

Common Clinical and Imaging Conditions Misdiagnosed as Multiple Sclerosis

A Current Approach to the Differential Diagnosis of Multiple Sclerosis



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KEYWORDS

- Multiple sclerosis • Differential diagnosis • Multiple sclerosis mimics
- Nonspecific white matter abnormalities • MRI

KEY POINTS

- The incidence and prevalence rates of multiple sclerosis (MS) are increasing; so are the number of misdiagnosed cases as MS. One major source of misdiagnosis is misinterpretation of nonspecific clinical and imaging findings and misapplication of MS diagnostic criteria resulting in an overdiagnosis of MS!
- The diagnostic spectrum of MS and related disorders includes the MS subclinical and clinical phenotypes, MS variants and inflammatory astrocytopathies, and other antibody-associated atypical inflammatory-demyelinating syndromes. The differential diagnosis of MS includes these disorders as well as some other diseases mimicking MS.
- There are several systemic diseases in which either the clinical or MRI or both findings may mimic MS; however, in most, a well-taken history and a thorough physical examination will reveal the symptoms and signs of the systemic disease and appropriate laboratory workup will confirm the non-MS diagnosis.
- Because nonspecific white matter abnormalities on brain MRI and other imaging findings that may mimic MS, as well as MS-nonspecific lesions, may be seen in people with MS, neurologists should be aware of all possibilities and they should be able to interpret the MRI findings independent of the radiology reports! Currently, the old school of taking a detailed history, a thorough neurologic examination, and a cerebrospinal fluid study are essential for the MS diagnosis. MRI is one other tool that is most often confirmatory, but may cause confusion at times too, necessitating a “think twice” approach before reaching a final diagnosis.

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INTRODUCTION

The prevalence of multiple sclerosis (MS) is on the increase,^{1,2} which in large is likely to be due to an increased awareness both by the medical and nonmedical communities. Patients are self-admitted or referred for a neurology consultation either because of clinical symptoms and signs or cranial and spinal MRI findings that are suggestive of “MS” or because of both. The raised admittance rates with a presumed diagnosis of MS, in turn, also results in increased misdiagnosed cases. The problem of misdiagnosis and difficulties in diagnosing MS have been reported before the introduction or widespread use of diagnostic tools, such as imaging, evoked potentials, and cerebrospinal fluid studies in neurology,³ which is certainly understandable. However, it seems that the most advanced tools that we have today have not changed this problem much. Indeed, in recent years, several studies confirmed this issue of incorrect MS diagnosis and further had emphasized that a significant number of these individuals who in fact did not have MS were even put on long-term MS treatments.^{4–8}

Currently, the most common cause of MS misdiagnosis seems to be nonspecific white matter abnormalities on brain MRI and misinterpretation and misapplication of radiographic diagnostic criteria, as well as the presence of vague or nonspecific neurologic symptoms considered to be related to MS.^{8,9} In fact, it has been shown that in up to one-third of “normal” people aged 20 to 45, transient neurologic symptoms, such as visual changes (including blurring, diplopia), weakness, poor balance and coordination, and speech difficulties of no clinical significance are reported without any underlying abnormality.^{9,10} It is also not uncommon to see people with dizziness, numbness, and similar sensory symptoms, without any underlying disease in medical practice too. When people with such symptoms present and by coincidence turn out to have a number of nonspecific white spots on their brain MRI, they easily may be misdiagnosed as having MS by the unexperienced physician. Interestingly, most of these cases end up receiving a final diagnosis of a psychiatric disorder or migraine or fibromyalgia,^{6,8} as most studies had shown psychiatric conditions are among the major causes of MS misdiagnosis.^{3,4,6,9} It is not uncommon for someone to come to a clinician with the fear of having MS because of disease suggestive symptoms, which in fact are due to somatization or of no clinical significance. Many times, the final diagnosis will end up being hypochondriasis, a somatoform disorder with anxiety or depression or malingering. However, if the clinician does not concentrate well in such patients’ history and examination in whom the MRI scan shows a few nonspecific white spots, then the psychiatric problem may be missed and the patient may be misdiagnosed as having MS. A well-taken history will reveal that psychiatric-based (somatic) symptoms cannot be easily localized and are not consistent with known neuroanatomical sites; they are multiple, show variations and fluctuations, but are always there! So, their symptoms will not be consistent with the classic definition of MS that is based on attacks being disseminated in time and space.⁹

Another major issue in the diagnosis and differential diagnosis of MS is a large number of other disorders that may mimic MS, such as the so-called atypical inflammatory-demyelinating diseases of the central nervous system (CNS) that include neuromyelitis optica spectrum disorders (NMOSD), acute disseminated encephalomyelitis (ADEM), and some other rare diseases within this group, several inherited disorders that have their onset at adolescent or adult age periods, as well as some infectious, neoplastic, or vascular disorders affecting mainly the young adult population.^{9,11–15} These disorders and their differential diagnosis from MS have been reviewed in detail in several publications and although some also are reviewed here, further specific information can be found in those publications.^{9,11–16}

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