Movement Disorders in Demyelinating Disorders: How Important Is This Historical Link Today?

Jean-Martin Charcot (1825–1893) was a French neurologist and anatomical pathologist. Born in Paris, he was trained by the famous neurologist Duchenne. Charcot worked and taught at the famous Hôpital de la Salpêtrière for more than 3 decades. His name has been associated with at least fifteen medical eponyms including Charcot joint (diabetic arthropathy), Charcot's artery (lenticulostriate artery), Charcot's disease (amyotrophic lateral sclerosis), Charcot's triad of acute cholangitis (right upper quadrant pain, jaundice, and fever), and Charcot's neurologic triad for multiple sclerosis (MS) (nystagmus, intentional tremor, and scanning or staccato speech), to name a few.[1] Reviewing and summarizing previous reports and adding his own clinical and pathological observations, Charcot was the first to identify MS and called the disease sclérose en plaques. He identified three signs of MS, nystagmus, intention tremor, and scanning or staccato speech (dysarthria). These are known as Charcot's neurologic triad. They were originally described by Charcot to distinguish it from Parkinson's Disease.[2] We know now that these clinical signs suggesting underlying movement disorder are neither unique to MS nor are they the most common features seen in this disease as we know it today. However, this unique and historically important link of movement disorder signs in demyelinating disease has been explored further in a very well-researched article published in this issue of the journal.[3]

Singh *et al*.,[3] through a meticulous review process, have described the association of various movement disorders in demyelinating diseases. Their task was difficult as the association is a highly complex one due to several reasons. Firstly, the spectrum of diseases constituting demyelinating disorders ranges from chronic conditions such as MS and neuromyelitis optic spectrum disorders (NMOSDs) to potentially fulminant situations such as acute disseminated encephalomyelitis (ADEM) and osmotic demyelination (OD). Secondly, each of the demyelinating diseases considered is inherently heterogeneous in course. MS and NMOSD can have a varying course from relapsing to progressive, whereas ADEM and OD are generally monophasic.[4] Thirdly, the nature of each of these diseases can vary. MS may be relatively benign or have a more aggressive nature with several relapses and accumulating deficits in a short period.[5] NMOSD patients may be either aquaporin 4 antibody-positive, myelin oligodendrocyte glycoprotein (MOG)-positive, or double seronegative with variations in the phenotype of each one of them and outcomes.[6] There are certain MOG-positive patients who do not satisfy the criteria of NMOSD and may present like ADEM.[7] Presentation of ADEM may be fulminant or relatively benign. Fourthly, although demyelinating diseases have the potential to occur anywhere along the entire neuraxis, individually, each of them may have a predilection for certain anatomical areas. For example, aquaporin 4 positive NMOSD may involve the cervical and dorsal cord more, whereas MOG positive disease is more likely to involve the caudal area. ADEM has cortical involvement with seizures being one of the manifestations, whereas OD may be pontine or extra-pontine, especially in basal ganglia presenting as locked-in state or parkinsonism.[8] Fifthly, from the time of Charcot, due to the therapeutic armamentarium available, the course of these diseases has been altered and the spectrum of clinical findings seen then may have somewhat changed. Lastly, movement disorders per se are a basket of clinical manifestations and include hyperkinetic and hypokinetic disorders. Depending on the circuit disrupted in the same anatomical area, the presentation can vary. As a result of the above, the theoretical possibilities of various permutations and combinations possible are phenomenal. However, in clinical practice, neither are movement disorders commonly seen in demyelinating diseases nor are the full spectrum seen. For example, tremor may occur in patients with MS, but parkinsonism is more likely to be an incidental finding. This has been well highlighted in the review by the authors.

After a PubMed search using key Medical Subject Heading (MeSH), they identified 199 articles, which they summarize systematically covering hyperkinetic and hypokinetic disorders. Although much of the published literature is on MS, they have done well to cover other relevant demyelinating diseases as well. Not surprisingly, tremor is the most common movement disorder seen in MS. Paroxysmal dyskinesias occur most commonly in NMOSD, whereas parkinsonism dominates in OD. In this review, two of the original three Charcot's triad of MS have been covered particularly well. It is well known that tremor in MS can be disabling, and treatment can be difficult. Therapeutic options range from drugs to neuro-stimulation, but response is less than satisfactory. It has also been reported with other demyelinating diseases. Evaluation of movement of the eyes, especially saccades, provides a host of important information such as localization of lesion and cognitive involvement. Patients with MS can have different types of nystagmus, but central positional nystagmus and opsoclonus are rarely reported.

There are other non-autoimmune conditions which affect myelin and may potentially cause movement disorders, and this link is relevant to them also. These include vasculopathy causing Binswanger disease (parkinsonism, especially lower body), toxic exposure (carbon monoxide, mercury, etc.), and leukodystrophies. For today's practicing neurologists, how important is the link between movement disorders and demyelinating diseases? The presence of a particular

movement disorder may not be the sole reason to diagnose a demyelinating disease, but its identification and specific treatment along with the primary disease therapy is important to improve the quality of life.

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