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An Essential Permissive Microenvironment as Primarily Passive Accumulation of Multiple Sclerosis Lesion Byproducts Redefines Disease Pathogenesis

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Abstract

A permissive micro-environment enhances the realization of events that are principally characterized by accumulative dynamics for further change that occur both in series and in parallel. The performance of significant participation of macrophage dysfunction is essential attribute definition of the transforming pathways of myelin breakdown products as first realized by dimensions of cooperative institution of accumulative process redefinitions. It is significant to consider the recharacterized implements of lesion segregation as systems of performance of phagocytosis and as further degradation of the lesion byproducts within the MS lesion pathways of consequence.

Keywords: Microenvironment; Pathogenesis; Multiple sclerosis

Introduction

Non-resolution of the active pathologic lesions and particularly the physicochemical changes as accumulation of lesion burden lies as the central events in the clinico-pathologic spectrum of multiple sclerosis. Effects memory T cells populate healthy CNS parenchyma in humans and also that CCR5-expressing lymphocytes as well as CCR5 ligands are enriched in the CNS of patients with MS [1]. The definition and incumbent aggregation and segregation of transforming pathologic changes account for the evolutionary course of Multiple sclerosis (MS). In MS, demyelinated CNS lesions fail to sufficiently demyelinate despite the presence of oligodendrocyte precursor cells capable of differentiating into mature oligodendrocytes; in fact MS lesions contain damaged myelin debris that can inhibit oligodendrocyte precursor cell maturation and hinder repair [2]. As such, such a concept contrasts with the evolution of active pathogenesis as derived from etiologic causation and from participating activity of the foci of demyelination and axonal transection.

Non-Resolution

The conceptual frameworks of non-resolution indicate a full display of forceful dynamics with no resolving dimensions. It is clear that derived phenomena of injury in the MS brain and spinal cord denote a series of primary determinants in non-resolution of the demyelination.

As such, the further cooperative inherent dimensions of such non-resolution indicate and implicate the derived segregation of various influences within the further breakdown events of the myelin sheaths. Evidence suggests that ablation of microglia/macrophages during the symptomatic phase of experimental autoimmune encephalitis [EAE] reduces CNS inflammation and may promote a permissive environment for demyelination [3]. It is within such frameworks of operative dimension that MS progression derives dynamics in the evolution especially of the multiple and various pathogenetic pathways in delimiting and further accentuating demyelinating lesions in the white

matter of the brain. Hyaluronan is abundant in chronic inflammation and contributes to lymphocyte activation, polarisation and migration and may create a permissive environment for autoimmunity [4].

Correlative Indices

Correlative indices of cooperative factors account for a redistribution of lesions that include the further parallel and in series dimensions of axon transection and also of the outline phenomena of neurodegeneration in MS patients.

Gamma-delta 17 T cells are important in breaking immunologic tolerance and enhancing inflammation in MS in terms of their biologic traits such as development, effector function, activation and plasticity [5].

Within such a scenario, the inevitable failure of resolution of the CNS lesions indicates and further specifies incumbent dimensions of persistence of pathologic damage foci as indicated especially by persistence of many cases with a relapsing/remitting clinico-pathologic course of the disease. In such terms, derived outline phenomena of additional lesions within the CNS account for redistribution of pathogenesis as a secondary causative series of transformations. In the course of such considered dimensions, the MS pathology is incumbent non-resolution of initial changes that lesion the myelin sheaths and the parent axons. Hence, it is significant to view the causative agents as directly significant in the resetting and further enhancement of the previously established MS lesion.

Targeting

The actual targeting of events of the MS process is hence a reconditioning of events within a milieu that is micro environmentally persistent in nature but that is enhanced passive resultant of integer processes of progression of persistent pathologic lesions primarily found within the CNS white matter.

In such terms, attributes of progressiveness are dysfunctional consequences of a non-resolving series of lesions that incorporate the specific dimensions for further dynamic transformation. It is within such conceptual frameworks of ongoing progression that MS includes the phenomenon of derived increments of pathology and of physicochemical segregation of the MS lesions.

Such prominence of non-resolving issues comes to define the dynamics of the MS disease process in terms especially of macrophage participation in the evolution of lesion transformation. Such derivative phenomena of phagocytic implications in pathogenesis are therefore involved in attribute factors in a series of transformations that include the redefinition of each MS lesion within the CNS.

Dietary cholesterol enhances repair of demyelinated lesion in the adult brain [6]. A permissive genetic disposition, a pro-inflammatory intestinal microbial profile and the accumulation of auto reactive cells in the gut-related lymphoid tissue are conceptual requirements in pathogenesis of MS [7]. The somatodendritic compartment directly suppresses myelination and oligodendrocytes are able to myelinate permissive structures in the absence of molecular cues [8].

In terms therefore of essential accumulative dimensions of acquisition, there is implicated a series of further progression steps within frameworks of an acquired nature. The immunologic etiologic agents are pronounced attributes of a T-helper pathway within the system profiles of such non-resolution. The further cooperative implications include a reconsideration of lesion burden that conclusively is derived from the various transforming dimensions of cooperative segregation of products of damage to the myelin sheath. Extracellular cues in modulation of re-myelination may include soluble, part of the extracellular matrix or mediators derived from cell-cell interactions [9].

Consequential Conformation of Lesions

In various conformational consequences of the myelin sheath there is implicated a macrophage dysfunctional panorama of postoperative dimensions that carry over the implicated segregation of byproducts of breakdown of the myelin sheaths. The cooperative implications of demyelination come to offer a series of transforming cellular attributes that directly activate macrophage dysfunctionalities. A new in vitro mouse oligodendrocyte precursor cell migration assay reveals a role for integrin-linked kinase operative in cell motility [10].

Immunosuppression therapy has a limited range of efficacy in MS, arguing for a paradigm shift to strategies that target oligodendrocyte lineage cells to achieve remyelination [11]. Further to such considerations, the active and passive pathogenesis of foci of catabolized myelin byproducts and the failed clear resolution of lesions are cooperative within systems of incremental dysfunctional states of participation in MS nature definition of original etiology and subsequent accumulative pathogenesis of lesion increment. Chondroitin sulphate proteoglycans are key modulators in pathology of the CNS [12].

Performance Indices

Performance redefinition is hence a direct consequence of post etiologic dimension as dictated by systems of

specific series of redefinition. The causative attributes of such postulates therefore constitute a series and parallel consequence within the performance dynamics of injury that allow a highly permissive spectrum for progression of accumulative lesions. It is within simple panoramas of increment that dynamics of MS progression are attributes of macrophage accumulation in their own right. Toll-like receptor4 is a key player in axonal debris clearance by microglia, thus allowing for a more permissive environment for axonal outgrowth [13].

The complexities of the various agents in such primarily consequential pathogenesis account for a redistribution of lesions that redefines the momentum of especially the relapsing/remitting disease course seen clinically in many patients with MS. Netrin-1 expression within demyelinating MS plaques inhibits oligodendrocyte precursor cell recruitment with eventual permanent demyelination failure [14].

Performance indices of non-resolution are hence consequences within frameworks of altered homeostatic control states as directly indicated by the macrophage dysfunctionalities within the non-resolving individual MS lesion in patients that suffer from the persistent evolution of the injury to the myelin sheath and transected axons. Diverting T helper cell trafficking through increased plasticity attenuates autoimmune encephalitis [15]. It is clearly in terms of the creation of a permissive series of parallel events that the complexity of lesion transformation accounts for difficulties in lesion definition in most patients suffering from MS.

Concluding Remarks

The confines of conscription within the accumulative dynamics of disease by-products are a failed dimension of the permissive micr- environment that dictates the clinico-pathologic indices of progression of the MS pathogenic pathways. In such terms, overall indices for transforming progression permit the redefinition of each pathologic stage in MS lesion characterization. It is within the system profile of modeled events that there emerges a realization of lesion accumulation in terms of permissive attributes in autoimmune processes of active versus passive acquisition of dynamics of turnover of macrophage dysfunctionality in phagocytosis and of removal of partly degradable by-produces of consequence in MS evolution in the individual patient. Such processes as depicted by permissive pathogenesis are therefore a hierarchal system of series and parallel events that target dyshomeostasis within micro environments of persistent disease activity.

References

1. Herich S, Scheider-Hohendorf T, Rohlmann A, Khaleghi Ghadiri M, Schulte-Mecklenbeck A, et al. (2019) Human CCR5high effector memory cells perform CNS parenchymal immune surveillance via GZMK-mediated transendothelial diapedesis. Brain 142(11): 3411-3427.

2. Zorina Y, Stricker J, Caggiano AO, Button DC (2018) Human IgM antibody rHIgM22 promotes phagocytic clearance of myelin debris by microglia. Sci Rep 8(1): 9392.

3. Nissen JC, Thompson KK, West BL, Tsirka SE (2018) Csf1R inhibition attenuates experimental autoimmune encephalomyelitis and promotes recovery. Exp Neurol 307: 24-36.

4. Nagy N, Kuipers HF, Marshall PL, Wang E, Kaber G, et al. (2019) Hyaluronan in immune dysregulation and autoimmune diseases. Matrix Biol 78-79: 292-313.

5. Papotto PH, Reinhardt A, Prinz I, Silva-Santos B (2018) Innately versatile: gammadelta17 T cells in inflammatory and autoimmune diseases. J Autoimmune 87: 26-37.

6. Berghoff SA, Gerndi N, Winchenbach J, Stumpf SK, Hofsang L, et al. (2017) Dietary cholesterol promotes repair of demyelinated lesions in the adult brain. Nat Commun 8: 14241.

7. Wekerle H (2016) The gut-brain connection: triggering of brain autoimmune disease by commensal gut bacteria. Rheumatology ? (Oxford) 55(S2): ii68-ii75.

8. Redmond SA, Mei F, Eshed-Eisenbach Y, Osso LA, Leshkowitz D, et al. (2016) Somatodendritic expression of JAM2 inhibits oligodendrocyte myelination. Neuron 91(4): 824-836.

9. Wheeler NA, Fuss B (2016) Extracellular cues influencing oligodendrocyte differentiation and (re) myelination. Exp Neurol 283: 512-530.

10. O'Meara RW, Cummings SE, Michalski JP, Kothary R (2016) A new in vitro mouse oligodendrocyte precursor cell migration assay reveals a role for integrin-linked kinase in cell motility. BMC Neurosci 17: 7.

11. Lopez Juarez A, He D, Richard Lu Q (2016) Oligodendrocyte progenitor programming and reprogramming: toward myelin regeneration. Brain Res 1638: 209-220.

12. Dyck SM, Karimi-Abdoirezaee S (2015) Chondroitin sulfate proteoglycans: key modulators in the developing and pathologic central nervous system. Exp Neurol 269: 169-187.

13. Rajbhandari L, Tegenge MA, Shrestha S, Ganesh Kumar, Malik A, et al. (2014) Toll-like receptor 4 deficiency impairs microglial phagocytosis of degenerating axons. Glia 62(12): 1982-1991.

14. Tepavcevic V, Kerninon C, Aigret MS, Meppiel E, Mozafari S, et al. (2014) Early netrin-1 expression impairs central nervous system remyelination. Ann Neurol 76(2): 252-268.

15. Califano D, Sweeney KJ, Le H, VanValkenburgh J, Yager E, et al. (2014) "Diverting T helper cell trafficking through increased plasticity attenuates autoimmune encephalomyelitis. J Clin Invest 124(1): 174-187.