NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Accommodating the Things That Cannot Be Changed: Diagnosis and Treatment of Multiple Sclerosis

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Part I – Mary's Medical Mystery

Mary Joe, a 35-year-old white female, lived in northern Oxford County, Maine. She disliked the long and chilly Maine winters, but that is where she and her husband had decided to settle in order to be close to family and her husband's job.

One of Mary's favorite things to do was to paint. She picked it up as a hobby in high school when she was stuck at home, sick with infectious mononucleosis (more commonly known as "mono"), and it had been her passion ever since. Mary was also the proud owner of a small art studio where she was building her professional portfolio and teaching weekly painting classes. Mary's business brought her a deep sense of pride and purpose, allowing her to marry her love of art and community.

Recently, in a rush to complete a fast-approaching deadline, Mary had spent an entire day painting. Despite this being routine, on this day something felt "off." After hours of standing and intense concentration, she felt numbness in her fingertips and right leg, and she grew slightly dizzy. The symptoms continued throughout the day but got weaker and disappeared by the end of the next day. Mary decided it would be best to stay seated and take breaks the next time she worked for an extended period of time, assuming she was just really tired and stressed, something she had never handled very well.

However, while resting that evening, Mary remembered what Lainey, her older sister, experienced prior to being diagnosed with a severe case of multiple sclerosis (MS). The doctors had said that Lainey's obesity and lifestyle of smoking and not being physically active contributed to the onset of her MS. Over the years Lainey's physical limitations grew, eventually causing her to lose her job. Lainey was diagnosed in her later twenties, and by the time she was 40, Mary and her husband had to assist her in even simple activities of daily living such as brushing her teeth or taking a shower. Lainey passed away from pneumonia complications three years later.

Caring for her sister while maintaining a business was stressful, and Mary had often felt exhausted and overwhelmed. At times, she felt numbness in her right hand, but she attributed it to poor posture, too many hours painting, or poor form when helping care for Lainey.

Now, still grieving her sister's loss, Mary spent many hours in the studio trying to focus on work. The exhaustion masked the emotional pain, but the numbness in her arm started becoming more frequent, radiating into her hand and becoming harder to dismiss.

Mary called her family medicine doctor, Dr. Goodwin, and was instructed to rest and see if she improved. Though Dr. Goodwin was concerned about Mary's symptoms, she lived in a notably rural area over two hours away from the clinic where he practiced, making it difficult for him to see her on such short notice. Additionally, the health insurance provided by Mary's husband's employer made several care options unavailable to her, such as telehealth, which is vital to those living in rural areas, making it more difficult to access adequate care. Thankfully, over the next few days, the

numbness and fatigue dissipated, and Mary felt a great deal of relief. Unfortunately, this was only the beginning of a recurrent symptomology.

One day, Mary woke up with extreme nausea and dizziness. When she sat up and looked around the room, she realized it was hard to bring her surroundings into focus. She became alarmed, and when she reached for her glasses, she noticed her right arm felt abnormally weak and heavy. She struggled to coordinate her movements to put on her glasses and felt that her right eye was significantly blurrier than the left. It was then that Mary decided to call Dr. Goodwin to schedule an appointment and make the long trip to the doctor's office.

Questions

1. What is multiple sclerosis (MS)?

2. Based on Mary's symptoms, does it seem that she too might have MS? Explain your rationale. Include which symptoms would suggest MS and which might not align with the disease.

3. Does family history of any type of MS increase the risk of developing this disorder? Explain.

4. Mary contracted mono when she was young. What is mono and what virus causes it?

5. What is the connection between mono and the development of MS (regardless of type)? You may need to do a literature search to answer this question.

6. Mary lives in Maine, a Northern state in the United States that is distant from the equator. How does this location impact her vitamin D levels, and how might this affect her immune system?

Part II – "Tapping" Into an Answer

At her appointment with Dr. Goodwin, Mary reiterated her symptoms, emphasizing the increase in symptom intensity and similarity to her sister's symptoms. After taking a detailed medical history and considering Mary's current state, Dr. Goodwin remarked that her symptoms closely resembled those of a pathology of the central nervous system (CNS). Dr. Goodwin referred Mary to a neurologist and ordered magnetic resonance imaging (MRI) of the CNS, as well as a lumbar puncture, commonly known as a spinal tap. An MRI is used to visualize the brain and spinal cord to detect lesions, while a spinal tap extracts cerebrospinal fluid (CSF) to analyze its contents. Mary was concerned about the financial cost that such tests would have, but Dr. Goodwin explained that Maine's Office of Rural Health and Primary Care would assist her with payments.

Two months later, following Mary's various tests, she sat down with her neurologist, Dr. Whittaker, to discuss the results. Dr. Whittaker explained that the MRI came back positive for several lesions in various parts of the CNS, including the right optic nerve, cerebellum, basal ganglia, and left somatosensory cortex. All the brain lesions measured at least 3 mm in diameter. Additionally, Mary's spinal tap revealed the presence of oligoclonal bands in her CSF, an immunoglobulin indicating inflammatory activity in the CNS.

Given these test results and Mary's symptoms, Dr. Whittaker diagnosed Mary with relapsing-remitting multiple sclerosis (RRMS), a progressive autoimmune disorder of the CNS. Dr. Whittaker explained to Mary that RRMS involves the destruction of myelin, a lipid that insulates neurons and allows them to propagate action potentials more efficiently, which improves neuronal communication. In RRMS, however, the immune system becomes overactive, targeting and destroying this healthy tissue, which causes formation of lesions. RRMS, as compared to other forms of MS, is less aggressive characterized by periods of pathology progression (relapse) and then periods of stagnation (remission). The symptoms of RRMS can range greatly, and they can be somewhat unpredictable, depending on where lesions form in the brain.

Dr. Whittaker continued to explain how RRMS was causing Mary's specific symptoms. Her MRI results showed a lesion on the right optic nerve, causing optic neuritis and vision problems in her right eye. Mary also had lesions in the cerebellum and basal ganglia, key players in the brain's ability to integrate and coordinate movement smoothly. The basal ganglia contain dopaminergic neurons responsible for communicating with the substantia nigra, another brain region needed to coordinate voluntary movements. Mary's numbness was also likely explained by the lesion in her somatosensory cortex.

Given all of this information, Mary was overwhelmed and distraught. The thought of living with an incurable disease that deeply affected and ultimately took her sister was difficult to imagine, let alone figuring out how to afford treatments and doctor's visits given her lack of adequate insurance. Luckily, Dr. Whittaker was able to give Mary some peace in explaining his treatment plan for her.

Dr. Whittaker prescribed Mary fingolimod, an oral medication used to slow the progression of RRMS, and modafinil, a medication commonly prescribed to individuals with MS to combat debilitating fatigue. Fingolimod alters activity of lymphocytes throughout the body, including the CNS. Modafinil is a dopamine reuptake inhibitor that increases the amount of dopamine in the CNS, resulting in wakefulness. The combination of these two therapeutics would slow the progression of Mary's RRMS and reduce the severity of her symptoms.

Also, Dr. Whittaker told Mary about state-funded programs in Maine to help pay for her prescriptions and doctor's visits since she lacked access to high quality health services. He also informed her about social support organizations in the state that provide social work services should she need additional psychological support.

Luckily, these medications worked effectively for Mary, and in the short term she exhibited no new lesion development or worsening symptoms.

Questions

1. RRMS is an autoimmune disorder where the body's immune system attacks the myelin sheaths of neurons. Why might the presence of oligoclonal bands in the cerebrospinal fluid be a positive finding in an RRMS diagnosis?

2. Why is it important that neurons in the central nervous system be able to propagate action potentials at a high velocity? How does loss of myelin impact neuronal communication and explain Mary's symptoms?

3. Consider the location of Mary's lesions as shown by the MRI. List the locations of the lesions and explain how each lesion contributes to her symptoms.

4. Mary was prescribed fingolimod to slow progression of RRMS. Fingolimod is an antagonist to sphingosine-1-phosphate receptors (S1PR), primarily the S1PR1 receptor found in lymphocytes, and regulates their migration. Upon activation of S1PR1, lymphocytes migrate from the lymph nodes into circulation where they can then perform various immune functions. What is an antagonist? Speculate as to why antagonizing these S1PR1 receptors would be an effective treatment for RRMS.

5. Mary was also prescribed modafinil, which is a dopamine reuptake inhibitor. What is a reuptake inhibitor and how does it affect dopamine levels? What is the connection between dopamine and wakefulness?

6. Positron emission topography (PET) scans have demonstrated decreased glucose metabolism of neurons in the basal ganglia of RRMS patients. The basal ganglia are important structures in the brain, primarily responsible for motor control and coordination, as well as communication with the substantia nigra via dopaminergic pathways. Given modafinil's mechanism of action, could it hypothetically be used to treat motor dysfunction in people with RRMS? Explain.

7. Mary's lack of access to adequate health coverage is a major stressor for her. However, Mary is lucky enough to live in a state where government subsidies are available to assist people like herself with healthcare costs and access. Provided services can include discounts on prescriptions, access to telehealth, and financial assistance for doctors' visits. How might Mary's journey toward her diagnosis and treatment have been different if she lived in a state where she was not offered these benefits? Consider her ability to pay for her medications and to access medical specialists when answering this question.

Part III – Turning Grief Into Growth

Inherent to RRMS, Mary continued to experience relapses, as there is no cure for RRMS. While symptoms of RRMS can vary in type and severity, a relapse is defined as worsening symptoms that occur at least thirty days after the most recent relapse, is at least 24 hours in duration, and is not directly related to an illness or other medical condition. Mary, like many other RRMS patients, found that no two relapses are the same. Some relapses can last for a day or months, and severity can vary from little impact on daily life to leaving some individuals bed bound.

One of the most life-altering relapses that Mary experienced was over one month long. Leading up to the flare, Mary was chronically stressed and exhausted. Mary's husband was laid off from his job. This news came on the heels of a refusal by Mary's health insurance to pay for her diagnostic tests and medications, leaving her with a seemingly insurmountable financial burden.

While this is an unfortunate reality for many individuals living in the American healthcare system, Mary was determined to maintain her studio and not give up on her art.

The stress of this financially difficult time made managing a chronic condition even more challenging, prompting a severe RRMS flare. Suddenly, Mary became so fatigued that she could not stay awake long enough to drive her car to and from work. She struggled walking the short distance from her bed to the bathroom and grew incontinent, a symptom she had not previously experienced. With muscle weakness, fatigue, and incontinence, Mary became bed bound. She could not clean the house, go shopping for groceries, or work a full shift at her art studio.

While researchers have not been able to pinpoint an exact cause or trigger of an RRMS flare, there are many lifestyle modifications that have been shown to benefit RRMS patients. Mary's doctor recommended adopting habits to help boost her immune system and decrease chances of infections that might cause inflammation. He recommended eating a healthy diet, exercising regularly, and managing stress levels. In addition, he suggested considering wearing a mask when going out to places where there are many people. To reduce fatigue and weakness, her doctor suggested using a handicap placard, so she did not have to walk long distances. While Mary initially felt ashamed to use this resource as her disability was not outwardly visible, she came to understand that her own self-advocacy was more important than others' perceptions of her.

While it took over a month, the flare did end and with it came insights about Mary's new life with a disability. Mary understood the importance of listening to her body and adjusting to how she felt in the moment. She started talking with a therapist and began to realize that while she could have a fulfilling life, life with MS would look different than before. After her initial diagnosis, Mary experienced numerous flares and she learned to be responsive to her fatigue and limit activity in times of exhaustion. To avoid overexertion, Mary learned she had to ask for help, though this was a challenge as she was proud of her independence. However, many people in her life felt fulfillment when they were able to assist her.

Mary met with an occupational therapist who helped her make changes in her studio to respond to her changing needs. She started painting in a room located closer to the restroom, and she started a bladder training program to help address her incontinence. In addition, she learned that keeping the air conditioning on during the summer helped decrease flare onset.

Through time, working closely with her health care team, Mary learned to manage her RRMS and lead a meaningful life without being a victim of her condition. While she still experiences flares, they are nowhere near as frequent or severe, which has enhanced her quality of life. Most of all, Mary has realized that her support system has made all the difference in her RRMS prognosis. Support from her family and healthcare team have been invaluable in allowing Mary to continue pursuing her passion for art, while also giving her a social safety net to rely on in times of struggle. Additionally, she has realized the power of self-advocacy in the disability community, which has been integral in her efforts to pursue a meaningful life despite her physical limitations. All of Mary's experiences have culminated in the understanding that social circumstance and access to adequate medical care are vital to receiving equitable healthcare.

Questions

1. When Mary was still learning how to navigate the world as an individual with a disability, she became depressed. Why do you think people with chronic disease, like RRMS, often have higher rates of depression?

2. Many people with RRMS experience worsening symptoms in hot environments. Hypothesize why this might be.

3. Workplaces are required under the Americans with Disabilities Act to provide "reasonable accommodations" to employees with disabilities. Evaluate what you think classifies an accommodation as "reasonable." Give examples of both reasonable and unreasonable accommodations.

Part IV – Social Determinants of Health

All too often, individuals living in the United States and elsewhere see Mary's story as less of a case study, and more of a constant reality. Access to adequate healthcare that is affordable and approachable is multidimensional, and dynamic social circumstances directly inform how individuals are able to receive needed medical care. An individual's income, address, social standing, access to quality education, ability to understand the healthcare system, and much more all play a role in dictating what medical care is accessible to them, and therefore disease diagnosis and progression. This idea, that social circumstances play an influential role in health and wellbeing, is articulated by the Social Determinants of Health (SDH), a universal model used to describe how an individual's physical, cultural, and social environments often serve as limiting factors to what forms of medical care or wellness one can attain.

SDH is comprised of five determinants, each of which plays a role in health outcomes, though the weighting of each determinant is different for each individual. These determinants include health care and quality, neighborhood and built environment, social and community context, economic stability, and education access and quality. Importantly, access to quality health care is only one pillar of this model, emphasizing the importance of outside environmental factors on health and wellbeing. Equally important is the inclusion of non-medical factors, driving home the vital perspective that health and wellbeing are not linearly correlated with quality medical care, but simultaneously informed by a host of unseen, sometimes taboo, social factors.

Questions

1. Navigate to https://my.clevelandclinic.org/health/articles/social-determinants-of-health to see what the Cleveland Clinic has to say about SDH (also known as social drivers of health, or SDOH). Use this resource as a tool to explore the five social determinants in greater detail. Another great resource to explore is Healthy People 2030 (https://odphp.health.gov/healthypeople/priority-areas/social-determinants-health). Now, with a greater understanding of SDH, reflect on Mary Joe's story. Which SDH were most influential in her ability, or lack thereof, to access needed medical care for her RRMS?

2. Predict how Mary's prognosis would change if she were unable to resolve issues with her health insurance. For context, one month's supply of fingolimod costs more than $8,000, and one visit to a neurologist (excluding testing and medication) is over $100.

3. SDH are far from an abstract concept. They are a direct manifestation of changes in our physiology because of the environment. Whether air pollution, access to controlled substances in disadvantaged neighborhoods, or exposure to toxins from impoverished living conditions, SDH directly change how our bodies work. With this in mind, identify an environmental condition in your own life, and assess how it may be protecting you from or predisposing you to disease (identifying positive environmental factors is just as valuable as identifying negative ones). For more information on how SDH impacts physiology, read the following article:
    - Braveman, P., & L. Gottlieb. (2014). The Social Determinants of Health: it's time to consider the causes of the causes. *Public Health Reports* 129(1, supp 2). <https://doi.org/10.1177/00333549141291S206>

4. One SDH that has a significant impact is social and community context. How might the cultural context in which a person lives impact their ability to access healthcare services? In answering this question, consider the following quote:

   > *While the term disparities is often used or interpreted to reflect differences between racial or ethnic groups, disparities can exist across many other dimensions as well, such as gender, sexual orientation, age, disability status, socioeconomic status, and geographic location. According to Healthy People 2030, all of these factors, in addition to race and ethnicity, shape an individual's ability to achieve optimal health. Indeed, the existing evidence on health disparities does reveal differential health outcomes across and within all of the aforementioned identity groups.* —National Academies of Sciences, Engineering, and Medicine. 2017. Communities in Action: Pathways to Health Equity. Washington, DC: The National Academies Press. https://www.ncbi.nlm.nih.gov/books/NBK425844/.

5. A key point surrounding the SDH is that they are universal. The experiences of economic struggle, cultural strife, attacks on education, etc., are not unique to any one country, state, or society. Therefore, an important aspect of employing the SDH model to enhance health and wellbeing is promoting awareness and education about how one's day-to-day social context impacts health. Consider how knowledge of SDH may apply to your life, or the lives of those around you (relatives, neighbors, friends). Draft an educational resource that reflects the importance of SDH on health and wellbeing. You may choose to create a brochure, poster, or even a script for a potential public service announcement. Regardless of the medium, your work should articulate how the five social determinants are integral to health and wellbeing to promote awareness of the widespread implications of this model. The following resources may be helpful to you in creating your work:
   - Whitman, A., N. De Lew, A. Chappel, V. Aysola, R. Zuckerman, & B.D. Sommers. (2022). Addressing social determinants of health: examples of successful evidence-based strategies and current federal efforts. [Report]. ASPE Office of Health Policy. <https://aspe.hhs.gov/reports/sdoh-evidence-review>
   - World Health Organization. (n.d.). Social determinants of health. [Webpage]. <https://www.who.int/health-topics/social-determinants-of-health>
   - American Academy of Family Physicians. (2019). Advancing health equity by addressing the social determinants of health in family medicine. [Position paper]. <https://www.aafp.org/about/policies/all/social-determinants-health-family-medicine-position-paper.html>
   - Office of Disease Prevention and Health Promotion. (n.d.). Healthy people 2030. [Webpage]. <https://odphp.health.gov/healthypeople>
   - HRSA National Health Services Corps. (2024). Social determinants of health: health care access and quality. [Executive summary]. <https://clinicians.org/wp-content/uploads/2024/02/Social-Determinants-of-Health-Health-Care-Access-and-Quality_Exec-Summary_Final-508.pdf>

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