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Review Article

A narrative review of transverse myelitis and multiple sclerosis: Associations and threats

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Abstract. The affiliation of multiple sclerosis (MS) with other immune system and inflammatory illnesses like transverse myelitis (TM) has been a theme of interest. Even though, previous investigations tried to elucidate the relationship between these two illnesses, it remained unclear because of restricted and incompatible information in this subject. In this review, we researched the etiology, pathophysiology, epidemiology and treatments of MS and TM according to accessible articles in valid databases. We figured out multiple sclerosis (MS) can be associated with transverse myelitis (TM) in a number of aspects and longitudinal expanse of brain and spinal cord lesions found by MRI, presence of DRB1*1501 allele, and etc. However, further research is fundamental to perceive the remarkable relationship between multiple sclerosis and transverse myelitis in field of neurodegenerative diseases. An appraisal of research studies published in various bibliographic databases including PubMed, Medscape, and Google scholar were used. A total of 57 articles were sought and reviewed. Results were classified into 6 specific subtitles including prevalence and incidence rates, complications, common cerebrospinal fluid (CSF) agents and factors, prognosis and diagnosis, treatment, and finally risk factors. Research articles were reviewed and analyzed for information regarding each subject. In this study, we aimed to review articles that detected links between TM and MS and those that described different aspects of these correlations. It was observed that in various aspects MS and TM had Strong as well as weak correlations. On the other hand, we discussed that the lack of common appropriate treatment caused the inability to restrict symptoms on patients in either disease. Further trials on candidate therapies may result in new reliable treatments with acceptable adverse effects.

Keywords: Transverse myelitis, multiple sclerosis, neurodegenerative, risk factor, sssociation.

Introduction

Multiple sclerosis (MS) is a chronic central nervous system disease with cognitive and depressive disorders [1]. The last reports revealed that MS pathogenesis is commonly observed in women more than in men and usually occurs in young adults [2-5]. In the last decades, MS prevalence significantly increased in European and American countries (up to more than 120 per 100,000) [2-6].

The symptoms of MS would present in different levels (e.g., mild, moderated, severe progression) [7]. Despite some studies suggested several hypothesizes, such as inflammatory mediated pathogenesis introduced by genetic deposition and environmental effects, the mechanisms of MS progression have remained unclear up to recent years [7-9]. Moreover, some other studies showed that different cytokines, induced by autoreactive T cells, play the main role in cerebral inflammation leading to MS progression [5, 10]. Therefore, it is still required to investigate new associations and pathogenesis mechanisms to provide more reliable treatments for MS.

Transverse myelitis (TM) is another neurological dysfunction that occurs in both brain hemispheres and would progress to the spinal cord as well [11]. Several reports in earlier years revealed that more than 9 million people present different TM symptoms worldwide, but approximately around 90% of them experience mild symptoms [12, 13]. TM has shown the most association with connective tissues disorders, such as systemic lupus erythematosus and Sjogren's syndrome [14]. Moreover, recent studies demonstrated that acute partial transverse myelitis (APTM) would remain monophasic or change its pathogenesis to MS symptoms [15]. On the other hand,

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other studies on APTM showed that shifting to MS may occur very rarely in some cases, but with a higher symptomatic presentation [16, 17]. However, attempts to explore new findings of the relationship between MS and TM have continued in the last two decades [18].

In recent years, several studies have been carried out to find new associations and develop novel therapies for neurological disorders. Therefore, in this study, we aim to review published articles to achieve links, promising treatments, and new common conditions for MS and TM patients.

Links between TM and MS

1. Prevalence and incidence

One of the first observations showed that around 3% of adult patients with TM completely convert to MS [19]. However, only 0.7% of patients with MS face acute TM, but the situation becomes different in the long term [20]. Further clinical observations revealed that approximately 80% of patients with partial TM may present MS symptoms in 3 years [21]. A multi-central evaluation in New Mexico showed that more than 20 percent of TM cases would be induced by MS mechanisms [22]. Therefore, their remarkably observed correlation between TM and MS shows novel connections [23].

2. Complications

Pediatrics with TM or MS have higher levels of working memory, social life, and attention problems [24].TM and MS patients would present the same complications, such as depression, pain, and fatigue [25]. Further studies showed that TM and MS patients have a higher risk for experiencing metabolic and cardiovascular disorders [26]. Therefore, patients with these disorders may face several life-long mental and psychological problems require us to find novel management and control their complications.

3. Common CSF agents and factors

Some studies tried to introduce new common agents between TM and MS. The evaluation of cerebrospinal fluids (CSF) in MS patients indicated that an increase in CSF concentration of oligoclonal bands (TM-related agents) has a significant correlation with MS and would develop MS symptoms after 34 months [22, 27-29]. Also, other trials showed that 14-3-3 proteins would elevate in patients with little recovered MS and acute TM [30, 31]. Earlier studies revealed that IL-17 would promote the level of IL-6 in inflammation disorders [32]. In 2008, Graber et al. demonstrated that IL-17 induces astrocytes to resect more IL-6 and develop TM and MS symptoms [33]. In contrast, other evaluations showed that MS agents found in CSF specimens had no reliable correlation with the development of recurrent TM [34]. Moreover, Myelin oligodendrocyte glycoprotein Immunoglobulin G is another diagnostic factor related to recurrent TM that provides MS-liked symptoms and caused multiple clinical misdiagnoses [35].

4. Prediction, diagnosis and prognosis

In 1998, Scott et al. introduced a novel prognosis for MS. In this study, they revealed that the correlation of neurological disorders with MS development is more significant in acute TM [36]. Further investigations showed that symmetric sensory disorders have a higher prevalence in TM, while ATM-related asymptomatic lesions are the most remarkable prognosis for MS [23, 36]. Studies on adolescent patients with partial ATM indicated that the presence of relapses and MRI abnormalities in the brain predicts MS and results in higher complications [38].

On the other hand, in some situations, imaging would result in a misdiagnosis. In a recent study, Asnafi et al. showed that longitudinal extensive TM would be mistaken with multiple MS. This misdiagnosis would be prepared with simple axial imaging in suspected cases [39]. Moreover, imaging has low reliable efficiency in distinguishing between idiopathic ATM and MS, as patients with idiopathic ATM have a lower chance to show MS symptoms [29, 40]. Therefore, we require further studies to figure out more criteria and provide diagnostic approaches with more efficiency [41].

5. Risk factors

Trials on antibody mutations indicated that the presence of immune system abnormalities is generally similar in both TM and MS. In a unique study, Ligocki et al. introduced antibody gene signature (AGS), as a novel risk factor for MS prediction. This study revealed that patients with a high concentration of AGS had a serious risk of MS appearance, but these results would not provide reliable biomarkers to certainly diagnose MS [42]. Another study on pediatric patients with MS and TM demonstrated that HLA-DRB1*1501 allele, vitamin D abnormality, and viral infections, such as Epstein-Barr virus and cytomegalovirus, would increase the risk of MS and TM development [43].

In 2008, Sellner et al. and revealed a complete list of MS risk factors. This observation indicated that partial ATM with IgG abnormalities, familial history of MS, serious complications at the beginning of symptoms, and brain MS-related lesions confirmed by MRI, alongside oligoclonal bands would convert to MS more than the others [44]. Moreover, further studies added gender (being female), smoking, and the appearance of HLA-DR15 to the previous risk factors of MS incidence [26]. In contrast, Saroufim et al. investigated that cardiovascular diseases, such as hypertension, would result in a higher risk of MS but have no relation with TM [45].

6. Treatments

To date, several common treatments have been developed for TM and MS. New observations showed that medical marijuana would provide promising results to control the complications of TM and MS [46].

Discussion and conclusion

In this study, we aimed to review articles that detected links between TM and MS and described different aspects of these correlations.

In 1998, Paty et al. showed that the simultaneous incidence of TM and MS, and their conversion to each other in short term [47]; but, other long-term studies indicated

tight correlations between MS and TM [48]. The 3-year term had been introduced as a cut-off for co-appearance of these disorders [49]. However, we would require to design longer observations with bigger sample sizes to achieve more knowledge about the long-term clinical presentations.

Multiple studies reported that TM and MS patients may suffer from the same complications as well. While young cases would face some mental health disorders, such as social life, working memory, and attention problems, the older patients may present non-communicable diseases [50, 51]. Thus, MS and TM patients may show different complications in various steps.

In the past years, several CSF biomarkers have been introduced to diagnose MS and TM. The presence of oligoclonal bands and IL-17 had a significant association with higher incidence of TM and MS [52, 53]. Despite these developments, we still have remarkable misdiagnoses in patients with different stages of TM or MS [54]. Therefore, further studies are needed to investigate more reliable biomarkers with higher efficiency in prognoses.

For the first observations, Scott et al. indicated that neurological symptoms in acute TM and MS patients would occur in the same patterns [55]. Based on further studies, MRI has been introduced as a relatively reliable approach in diagnosing these neurological disorders [48, 56]. On the other hand, the other observations showed that diagnosis with MRI would not be appropriate to detect all presentations. Therefore, the specialists recently have serious doubts to rely on this procedure [57]. Further studies would figure out novel promising methods to distinguish TM and MS in the future.

In the end, considering we expand searches in different databases, we have a lack of appropriate common treatment to restrict symptoms which follow complications in patients with TM and MS. Further trials on candidate therapies may result in new reliable treatments with acceptable adverse effects.

Conflict of Interest

The authors declare no conflicts of interest.

References

1. Tobin WO. Management of multiple sclerosis symptoms and comorbidities. Tobin WO. Management of Multiple Sclerosis Symptoms and Comorbidities. Continuum (Minneap Minn). 2019;25(3):753-772.

2. Wallin MT, Culpepper WJ, Nichols E, Bhutta ZA, Gebrehiwot TT, Hay SI, et al. Global, regional, and national burden of multiple sclerosis 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet Neurology. 2019;18(3):269-285.

3. Evans C, Beland S-G, Kulaga S, Wolfson C, Kingwell E, Marriott J, et al. Incidence and prevalence of multiple sclerosis in the Americas: a systematic review. Neuroepidemiology. 2013;40(3):195-210.

4. Kingwell E, Marriott JJ, Jetté N, Pringsheim T, Makhani N, Morrow SA, et al. Incidence and prevalence of multiple sclerosis in Europe: a systematic review. BMC neurology. 2013;13(1):1-13.

5. Saroufim P, Zweig SA, Conway DS, Briggs FB. Cardiovascular conditions in persons with multiple sclerosis, neuromyelitis optica and transverse myelitis. Mult Scler Relat Disord 2018;25:21-25.

6. MS MSIFLao. mapping multiple sclerosis around the world 2013 [Available from: http://www.msif.org/about-ms/publications-and-resources/2013.

7. Scott TF, Bhagavatula K, Snyder PJ, Chieffe C. Transverse myelitis: comparison with spinal cord presentations of multiple sclerosis. Neurology 1998;50(2):429-433.

8. Mohan N, Edwards ET, Cupps TR, Oliverio PJ, Sandberg G, Crayton H, et al. Demyelination occurring during anti–tumor necrosis factor α therapy for inflammatory arthritides. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology 2001;44(12):2862-2869.

9. Jeffery DR, Mandler RN, Davis LE. Transverse myelitis: retrospective analysis of 33 cases, with differentiation of cases associated with multiple sclerosis and parainfectious events. Arch Neurolo 1993;50(5):532-535.

10. Young J, Quinn S, Hurrell M, Taylor B. Clinically isolated acute transverse myelitis: prognostic features and incidence. Mult Scler J 2009;15(11):1295-1302.

11. Group TMCW. Proposed diagnostic criteria and nosology of acute transverse myelitis. Neurology 2002;59(4):499-505.

12. Berman M, Feldman S, Alter M, Zilber N, Kahana E. Acute transverse myelitis: incidence and etiologic considerations. Neurology 1981;31(8):966-971.

13. Paine RS, Byers RK. Transverse myelopathy in childhood. AMA Am J Dis Child 1953;85(2):151-163.

14. Mok CC, Lau CS, Chan E, Wong R. Acute transverse myelopathy in systemic lupus erythematosus: clinical presentation, treatment, and outcome. Journal Rheumatol 1998;25(3):467-473.

15. Garg N, Smith TW. An update on immuno-pathogenesis, diagnosis, and treatment of multiple sclerosis. Brain Behavior 2015;5(9):e00362.

16. Sellner J, Lüthi N, Bühler R, Gebhardt A, Findling O, Greeve I, et al. Acute partial transverse myelitis: risk factors for conversion to multiple sclerosis. Eur J Neurol 2008;15(4):398-405.

17. Sellner J, Lüthi N, Bühler R, Gebhardt A, Findling O, Greeve I, et al. Acute partial transverse myelitis: risk factors for conversion to multiple sclerosis. Eur J Neurol 2008;15(4):398-405.

18. Montalban X. The importance of long-term data in multiple sclerosis. J Neuro 2006;253(6):vi9-vi15.

19. Lipton HL, Teasdall RD. Acute transverse myelo-pathy in adults: a follow-up study. Arch Neurol 1973;28(4):252-257.

20. Paty D, Hashimoto S, Ebers G. Management of multiple sclerosis and interpretation of clinical trials. Multiple sclerosis Philadelphia: FA Davis, 1998:445-447.

21. Ford B, Tampieri D, Francis G. Long-term follow-up of acute partial transverse myelopathy. Neurology 1992;42(1):250-252.

22. Jeffery DR, Mandler RN, Davis LE. Transverse myelitis: retrospective analysis of 33 cases, with

differentiation of cases associated with multiple sclerosis and parainfectious events. Archives of neurology. 1993;50(5):532-535.

23. Lynn J. Transverse Myelitis- The Multiple Sclerosis Connection. Transverse Myelitis Association. 2001;4.

24. Tan A. Neurocognitive and Psychosocial Profiles of Pediatric Multiple Sclerosis and Transverse Myelitis 2018.

25. Simpson AC. Psychology in neuromyelitis optica, transverse myelitis, and multiple sclerosis: a cross-sectional study of fatigue, pain, and depression associated with disability: Boston University; 2013.

26. Simon K, Schmidt H, Loud S, Ascherio A. Risk factors for multiple sclerosis, neuromyelitis optica and transverse myelitis. Multiple Sclerosis Journal. 2015;21(6):703-709.

27. Moulin D, PATY DW, EBERS GC. The predictive value of cerebrospinal fluid electrophoresis in 'possible'multiple sclerosis. Brain. 1983;106(4):809-816.

28. Scott TF, Kassab SL, Singh S. Acute partial transverse myelitis with normal cerebral magnetic resonance imaging: transition rate to clinically definite multiple sclerosis. Multiple Sclerosis Journal. 2005;11(4):373-377.

29. Calvo ÁC, Martínez MAM, Alentorn-Palau A, Escuer JB, Pinel LR, Martínez-Yélamos S. Idiopathic acute transverse myelitis: outcome and conversion to multiple sclerosis in a large series. BMC neurology. 2013;13(1):1-8.

30. Irani DN, Kerr DA. 14-3-3 protein in the cerebrospinal fluid of patients with acute transverse myelitis. The Lancet. 2000;355(9207):901.

31. Martínez–Yélamos A, Saiz A, Sanchez–Valle R, Casado V, Ramon J, Graus F, et al. 14-3-3 protein in the CSF as prognostic marker in early multiple sclerosis. Neurology. 2001;57(4):722-724.

32. Hwang S-Y, Kim J-Y, Kim K-W, Park M-K, Moon Y, Kim W-U, et al. IL-17 induces production of IL-6 and IL-8 in rheumatoid arthritis synovial fibroblasts via NF-κB- and PI3-kinase/Akt-dependent pathways. Arthritis Res Ther. 2004;6(2):1-9.

33. Graber JJ, Allie SR, Mullen KM, Jones MV, Wang T, Krishnan C, et al. Interleukin-17 in transverse myelitis and multiple sclerosis. Journal of neuroimmunology. 2008;196(1-2):124-132.

34. Ungurean A, Palfi S, Dibo G, Tiszlavicz L, Vecsei L. Chronic recurrent transverse myelitis or multiple sclerosis. Functional neurology. 1996;11(4):209-214.

35. Perez GS, Wisdom PJ, Anadani N. (CRS06) A Long-Standing Case of Recurrent Transverse Myelitis Due to Myelin Oligodendrocyte Glycoprotein (MOG)--IgG Antibody Mimicking Multiple Sclerosis. International Journal of MS Care. 2020;22.

36. Scott TF, Bhagavatula K, Snyder PJ, Chieffe C. Transverse myelitis: comparison with spinal cord presentations of multiple sclerosis. Neurology. 1998;50(2):429-433.

37. Nakashima I, Fujihara K, Takase S, Itoyama Y. Decrease in multiple sclerosis with acute transverse myelitis in Japan. The Tohoku journal of experimental medicine. 1999;188(1):89-94.

38. Meyer P, Leboucq N, Molinari N, Roubertie A, Carneiro M, Walther-Louvier U, et al. Partial acute transverse myelitis is a predictor of multiple sclerosis in children. Multiple Sclerosis Journal. 2014;20(11):1485-1493.

39. Asnafi S, Morris P, Pittock S, Weinshenker B, Palace J, Messina S, et al. The Frequency of Longitudinally Extensive Transverse Myelitis in Multiple Sclerosis in the Era of Glial Biomarkers; A Population-Based Study (P4. 2-055). AAN Enterprises; 2019.

40. Kim HJ, Chang KH, Kim SH, Kim KK, Lee YS, Lee KW. Differentiation between idiopathic acute transverse myelitis and myelopathic multiple sclerosis by MRI. Journal of the Korean Neurological Association. 1999;17(5):651-660.

41. Torisu H, Kira R, Ishizaki Y, Sanefuji M, Yamaguchi Y, Yasumoto S, et al. Clinical study of childhood acute disseminated encephalomyelitis, multiple sclerosis, and acute transverse myelitis in Fukuoka Prefecture, Japan. Brain and Development. 2010;32(6):454-462.

42. Ligocki A, Rounds W, Cowell L, Chaudhary P, Xiang D, Guidry P, et al. Comparison of antibody gene mutation patterns in first attack optic neuritis and transverse myelitis leading to Multiple Sclerosis (47.18). Am Assoc Immnol; 2011.

43. Weinfurtner K, Graves J, Mowry E, Krupp L, Belman A, Milazzo M, et al. Risk Factors for Transverse Myelitis Compared with Multiple Sclerosis, Neuromyelitis Optica, and Other Neurologic Disorders in Pediatric Patients (P02. 121). AAN Enterprises; 2013.

44. Sellner J, Lüthi N, Bühler R, Gebhardt A, Findling O, Greeve I, et al. Acute partial transverse myelitis: risk factors for conversion to multiple sclerosis. European journal of neurology. 2008;15(4):398-405.

45. Saroufim P, Zweig SA, Conway DS, Briggs FB. Cardiovascular conditions in persons with multiple sclerosis, neuromyelitis optica and transverse myelitis. Multiple sclerosis and related disorders. 2018;25:21-25.

46. Gyang T, Hyland M, Samkoff L, Goodman A. "Real world" experience of medical marijuana in symptomatic management of multiple sclerosis and transverse myelitis (P1. 421). AAN Enterprises; 2018.

47. Paty D, Hashimoto S, Ebers G. Management of multiple sclerosis and interpretation of clinical trials. Multiple sclerosis Philadelphia: FA Davis. 1998:445-447.

48. Lynn J. Transverse Myelitis—The Multiple Sclerosis Connection. Transverse Myelitis Association. 2001;4.

49. Ford B, Tampieri D, Francis G. Long-term follow-up of acute partial transverse myelopathy. Neurology. 1992;42(1):250-252.

50. Tan A. Neurocognitive and Psychosocial Profiles of Pediatric Multiple Sclerosis and Transverse Myelitis 2018.

51. Simon K, Schmidt H, Loud S, Ascherio A. Risk factors for multiple sclerosis, neuromyelitis optica and transverse myelitis. Multiple Sclerosis Journal. 2015;21(6):703-709.

52. Scott TF, Kassab SL, Singh S. Acute partial

transverse myelitis with normal cerebral magnetic resonance imaging: transition rate to clinically definite multiple sclerosis. Multiple Sclerosis Journal. 2005;11(4):373-377.

53. Graber JJ, Allie SR, Mullen KM, Jones MV, Wang T, Krishnan C, et al. Interleukin-17 in transverse myelitis and multiple sclerosis. Journal of neuroimmunology. 2008;196(1-2):124-132.

54. Ungurean A, Palfi S, Dibo G, Tiszlavicz L, Vecsei L. Chronic recurrent transverse myelitis or multiple sclerosis. Functional neurology. 1996;11(4):209-214.

55. Scott TF, Bhagavatula K, Snyder PJ, Chieffe C. Transverse myelitis: comparison with spinal cord presentations of multiple sclerosis. Neurology. 1998;50(2):429-433.

56. Meyer P, Leboucq N, Molinari N, Roubertie A, Carneiro M, Walther-Louvier U, et al. Partial acute transverse myelitis is a predictor of multiple sclerosis in children. Multiple Sclerosis Journal. 2014;20(11):1485-1493.

57. Calvo ÁC, Martínez MAM, Alentorn-Palau A, Escuer JB, Pinel LR, Martínez-Yélamos S. Idiopathic acute transverse myelitis: outcome and conversion to multiple sclerosis in a large series. BMC neurology. 2013;13(1):1-8.