Tumefactive Multiple Sclerosis: a Case Analysis

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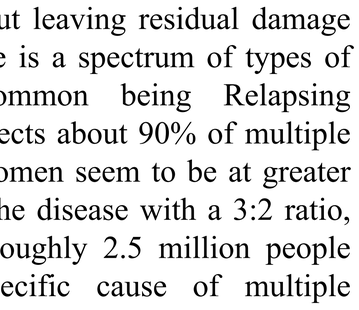
Abstract

Multiple sclerosis is a chronic autoimmune disease that overtime destroys the connections between neurons. The disease presents itself differently and uniquely among all cases. The pathology of the disease is not linear and can be quite difficult to diagnose and treat. One particularly rare case of MS is tumefactive MS characterized by large areas of destroyed tissue. This study would look at the clinical presentations of tumefactive MS patients and how to effectively look at epidemiology and pathology.

Introduction

Multiple Sclerosis (MS) is a complex chronic autoimmune disease of the central nervous system (CNS), characterized by demyelination of neurons, forming lesions, plaques and scaring of the myelin sheath. These plaques cut off electrical impulses being sent between neurons to communicate actions, resulting in a wide variety of disabilities. Early symptoms can include fatigue, vision problems, cognitive issues, and in severe chronic cases, can lead to paralysis. This process of demyelination is followed a process of remyelinating, where the site "heals" itself (and symptoms temporarily go away) but not without leaving residual damage (Fig. 1 and 2). There is a spectrum of types of MS, the most common being Relapsing Remitting, which effects about 90% of multiple sclerosis patients. Women seem to be at greater risk for developing the disease with a 3:2 ratio, with MS affecting roughly 2.5 million people worldwide. The specific cause of multiple sclerosis is unknown; however, several genetic and environmental factors have been linked to the disease: chronic stress, smoking, lack of vitamin D, exposure to the Epstein-Barr virus, etc. The typical age of onset is around 27 years old, but diagnosis can generally occur anywhere from 15-40 years old. Tumefactive MS is the presence of a lesion (where the myelin has been damaged or destroyed), that is greater than 2 centimeters in diameter. Misdiagnosis is very common with a lesion like this, because not only can it mimic a malignant glioma or cerebral abscess, but also on biopsy can be misidentified as a neoplasm. Because of the overly common misdiagnosis, tumefactive MS is not treated properly and can develop severe symptoms quickly.

Fig. 1. shows a comparison between a healthy brain, vs. a brain with damaged neurons from MS. The whiter areas show the sections scares, also known as "sclera"



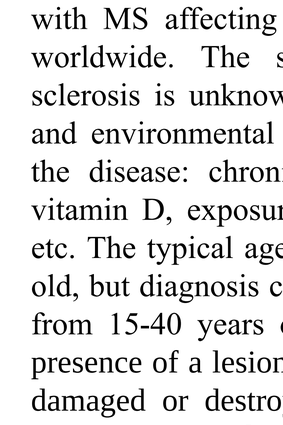


Fig. 2. presents a diagram showing the process a neuron goes through of demyelination and remyelination. After the neuron has been damaged beyond repair, it can often break off completely.

Review of Literature

A Case Control Study of Association between Socio-Demographic, Lifestyle, and Medical History[1]
Ghadirian, P, et al.

Roughly 400 people, half being controls, and half having MS, were looked at for the influences of genetic and environmental links of developing MS. A significant risk was observed between developing Multiple Sclerosis and smoking 20-40 cigarettes a day. Cases of patients with exposure to house animals like cats, dogs, and birds for several years prior to diagnosis were higher compared to the controls (Fig. 3). The reasons for this could be that these animals are involved as exogenous causative agents of disease. Concussion was also seen as a possible links, due to its possible disruption of the blood-brain barrier, which is how immune cells get to the neuron (Fig. 4).

Fig. 3. and 4 show the results that many of the variables tested, (including exposure to disease, having domestic animals, and smoking) are correlated with the development of multiple sclerosis.

TABLE II
Risk of Multiple Sclerosis Associated with Sociodemographic Characteristics

Variable	Cases	Controls	*OR (95% CI)
Marital status			
Never-married	42	42	1.0
Ever-married	158	160	0.9 (0.6-1.6)
Cigarette smoking			
Never-smoked	62	83	1.0
Ever-smoked	138	119	1.6 (1.0-2.4)
0<10/day	15	27	0.7 (0.3-1.5)
10-20/day	34	34	1.4 (0.8-2.4)
20-40/day	71	50	1.9 (1.2-3.2)
40+/day	16	4	5.5 (1.7-17.8)
Physical activities			
Much less active	1	2	0.9 (0.1-8.6)
Less active	44	55	1.2 (0.7-1.9)
As active	64	87	1.0
More active	68	42	2.3 (1.4-3.9)
Much more active	23	16	2.4 (1.1-5.0)
Education			
< 18 years	177	156	1.0
≥ 18 years	23	46	0.4 (0.3-0.8)

*OR = Odds ratio adjusted for age, sex, smoking and education

TABLE III
Risk of Multiple Sclerosis Significantly Associated with Domestic Animals

	Cases/Controls	*OR (95% CI)
Cats	127/156	0.5 (0.3-0.8)
All	36/50	0.3 (0.1-0.8)
Males	91/106	0.6 (0.3-1.0)
Females	32/36	0.6 (0.3-1.1)
For less than 5 years	23/32	0.4 (0.2-0.8)
For 5 to 10 years	64/83	0.4 (0.3-0.7)
For 10 years or more		
Birds		
All	84/54	1.9 (1.0-2.3)
Males	18/18	1.1 (0.5-2.4)
Females	66/36	2.5 (1.5-4.2)
For less than 5 years	41/29	1.8 (1.0-3.0)
For 5 to 10 years	16/12	1.4 (0.6-3.2)
For 10 years or more	20/7	3.6 (1.4-8.9)

* OR = Odds ratio adjusted for age, sex, smoking and education

TABLE IV
Risk of Multiple Sclerosis Significantly Associated with Medical History and Familial History of Diseases and Conditions, Before the First Onset of the First MS Symptoms

Disease	Cases/Controls	*OR (95% CI)	Cases/Controls	*OR (95% CI)
Multiple sclerosis	–	–	15/5	3.4 (1.2-9.7)
Cranial trauma without loss of consciousness	16/5	4.0 (1.4-11.4)	10/13	0.9 (0.4-2.1)
Only events before first MS symptoms	14/5	3.4 (1.2-10.1)		
Eye (vision)	19/4	4.9 (1.6-15.0)	24/12	2.2 (1.1-4.6)
Only events before first MS symptoms	6/4	1.4 (0.4-5.2)		
Mumps	81/70	1.3 (0.9-2.0)	46/30	1.8 (1.1-3.0)
Measles	108/97	1.3 (0.8-1.9)	49/32	1.7 (1.0-2.8)
Rubella	15/15	0.9 (0.4-2.0)	25/11	2.5 (1.2-5.4)
Cancer	8/0	infinity	63/48	1.5 (1.0-2.5)
Only events before first MS symptoms	5/0	infinity		
Auto-immune diseases	6/1	6.5 (0.8-55.1)	21/7	3.4 (1.4-8.3)
Only events before first MS symptoms	4/1	3.8 (0.4-34.4)		

* OR = Odds ratio adjusted for age, sex, smoking and education
Familial history (father, mother, sons, daughters, brothers and sisters)

Adverse Childhood Experiences are linked to Age of Onset and Reading Recognition in MS[2]
Shaw, M T, et al.

67 patients aged 18-70 with definitive diagnosis of multiple sclerosis were studied to see the link between early childhood stress and multiple sclerosis. The Adverse Childhood Experience Survey (ACES) was used to define the severity of childhood trauma. 10 questions are asked about stressful events occurring prior to the age of 18, and for every question applies, a number is added to the ACES score, 10 being the highest. that was seen that those with a greater number of Adverse Childhood Experiences had an earlier age of onset (Fig. 5). Childhood maltreatment influences physiological dysregulation by changing allostatic mechanisms because of increased glucocorticoid activity.

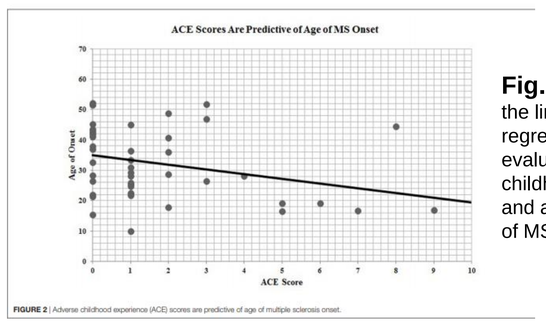


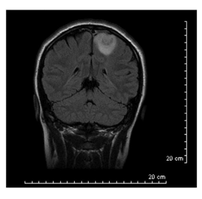
FIGURE 2 | Adverse childhood experience (ACE) scores are predictive of age of multiple sclerosis onset.

Fig. 5. shows the linear regression evaluated between childhood stress and age of onset of MS.

Tumefactive Multiple Sclerosis: an uncommon diagnostic Challenge[3]
Kaeser, Martha A., et al.

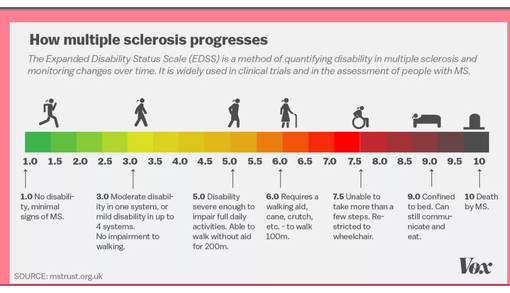
A 30 year old women presented to a chiropractic teaching clinic with a sudden right foot drop. She was initially diagnosed with a peripheral nerve lesion, until on MRI it was discovered that she had a large mass (Fig. 6.) in the left parietal lobe, consistent
with tumefactive MS. Tumefactive MS shares characteristics of a cerebral abscess or malignant glioma, and can even represent itself on biopsy as a neoplasm. Symptoms of tumefactive MS often include headache, cognitive issues, mental confusion, aphasia, apraxia and/or seizures.

Fig. 6. shows the MRI scan of intraaxial lesion in the superior aspect of the left parietal lobe.



Na MRI reveals persistent sodium accumulation in tumefactive MS lesions[4]
Huhn, Konstantin, et al.

Shared features between enlarged MS lesions, tumefactive demyelination and "Balo-like" lesions make them hard to differentiate on MRI. NaMRI is a way of looking at sodium accumulation. MS patients have displayed higher sodium levels within acute acute inflammatory lesions. This study looked at their relationship to tumefactive lesions. Tumefactive demyelination showed elevated sodium levels, consistent with other research, however, these enlarge lesions showed the highest levels of sodium accumulation in contrast. With intervention, acute MS lesions begin to decline until plateau is reached, whereas even 5 weeks after intervention of the tumefactive lesions, sodium levels stayed elevated despite reconstruction of the blood-brain barrier.



Potential Methodology

With the patient charts and work done through the Multiple Sclerosis Comprehensive Care Center (a part of the NYU Langone Medical Center), an analysis of cases will be conducted, looking at patient demographics, diagnoses, MRI, and biopsy. From this, we will look into the relationships displayed between several different factors such as: initial diagnosis and/or potential misdiagnosis, size of lesions and plaques, and other variables that may come up.

References

(1)Ghadirian, P, et al. "A Case-Control Study of the Association between Socio-Demographic, Lifestyle and Medical History Factors and Multiple Sclerosis." *Advances in Pediatrics.*, U.S. National Library of Medicine, 2001.
(2)Shaw, M T, et al. "Adverse Childhood Experiences Are Linked to Age of Onset and Reading Recognition in Multiple Sclerosis." *Advances in Pediatrics.*, U.S. National Library of Medicine, 2 June 2017.
(3)Kaeser, Martha A., et al. "Tumefactive Multiple Sclerosis: An Uncommon Diagnostic Challenge." *Advances in Pediatrics.*, U.S. National Library of Medicine, 10 Mar. 2011.
(4)Huhn, Konstantin, et al. "23Na MRI Reveals Persistent Sodium Accumulation in Tumefactive MS Lesions." International Journal of Gerontology, Elsevier, 7 June 2017.

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