagnosis of exclusion.’\(^8\) The criteria needed to make an accurate diagnosis of relapsing remitting or primary progressive MS include: imaging that demonstrates dissemination of space and time, clinical presentation that indicates demyelination, and an absence of features that suggest an alternative diagnosis.\(^8\) However, if the clinical presentation or diagnostic imaging does not meet MS criteria, then further investigation is warranted in order to exclude alternative diagnoses.

Acute disseminated encephalomyelitis (ADEM) is a rare inflammatory, demyelinating disease of the CNS that is typically transient in nature.\(^4,6\) This disease presents with rapid and progressive symptoms with the greatest deficits occurring within a few days of onset, but typically results in gradual improvement of deficits over time.\(^4\) The diagnostic process is primarily clinically based with the support of neuroimaging, due to the lack of a biological marker.\(^4\) Additionally, it requires the exclusion of other potential diagnoses that may present similarly such as MS.\(^6\) Typically, ADEM has been shown to affect children and young adults, with only rare cases known in older adults.\(^6\) The diagnosis of ADEM has typically been associated with a viral illness or vaccination, but a causal relationship has not been proven.\(^6,9\) The presentation most commonly seen involves multifocal neurological deficits and multiple symptoms being presented due to the various areas of the CNS affected.\(^4\) The more commonly reported symptoms involve weakness of the upper and/or lower extremities, ataxia, cranial nerve palsies, seizures, fever, malaise, irritability, somnolence, headache, nausea, vomiting, meningeal signs, peripheral nervous system involvement, and impairment in speech.\(^4,9\) Initial onset of symptoms of ADEM can typically occur anywhere from 2 days up to 4 weeks after a viral infection or vaccination.\(^6\) Symptom presentation involves sudden onset of encephalopathy, which is defined as a behavioral change or altered state of consciousness that involves multifocal neurological deficits, and typically results in hospitalization within a week of symptom onset.\(^6\)

Similar to the diagnostic course of MS, there are common MRI findings that help support the diagnosis of ADEM and exclude it from other CNS demyelinating diseases.\(^4\) In the case of ADEM, analysis of CSF is typically necessary for diagnosis and is utilized in order to help exclude the possibility of an acute CNS infection.\(^4\) Although cerebral tissue is typically not available for assessment, the gold standard for diagnosis is histopathology of the brain.\(^4\) Therefore, clinical presentation, neuroimaging, and CSF findings are utilized. Unlike MS, the diagnosis of ADEM is a ‘diagnosis of exclusion’ and requires a comprehensive exam and diagnostic screening in order to avoid misdiagnosis. Aside from eliminating alternate diagnoses, the following criteria must be met in order to be considered ADEM: first polyfocal clinical CNS event with expected inflammatory demyelinating cause, encephalopathy, brain MRI abnormalities consistent with demyelination during the acute phase (3 months), and no new clinical or MRI findings reported 3 months or more after the initial onset.\(^9\) If this criteria is met, then it is classified as ADEM with a monophasic disease course.\(^9\) In general, ADEM is considered to be a monophasic disease, but there is now evidence of cases that involve recurrent ADEM that is defined as multiphasic disseminated encephalomyelitis (MDEM).\(^9\) This multiphasic classification of ADEM involves a second ADEM episode 3 months after initial disease onset.\(^9\) ADEM has also been linked to the development of MS if an individual presents with a non-ADEM...
demyelinating relapse and new MRI findings that meet the criteria for DIS, 3 months after the initial ADEM episode. Therefore, follow-up imaging after initial onset of disease may be an important prognostic factor for ADEM.

Due to the lack of concrete diagnostic markers for ADEM, and the initial presentation of MS being similar to ADEM, it is important to be aware of the difficulty differentiating the two at initial symptom onset. Misdiagnosis of MS was reported to be as high as 10%. Furthermore, 95% of neurologists specializing in MS reported having at least one patient in the past year that was misdiagnosed with MS, and therefore treated improperly for their condition. As a result, it is our role as health care providers in various settings to be well aware of these potential differential diagnoses that can impact treatment and prognosis. The purpose of this case report is to compare and contrast the clinical presentation, pathogenesis, and diagnostic criteria of MS and ADEM, in order to better understand how to differentiate these two inflammatory demyelinating diseases of the CNS. The acute management of a patient presenting with symptoms of one of these demyelinating diseases will be discussed to highlight the importance of having an evolving knowledge of differential diagnoses in order to comprehensively evaluate and provide an appropriate plan of care.

Case Description
Patient History and Systems Review
The patient was a 35-year-old female who presented to the Emergency Department (ED) with primary complaint of dizziness for 1 week. The day prior to admittance, the patient’s symptoms began to worsen as she started to experience nausea, vomiting, unsteady gait, and slurred speech. The patient’s sister described the dizziness as a “room spinning sensation.” The patient’s sister drove her to the ED and proceeded to answer a majority of the subjective history due to the patient’s minimal verbalization. The patient’s sister reported that the patient appeared to be off balance and veering off to the left when walking to go to the bathroom last night. The patient’s sister notes that she has been dry heaving frequently and experiencing mild tingling in her left hand since last night. The patient required assistance from the wheelchair to the cart in order to be transferred due to the patient’s recent onset of ataxic gait.

The patient’s past medical history was significant for iron-deficiency anemia due to a heavy menstrual cycle, which she was experiencing upon admittance to the ED. Interestingly, 1 month prior to hospital admission, she was experiencing intermittent vertigo episodes. The patient’s medical history implied that she had received prior treatment for this recent onset of vertigo without success, and that she had only experienced relief from temporary use of meclizine. The ED examined the patient and reported that the she appeared to have slight vertical nystagmus, a left gaze preference, and a urinary tract infection (UTI). Upon admittance to the ED, the patient was transferred to the neurology unit for further examination and treatment.

Differential Diagnoses & Diagnostics
After considering the patient’s previous medical history and presentation in the ED, the initial differential diagnoses included intracranial mass or bleed, posterior infarct, benign paroxysmal positional vertigo (BPPV), vestibular lesion, infection, or an autoimmune presentation. As a clinician, it is beneficial to not only spend time comprising a comprehensive differential diagnoses list, but also problem-solving the various ways in which these diagnoses can be objectively investigated.

A patient may undergo a Computerized Tomography Angiography (CTA) in order to rule out evidence of an acute bleed or intracranial mass. The next form of testing could involve the use of a Magnetic Resonance Imaging (MRI) in order to determine the presence of deficient blood supply to a territory in the cerebrum or cerebellum. Due to the presence of slurred speech, left sided weakness, and visual changes it is imperative to rule out any signs of impaired blood supply to the brain. Therefore, these scans are time sensitive and considered first priority. Assessing for the presence of BPPV using the Dix Hallpike maneuver would be considered a lesser priority. BPPV is an onset of vertigo that involves positional changes, which was not reported in the patient’s history and would not
explain some of the more severe symptoms such as the left sided weakness or slurred speech. Therefore, due to the extensiveness of the patient’s impairments, BPPV would be a less likely diagnosis to explain the entire clinical picture. In order to assess for a vestibular lesion, there are a number of tests to perform including a traditional oculomotor exam to assess for the presence of nystagmus, smooth-pursuit, or saccadic eye movements, the alternate cover test to assess for skew deviation, and head-shake nystagmus to assess the direction of nystagmus. Vertical nystagmus that changes direction typically represents a centrally driven nystagmus, whereas a horizontal nystagmus tends to demonstrate a peripherally driven nystagmus. A panel of blood work would be necessary in order to indicate the presence of infection. Based on the ED exam, it is known that the patient has a UTI, but there could be a more complex underlying infection. Additionally, the use of MRI and cerebrospinal fluid (CSF) via a lumbar puncture would be utilized in order to assess for the presence of an autoimmune disease. This is a more likely diagnosis due to the patient’s age, gender, and sudden onset of severe neurological symptoms. In order to support or refute these diagnoses, further diagnostic testing was performed and is outlined in Table 1.

Table 1. Diagnostic test results of CTA, MRI, and lumbar puncture.

<table>
<thead>
<tr>
<th>EMERGENCY DEPARTMENT: DAY 1</th>
<th></th>
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</table>
| CTA Head                    | 1. No evidence for acute intracranial hemorrhage, mass effect or edema.  
2. No evidence for aneurysm or cerebral vascular occlusive disease.  
3. Low-lying cerebellar tonsils may represent Chiari morphology. |

<table>
<thead>
<tr>
<th>NEUROLOGICAL UNIT: DAY 2</th>
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</table>
| MRI Brain (without contrast) | 1. Numerous bilateral FLAIR hyperintensities within the supratentorial and infratentorial brain and upper cervical cord. **These most likely represent demyelinating disease.** Areas of active disease suspected which can be further assessed with postcontrast imaging.  
2. Chiari 1 malformation with mild to moderate crowding at the craniocervical junction. |
| MRI Brain (with contrast)  | 1. Numerous supratentorial and infratentorial lesions some of which demonstrate enhancement. **Findings would be compatible with chronic demyelinating disease with superimposed active demyelination.** |
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MRI Cervical Spine

1. Multiple small T2 hyperintense likely demyelinating lesions in the left upper aspect of the cervical cord with minimal if any enhancement. Numerous more clearly enhancing lesions and some non-enhancing lesions are more evident on earlier brain MRI, most compatible with chronic demyelinating plaques with superimposed areas of active demyelination.
2. Chiari I malformation. No syringohydromyelia in the cervical cord.

Cerebrospinal Fluid

Glucose normal (67)
Protein increased (62)
Increased total count (15), WBC (12), RBC (3), lymphocytes (94), plasma cell
Decreased monocytes (4)
Negative meningitis/encephalitis panel
Pending: oligoclonal bands (see below)

NEUROLOGICAL UNIT: DAY 6

Cerebrospinal Fluid

Oligoclonal bands: 7 (Normal < 4)

Examination

On Day 3 of admission, the patient was evaluated by physical therapy (PT) at bedside in order to obtain a history with no family present. This portion of the exam was made challenging because the patient was very limited in her ability to verbalize and express her thoughts. Additionally, the patient appeared to require additional processing time to comprehend the questions being asked. The patient primarily communicated with small nods and occasional slow, drawn out words such as “yes” and “no.” The patient appeared very lethargic and consistently closed her eyes throughout the session. During this exam, it was revealed that the patient worked with individuals with disabilities, lived with her family, and depended on the assistance of her family to complete various everyday tasks.

Upon examination, the patient required significant assistance to complete functional mobility tasks. The patient required maximal assistance to complete supine to sit transfers as well as maximal assistance in order to maintain static balance while sitting at the edge of the bed with only brief bouts of moderate assistance required. When trying to encourage the patient to demonstrate strength and mobility of upper and lower extremities against gravity, the patient did not initiate any movement with the left upper extremity. The patient achieved a 3/5 for the right upper extremity and bilateral lower extremities by demonstrating full range of motion of shoulder flexion and knee extension against gravity. The patient was transferred from sitting to standing with maximal assistance but showed progress in standing and required moderate assistance to stand for about 5 seconds. The information obtained from the PT initial examination is summarized in Table 2 below. Additionally, a number of diagnostic tests were performed by the neurology medical team, which can be found in Table 2 below. Based on the initial exam, the patient presented with severe generalized weakness, greater strength deficits in her left than her right, diminished truncal control, reduced activity tolerance, and an inability to communicate effectively using verbalized responses. As a result of the patient’s deficits and progressive weakness, the discharge recommendation was acute inpatient rehabilitation.
Table 2. Initial assessment of functional mobility, balance, and strength.

<table>
<thead>
<tr>
<th>Physical Therapy Evaluation: Day 3</th>
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</thead>
<tbody>
<tr>
<td><strong>Functional Mobility</strong></td>
</tr>
<tr>
<td>Supine &lt;&gt; sit: Maximal Assistance</td>
</tr>
<tr>
<td>Sit &lt;&gt; stand: Maximal Assistance</td>
</tr>
<tr>
<td>Gait: Not tested</td>
</tr>
<tr>
<td><strong>Balance</strong></td>
</tr>
<tr>
<td>Static sitting: Maximal Assistance</td>
</tr>
<tr>
<td>Brief moments of Moderate Assistance</td>
</tr>
<tr>
<td>Dynamic balance: Maximal Assistance</td>
</tr>
<tr>
<td>Static Standing: Moderate Assistance</td>
</tr>
<tr>
<td><strong>Strength</strong></td>
</tr>
<tr>
<td>RUE: 3/5</td>
</tr>
<tr>
<td>RLE: 3/5</td>
</tr>
<tr>
<td>LUE: 1/5</td>
</tr>
<tr>
<td>LLE: 3/5</td>
</tr>
<tr>
<td><em>Did not apply resistance due to decreased arousal and impaired activity tolerance</em></td>
</tr>
<tr>
<td><strong>Coordination</strong></td>
</tr>
<tr>
<td>RUE: Intact</td>
</tr>
<tr>
<td>LUE: Dysmetria on rapid alternating movement</td>
</tr>
<tr>
<td>Finger to Nose: Dysmetria on LUE</td>
</tr>
<tr>
<td>Heel on Shin: Intact bilaterally</td>
</tr>
<tr>
<td><strong>Reflexes</strong></td>
</tr>
<tr>
<td>Patellar: 3+ bilaterally</td>
</tr>
</tbody>
</table>

**Interventions**

The patient was admitted to the neurology unit for a total of 16 days. Throughout her time on the neurology unit, she went through different courses of treatment. On Day 2, the patient was administered a high dose steroid, methylprednisolone, for 5 days. During this time, the patient remained withdrawn, demonstrated flat affect, and her motor weakness on the left continued to be significantly worse than the right. On Day 5, the patient received a psychiatric consult for her depressed mood and loss of interest in communicating or participating with family and health care professionals. After the 5 days of high dose steroids, the patient was switched over to prednisone. Due to minimal improvement in symptoms, the patient had a catheter placed on Day 8 for plasma exchange (PLEX). Though the patient was planned to have 5 treatments of PLEX, she only received 4 treatments due to a complication with the catheter placement prior to discharge. Unfortunately, the patient did not demonstrate notable improvements in strength or speech capabilities after the PLEX treatments. During her admission, she was also given diazepam, meclizine, and ondansetron for her dizziness. Patient appeared to demonstrate improvements in dizziness throughout admission.

From a therapy standpoint, the focus of treatment sessions included bed mobility, transfers from the edge of bed, and encouraging any active range of motion available to bilateral upper and lower extremities, especially on the more impaired left side. Though the intent was to have the patient treated 5x per week by PT in order to progress in functional mobility, various factors hindered the therapy program. Limiting factors of therapy sessions included decreased arousal level, episodes of severe dizziness, and inability to communicate. The PLEX treatment also made it more challenging to coordinate appropriate times for therapy sessions due to the length of the treatment as well as the post-treatment fatigue that ensued. The patient was seen for a total of 7 physical therapy sessions throughout her length of stay.

Throughout the course of therapy, the patient demonstrated fluctuation in her level of assistance required for bed mobility, transfers, and static and dynamic sitting and standing. This may have been influenced by her state of consciousness, sleep quality, steroid and PLEX treatments, and continued heavy menstrual cycle throughout half of her length of stay. By the last treatment session, the patient
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demonstrated improved effort to verbally communicate, but it was still quite challenging for her to clearly articulate and verbalize her thoughts. She showed improvements with bed mobility by initiating bilateral lower extremity movement toward the edge of bed, but moderate assistance was still required to complete the full transfer due to impaired upper extremity strength and truncal control. The patient also required varying levels of assistance for static and dynamic sitting at the edge of the bed due to decreased endurance, impaired truncal control, and a tendency to shift toward the weaker left side once fatigued. The patient was able to progress and complete 5 sit to stand transfers with maintenance of standing balance for 5 seconds with moderate assistance but required significant verbal encouragement to maintain upright posture before requiring a seated break. The patient required maximum assistance to transfer to the commode due to poor truncal stability, strength deficits, and impaired balance. During treatment sessions, she frequently became overheated and sick, requiring maximal assistance to transfer back to bed. The patient’s primary deficits at discharge included generalized muscle weakness (left > right), impaired endurance, lack of body awareness, impaired balance, and inability to ambulate.

Discussion

Based on the initial presentation of the patient upon admission, there were symptoms that reflect both MS and ADEM. The patient’s ataxia, nystagmus, sensory symptoms (i.e. tingling in left hand), and asymmetric limb weakness could have been reflective of MS. Additionally, weakness in her upper/lower left extremity, ataxia, nausea, vomiting, malaise, somnolence, peripheral nervous system involvement, and impairment in speech could reflect ADEM. Based on the demographics of the patient, she was more likely to fit the clinical picture of MS. Relapsing-remitting MS tends to affect women with average onset of 30-years-old. In comparison, the literature primarily focuses on ADEM affecting children and young adults, with only rare cases known in older adults. However, the research is not specific in terms of what defines a “young adult,” therefore appropriate age demographics for this classification remain vague.

Upon admission, the patient received a myriad of diagnostic tests in order to begin the elimination process of differential diagnoses. A head CTA was performed in order to rule out any evidence of a bleed that would require immediate intervention. Fortunately, the patient did not have any vascular involvement. MRI of the brain was found to have numerous lesions in the supratentorial and infratentorial brain and upper cervical spinal cord with contrast imaging confirming active demyelination. As previously discussed, there needs to be lesions represented in 2 out of the 4 areas of the CNS: periventricular, juxtacortical, infratentorial, or spinal cord in order to satisfy the 2010 McDonald MRI criteria for MS. Therefore, the demonstration of numerous lesions in the infratentorial and cervical spinal cord would satisfy the DIS needed for the diagnosis of relapsing-remitting MS. Primary progressive MS requires slightly different imaging criteria, but it would be too premature to diagnose due to the acuity of the disease onset and the need for one year of disease progression to be evident for diagnosis. In comparison, ADEM has also been commonly shown to have multiple bilateral supratentorial white matter lesions in MRI, which would also coincide with the patient’s findings. Additionally, patients with ADEM typically demonstrate lesions in the thalamus, basal ganglia, brainstem, or cerebellum, which the patient did not demonstrate. The representation of white matter lesions in ADEM are typically multiple, bilateral, asymmetrical, and randomly distributed in the cerebrum, cerebellum, brainstem, and spinal cord. This wide distribution of lesion location throughout the CNS further enhance the difficulty of having defining features for diagnosing ADEM. To further differentiate lesion patterns in these two diseases, MS typically has lesions in the subcortical white matter, periventricular area, and corpus collosal whereas ADEM commonly has lesions in the cortical and deep gray matter areas such as the basal ganglia. The MRI of the cervical spine demonstrating demyelinating lesions does not further support one diagnosis over the other due to both MS and ADEM having lesions involving the spinal cord. Follow-up MRI can further assist in differentiation of these two diseases and confirm ADEM diagnosis in retrospect. For example, based on the monophasic ADEM criteria, there should not be presentation of new lesion development after 3 months since
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disease onset. Furthermore, in a majority of patients there is a complete or partial resolution of the MRI abnormalities that were previously found at initial onset. Whereas MS requires lesions to represent development over time, otherwise known as DIT, in order to demonstrate two different attacks and representation of at least two lesions on MRI findings. Therefore, follow-up imaging is important not only to confirm the initial diagnosis of ADEM, but also to ensure that there is no new developments that could warrant subsequent episodes or change in disease progression.

The CSF analysis assists in further differentiating between MS and ADEM. CSF findings in MS typically represent normal or mildly increased white cell count, elevated protein, and abnormal oligoclonal bands (OCBs). In comparison, CSF analysis for ADEM is usually not noteworthy due to the lack of confirming features. CSF findings characteristically represent high percentage of lymphocytes and monocytes, elevated protein, normal glucose, and OCBs are typically absent or transient in ADEM. Based on the findings from the literature, it would appear that the patient’s CSF analysis is more representative of MS due to the increased protein, elevated white cell count, and positive OCBs.

Throughout the patient’s length of stay, she was treated with methylprednisolone, prednisone, and PLEX while also being given various medications for her dizziness for acute management of her symptoms. Treatment of MS typically utilizes immunomodulator drugs for symptom management. For acute management, corticosteroids such as methylprednisolone and adrenocorticotropic hormone (ACTH) are used for their anti-inflammatory and immunomodulatory effects. For long-term management of MS, immunomodulatory therapies (IMT) have been used and also one of the reasons for improvement in treatment in the last 20 years. There are currently 12 medications that are available for those with MS that are available as injections, infusions, or orally depending on the specific drug. These IMT aim to reduce the frequency of relapses and the number of MRI lesions in order to slow disease progression. IMT have been shown to be the most effective for relapsing-remitting MS and clinically isolated syndrome, but there is limited evidence for progressive forms of MS (i.e. PPMS, SPMS). The mechanism underlying relapsing-remitting MS has become better understood and allows for the development of disease-modifying drugs to be available. Due to the lack of understanding behind the pathogenesis of PPMS and SPMS, there are minimal options available and providing efficacious therapeutic interventions is quite challenging. In contrast, there is no standard treatment for ADEM. The literature widely supports administering high doses of corticosteroids such as methylprednisolone or dexamethasone for 3-5 days with oral prednisone to follow-up. During this time, patients should be monitored closely for changes in blood pressure, urine glucose, and serum potassium. Numerous case studies have also shown the use of intravenous immune globulin (IVIg) for 2-5 days as a second-line treatment for individuals that did not respond to steroid treatment or who were experiencing side effects from steroid treatment. The use of PLEX has been shown to be a potentially effective treatment for both ADEM and MS, especially in individuals who are unresponsive to steroid treatment. This treatment should be started as soon as the use of steroids has been deemed ineffective. Overall, the acute management of either disease will initially focus on administration of high dose steroids in order mitigate the effects of the large inflammatory response caused by the disease onset. However, long-term management of MS with immunomodulatory or immunosuppressive drugs is not appropriate for ADEM, which is another reason why proper distinction between MS and ADEM has therapeutic importance.

Although symptom onset, imaging characteristics, and initial treatment interventions demonstrate overlap, the prognosis of these two diseases are very distinct. In general, the prognosis for ADEM is optimistic. Improvement is typically shown within days of beginning treatment with a return to baseline function occurring within weeks. Full recovery has been demonstrated in about 57-89% of patients and about 20-30% will demonstrate only minor deficits. Some of the more commonly reported residual effects include: focal motor deficits ranging from mild clumsiness to severe hemiparesis, visual problems ranging from mildly diminished visual acuity to blindness, and seizure development. However, if symptoms should arise again, imaging follow-up could help determine the presence of a recurring episode representative of multiphasic ADEM or potentially the transition to another
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demyelinating disease such as MS.9 In contrast, the course of MS is completely variable and highly dependent on the classification. CIS is a classification of MS that involves a single exacerbation with clinical symptoms that represent a demyelinating disease, but the MRI does not fully meet the criteria for RRMS, whereas RIS is a classification of MS that involves abnormal MRI findings suggestive of MS without any previous clinical symptoms.8 Together, these two classifications would likely meet the criteria for RRMS. Therefore, it can be speculated that individuals with these classifications might be more likely to progress in symptoms and advance to a different classification of MS in the future. RRMS is characterized by episodes of exacerbations of symptoms in which the individual will either partially or fully recover followed by periods of clinical stability.8 Disease-modifying drugs can help prolong episodes of stability and reduce occurrence of exacerbations.5 PPMS and SPMS are both more aggressive in nature and have less therapeutic options available to slow the progression of the disease, which results in a poorer prognosis.6 Since MS and ADEM can result in two very distinct disease courses, the therapeutic interventions used and overall prognosis can be significantly impacted.

The focus of this case report was to highlight the clinical course of a 35-year-old woman that was admitted to the hospital with a differential diagnosis of MS versus ADEM. During her final week on the neurology unit, she was diagnosed with MS. She received a myriad of treatments with minimal symptom improvement and was discharged to pursue further therapeutic interventions in acute inpatient rehabilitation. She was a typically functioning adult with sudden worsening of symptoms that resulted in debilitating deficits. Interestingly, her symptoms started 1 month prior when she was diagnosed with and received treatment for intermittent vertigo without success. Unfortunately, the medical records were not specific in what type of treatment she received or by what type of health care provider. Other neurological symptoms may not have been evident at the time of this initial onset of vertigo, but what if it had been? Or what if she had sought treatment for her vertigo from multiple providers without success (i.e. primary health care provider, physical therapist, etc.)? The ability to perform a comprehensive evaluation and have an evolving knowledge of differential diagnosis are essential in order to be a successful healthcare provider. This case report emphasizes the importance of this concept to primary care providers, as well as thoroughly reviews the similarities and differences between two inflammatory demyelinating diseases that can have a similar clinical presentation in order to provide a valuable resource to providers.

References