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Original Research Article

Mechanism of Neuroinflammation in Traumatic Brain Injury

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Abstract:To understand the interaction between inflammatory factors,blood-brain barrier and immune cells after traumatic brain injury(TBI).We review the recent literatures about inflammation post TBI.Microglia,astrocyte as well as inflammatory cytokines in inflammation are mentioned.In addition,interaction between immune cells through cytokines are mainly elaborated,in order to provide reference for treatment towards to TBI and other symptoms caused by acute brain injury.
Keywords:TBI;Neuroinflammation;Cytokines;Blood-brain barrier

1 Introduction

Traumatic brain injury(TBI)is a major cause of death and disability among children and young adults and has become increasingly prevalent in the elderly[1].TBI leads to complex pathological processes and Multiple neurodegenerative diseases which Extremely reduce the patient's quality of life[1,2].This research focus on the mechanism of neuroinflammation caused by changes of BBB,the interaction between immune cells and cytokines in TBI,in order to provide reference for future relevant experiments and provide strategies for treatment.

2 Dysfunction of BBB and Neuroinflammation

BBB tightly regulate the movement of metabolic substances between the blood stream and the brain[3].BBB disruption is a major risk factor for high mortality and morbidity in TBI patients,occurs within hours following TBI,and intriguingly,persisting in a high proportion of late survivors is considered[4].

Neuroinflammation has a significant pathophysiological role in the development of post-TBI secondary brain damages[5,6].Trauma could cause a direct damage to BBB,resulting in infusion of a large number of inflammatory molecules as well as the transmigration of effector immune cells into CNS,those which once inside the brain,act on CNS innate cells can induce the BBB dysfunction and neuronal damage[6].

3 Immune cells involving in the formation of neuroinflammation.

Microglia monitors changes of the CNS environment and plays a key role in cerebral pathological changes.Many studies have reported a very close spatiotemporal interaction between BBB dysfunction and microglial activation[7].Microglial response to BBB dysfunction is an entire part of the innate immune and inflammatory response.This response of microglial cells has been reported to have a profound paracrine effect on the BBB,contributing to its dysfunction[8].The M1 phenotype is considered inflammatory and is known to produce inflammatory cytokines,chemokines,nitric oxide and reactive oxygen species[9].As the number of M1 cells increases,the phagocytic ability appears to decrease,and there is increased secretion of inflammatory cytokines,chemokines and other neurotoxic mediators,leading to widespread cellular damage[10].

Astrocytes maintain intimate communication with the cerebral vasculature through astrocytic"end-feet,"forming and regulating the BBB.Under pathological insults,astrocytes usually respond by astrocytic hypertrophy and proliferation[11].Meanwhile,reactive astrocytes produce diverse cytokines,chemokines and factors for tissue damage or repair[11],depending on the temporal and spatial progression of astrocytic reaction,as well as the interaction between astrocytes with multiple cell populations[12].

4 Cytokines involving in the formation of neuroinflammation.

TNF is a transmembrane protein and produced primarily by monocytes[13].It can lead to activation of transcription factors by various signal channel,causing the upregulation of oxidative stress inducers and TNF-a[14].In response to injury,TNF-a functions to restore brain homeostasis during acute inflammation,acting as a defensive guard to protect against CNS injury,infection,neurodegen eration and neurotoxicity.

The primary functional properties of IL-1 family members are primarily inflammatory.IL-1 family members play a key role in the inflammation during acute injury[15].The IL-1βpromotes inflammatory diseases,and its receptor IL-1R1 is distributed throughout the brain[16].As reported earlier,IL-1βreleases neurotransmitters that mediate some neurological pathologies influencing the behavior through dopamine and serotonin neurotransmitter production[17].The production of IL-1βis induced in macrophages by bacterial infections and their products can pass through the endothelium of blood vessels and affect cytokines released by cerebral perivascular

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blood vessel macrophages and brain microglia cells[18].We also mentioned IL-33,together with IL-1β,shares the IL-1R3 receptor and deteriorates inflammation[17].IL-33 is expressed by several immune cells, is involved in neurological disorders[17].IL-33 activates immune cells including microglia and astrocytes,important cells in the mediation of neuroinflammatory states[19].

5 Discussion

After TBI,the strong external pressure causes the tissue damage of the brain parenchyma,which also leads to the disruption of BBB.Brain parenchymal cells will produce a variety of damage-associated information,which can activate immune cells in the brain for immune response.Microglia,astrocyte and immune cells are involved in the innate immune regulation and can quickly transfer to the damaged area during acute injury.In response to the special environment under the state of injury,the activated immune cells will undergo phenotypic changes,such as M1 type of microglia cells and A1 type of astroglia cells.In order to enhance the phagocytosis of damaged debris and pathogens,immune cells will produce a variety of inflammatory factors,chemokines,free radicals and proteases,to further expand phagocytosis,which may also damage tissues and cells of CNS without any difference,leading to the gradual formation of neuroinflammation[6].

Within the central nervous system,inflammation is a protective mechanism that restores damaged glial and neuronal cells. However,a long-term or an excessive inflammatory response may inhibit neuronal regeneration and cause cellular injury.There is a mechanism of sharing cytokines among immune cells,which can expand the role cells are playing,enabling them to respond quickly and efficiently under different conditions.

6 Conclusions

All neurodegenerative diseases possess a neuroinflammatory Component.After acute brain injury causes initial shock damage to the brain,it will also lead to more serious secondary damage.The subsequent development of neuroinflammation will results diverse Neurodegenerative disease.

Understanding the mechanism of interaction of cells,inflammatory cytokines and BBB post injury may provide more ideas for treatment.Reasonable suppression of immune response may reduce the harm caused by secondary injury.Specific treatment methods need to be explored and verified through more experiments and clinical trials.

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