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## The importance of assessing life stress exposure in multiple sclerosis: A case report

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This case report describes associations between childhood adversity, adult stress exposure, and Multiple Sclerosis (MS) to highlight the intersection between mental health and neurological illness in persons with MS (PwMS). We focus on a high-adversity, high-resource patient who self-referred to mental health services for depression and suicidal ideation, without ever being screened for past or current stress exposure. MS and common comorbid symptoms (e.g., fatigue, depression, suicidality) may be affected by adversity and compounded by pandemic-related stressors, including socio-political and economic sequelae. This case illustrates the potential benefit of screening for lifetime stressors as a mechanism to improve case conceptualizations, enable referrals to mental health specialists to promote coping and resiliency, reduce future MS morbidity, and illuminate stress as an important research focus that deserves further exploration in PwMS.

#### 1. Introduction

Adverse Childhood Experiences (ACEs) are major life stressors that occur before age 18, some of which can be traumatic. These experiences include physical, sexual or emotional abuse, neglect, and household dysfunction, such as parental mental illness, substance use, imprisonment, and divorce. ACEs, frequently assessed using the ACEs questionnaire (Felitti et al., 1998), are widely prevalent in the United States, with a majority (61%) of American adults having experienced at least one ACE (Centers for Disese Control and Prevention, 2020).

The consequences of experiencing ACEs can be long-term and profound, including multi-system damage stemming from chronic systemic inflammation (Furman et al., 2019). Indeed, a dose-response relationship has been found between the number of ACEs experienced and numerous adverse outcomes associated with Multiple Sclerosis (MS), as well as many neurodegenerative and autoimmune diseases, including increased perception of pain, fatigue, sleep disturbance, substance use, obesity, suicidality and other mental illness (Felitti et al., 1998; Centers for Disese Control and Prevention, 2020; Furman et al., 2019; Tesarz et al., 2016; Albott et al., 2018). Furthermore, ACEs, through an increased likelihood for tobacco use and obesity, can indirectly increase the risk for developing MS and impact disease progression and symptoms (Artemiadis et al., 2011). Additionally, ACEs increase the perception of stress in adulthood, which has been linked to MS onset and relapse rates (Albott et al., 2018; Shaw et al., 2017).

Despite these findings, the direct role that childhood stressors play in the pathogenesis and symptomatology of MS remains unclear. This is mainly due to scarce literature with diverse methods and mixed findings. Nevertheless, studies have documented evidence supporting significant associations between childhood stressors and age of MS onset, relapse rates, fatigue, and disability (Shaw et al., 2017; Pust et al., 2020; Slavich and Shields, 2018). Moreover, the current pandemic, economic, and socio-political stressors, compounded by constant and sometimes divisive social media coverage, may further trigger those with a history

of traumatic stressors to exhibit reduced coping and an increased risk for anxiety and other mental or physical symptoms in the MS population. These complex stressors may also contribute to medication non-adherence or vaccine hesitancy through concerns of COVID-19 risk in the context of immunosuppression.

### 2. Case report

To demonstrate how these connections can intersect in PwMS with a relatively common course, we present a case report involving a 58-year-old black woman who was diagnosed with relapsing-remitting MS at age 38. She experienced paresthesias that commenced during years of increased stress from the failing health, and eventual death of her mother. Assuming her intermittent symptoms were from stress, she delayed seeking medical attention until a year later. She presented to primary care for headaches and parathesias, and was subsequently diagnosed with left optic neuritis by an ophthalmologist when she developed periorbital pain and optic disk swelling. She was then referred to neurology and received her first MRI early the following year, which demonstrated four foci of increased signal in the periventricular white matter.

A repeat MRI that was completed four years later showed an additional one-centimeter left frontal periventricular lesion, and a smaller right frontal non-enhancing lesion. She remained relatively stable over the next nine years until gait issues prompted another MRI, which then revealed at least 20 ovoid shaped non-enhancing lesions in the periventricular white matter, extending to the corona radiata. She received her first cycle of Ocrelizumab in the winter of 2019 and has been tolerating the new medication well. She received her second cycle without delay despite the COVID-19 pandemic. However, she was at risk of missing her third cycle, in part due to recent deteriorating mental health.

In the fall of 2020, she presented to a psychiatric partial hospitalization program after eight months of progressively worsening

depression and suicidal ideation in the context of multiple psychosocial stressors. She recounted significant martial strain caused by spousal alcohol abuse which became more apparent while working from home due to the pandemic. This triggered childhood memories of her father, whom she described as a physically and emotionally abusive "functioning alcoholic." She recently moved out and now resides alone with continued thoughts of divorce. She expressed concerns regarding working from home as she has always viewed work as her "escape" from the stressors of her life. Due to her depression, she reported falling behind at work. She also reported increasingly severe depressive symptoms including low mood, anhedonia, early morning awakening, fatigue, worthlessness, frequent tearfulness, anorexia, poor concentration, and suicidal thoughts with a plan to overdose on prescription medications.

An ACE assessment was completed. The presence of significant childhood abuse, neglect, and household dysfunction resulted in a high ACE score of seven (range: 0-10). Despite these adverse life stressors, she earned excellent grades in high school and a college degree, providing evidence for adequate coping during parts of her life. Unlike most patients who receive hospital-based psychiatric treatment, she had the wherewithal to self-refer for treatment, which mitigated her suicidality. However, she had never previously been screened for past or current stressor exposure, despite having a clear history of serious stress-related symptoms.

### 3. Discussion

This report describes the clinical course of a PwMS, highlighting the role that major life stressors can play in promoting chronic disease and symptomatology. The patient's common experiences throughout the MS disease and diagnosis pathway lends support to the possibility that unaddressed stressors may play a similar role in affecting the lives, health, and wellbeing of other PwMS. The report depicts missed opportunities for assessing stress exposure in PwMS, which is rarely done on a formalized basis, particularly regarding childhood. Although early adversity may be especially relevant in this clinical context, stressors occurring after age 18 can also be impactful, thus highlighting the importance of adopting a lifespan approach. Notably, the Stress and Adversity Inventory (STRAIN; https://www.strainsetup.com) is the only instrument for systematically assessing lifetime stress exposure and it can be easily completed online by patients at home in about 18 minutes during the pre-appointment process (Slavich and Shields, 2018). The information collected can help estimate patients' risk of experiencing stress-related symptoms such as anxiety, depression, fatigue, pain, and relapse.

This case report also highlights inconsistent screening practices across subspecialties. This particular patient saw three different specialties during the diagnosis process, indicating three missed opportunities to assess this patient's stress exposure and mental health status. It is noteworthy that the American Academy of Neurology recommends screening for past and current trauma in patients with neurological conditions, and assisting patients with history of trauma to understand (a) how it may be impacting their disease/behavior, and (b) that referral to mental health services may be helpful even if the trauma is not currently happening (Schulman and Hohler, 2012). Although these recommendations could also apply to primary care, neurologists are in a unique position to screen for stress exposure, and close the referral gap for PwMS.

Case conceptualizations can be enhanced by including patients' stress histories, which can facilitate clinician and patient awareness of potential vulnerabilities. As witness to the high prevalence of depression, anxiety, and suicidality in PwMS, providers in neurology practice settings are ideally situated to help PwMS understand links between stress and symptoms, as well as the importance of improving mental health, coping, and resilience skills for enhancing whole-body health. Screening is especially important in the context of the pandemic, which

represents a complex multi-faceted stressor encompassing social, work, health, and financial challenges. Such efforts hold the potential to reduce MS-related symptom severity, enhance quality of life and increase stress-related resilience.

It is crucial that all providers are comfortable having conversations surrounding screening and referrals for these services. This may be especially relevant for pediatric MS providers given the access youth may have to social media or online content which may create potential for secondary traumatization or skewing their developing self-schemas (e.g., self-identity, self-esteem) for how they interact with the world in the context of having a chronic disease. To learn more about providing trauma-informed health care, there are resources available through the Trauma Informed Care Implementation Resource Center (traumainformedcare.chcs.org) and National Child Traumatic Stress Network (nctsn.org).

Cognizant of comorbid mental health complications associated with MS, neurology providers should have a low threshold for assessing and referring for improved management of life stress and coping in PwMS. Practitioners may be unsure about whether to prioritize or implement stress screening given the relatively scarce literature documenting associations between childhood stressors and MS. However, we have identified ten studies to date that have assessed ACEs (single or multiple) and MS prevalence or clinical outcomes such as age at onset, disability, relapses, or fatigue (Shaw et al., 2017; Pust et al., 2020; Slavich and Shields, 2018). While additional research is needed to better understand how life stress can be best assessed and managed in patients with MS, incorporating this information into practice can improve case conceptualizations and the therapeutic alliance.

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#### Informed consent

Written informed consent was obtained from the patient for her information to be published in this case report.

# **Declaration of Competing Interest**

The authors declare no conflicts of interest.

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