

Inflammatory and Immune Responses in Acute Stroke: A Narrative Review Based on the Traditional Chinese Medicine Theory of “Toxin Damaging Brain Collaterals”

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Abstract:

Stroke is a leading cause of death and long-term disability worldwide. In the acute phase, inflammatory and immune responses play a pivotal role in secondary brain injury and functional outcomes. The Traditional Chinese Medicine (TCM) theory of “toxin damaging brain collaterals” proposes that the core pathogenesis in acute stroke is the rapid invasion of pathogenic toxins into brain collaterals, causing sudden, severe, and fluctuating injury. This narrative review integrates modern biomedical findings on inflammatory and immune mechanisms with TCM pathophysiology, systematically summarizing acute stroke manifestations at molecular, cellular, and systemic levels, including microglial activation, elevated pro-inflammatory cytokines, blood-brain barrier disruption, infiltration of peripheral immune cells, microcirculatory impairment, oxidative stress, and excitotoxic neuronal injury. Evidence suggests that the TCM classifications of fire-toxin, stasis-toxin, phlegm-toxin, and wind-toxin correspond to different phases and patterns of acute inflammatory responses, demonstrating a high degree of compatibility between TCM pathogenesis and modern biomedical mechanisms. TCM interventions, through regulation of inflammation, improvement of microcirculation, protection of the blood-brain barrier, and neurofunctional support, exhibit holistic and multi-target regulatory effects. This integrative perspective provides theoretical guidance for acute stroke management and highlights the importance of combined TCM and conventional approaches in health care and nursing.

Keywords:

Stroke, Acute Phase, Toxin Damaging Brain Collaterals, Inflammation, Immune Regulation, Integrative Medicine

1. Introduction

Stroke, characterized by high incidence, disability, and recurrence rates, remains a major public health challenge globally. With the acceleration of population aging and the growing prevalence of vascular risk factors, the incidence of stroke continues to rise. Acute stroke treatment modalities, such as intravenous thrombolysis and mechanical thrombectomy, have improved patient outcomes but remain limited by

incomplete reperfusion, secondary injury, and neurological deterioration. Substantial evidence indicates that inflammatory and immune responses are central to acute brain injury [1]. These responses are rapidly initiated, broadly impactful, and involve systemic immune modulation. Conventional interventions, primarily single-target pharmacological treatments, often demonstrate limited efficacy due to the complex, multi-stage nature of post-stroke inflammation [2]. The TCM theory of “toxin damaging brain collaterals” posits that the acute pathogenesis of stroke is driven by the rapid invasion of pathogenic toxins into brain collaterals, resulting in sudden, severe, and fluctuating injury. This conceptualization aligns closely with the features of acute inflammatory and immune responses observed in modern biomedical research. Consequently, exploring acute stroke inflammation and immunity from an integrative TCM perspective provides valuable theoretical and clinical insights [3].

2. Theoretical Background

2.1. Overview of the “Toxin Damaging Brain Collaterals” Theory

The “toxin damaging brain collaterals” theory is a modern development in TCM stroke research that synthesizes classical concepts with clinical experience. It emphasizes that pathogenic toxins are highly aggressive and capable of rapidly damaging brain collaterals, leading to disturbances in consciousness, limb paralysis, facial asymmetry, and other acute neurological deficits [4]. In the acute stage of stroke, toxins may originate from external heat, internal phlegm-stasis accumulation, or abrupt disruptions in qi and blood flow. According to their characteristics and clinical manifestations, these toxins can be categorized as fire-toxin, stasis-toxin, phlegm-toxin, and wind-toxin. Fire-toxin manifests as acute inflammation, stasis-toxin as impaired circulation, phlegm-toxin as obstruction with fluid accumulation, and wind-toxin as fluctuating neurological function. This theoretical framework provides a holistic understanding of the rapid progression and variability observed in acute stroke [5].

2.2. Modern Inflammatory and Immune Mechanisms

From a biomedical perspective, acute stroke triggers multi-level inflammatory and immune responses. Within minutes of ischemia, resident microglia activate and release large quantities of pro-inflammatory cytokines, including interleukin-1 β , interleukin-6, and tumor necrosis factor-alpha, initiating cascades that increase blood-brain barrier permeability and promote peripheral immune cell infiltration [6]. Neutrophils infiltrate early, releasing proteases and reactive oxygen species that exacerbate local tissue damage, while subsequent monocyte and macrophage recruitment further modulates the inflammatory environment [7]. Cerebral ischemia also impairs microcirculation and induces microthrombosis, contributing to hypoperfusion despite large vessel recanalization. Excessive glutamate accumulation triggers excitotoxicity and intracellular calcium overload, activating destructive enzymes that result in neuronal apoptosis or necrosis. Elevated oxidative stress, coupled with impaired antioxidant defenses, aggravates neuronal injury including lymphocyte depletion and immunosuppression, increases susceptibility to infections. These rapid, severe, and fluctuating pathological features correspond closely to the TCM description of acute toxin-mediated brain injury [8].

3. Correspondence Between Inflammation and TCM Pathogenesis

The classifications of fire-toxin, stasis-toxin, phlegm-toxin, and wind-toxin can be mapped to specific aspects of acute inflammatory responses. Fire-toxin parallels microglial activation and cytokine storms, reflecting acute, intense inflammation. Stasis-toxin corresponds to microcirculatory impairment and microthrombus formation, explaining persistent ischemia and reperfusion challenges. Phlegm-toxin relates to blood-brain barrier disruption and cerebral edema, capturing fluid accumulation and associated neuronal dysfunction [9]. Wind-toxin corresponds to fluctuating neurological function, reflecting dynamic excitotoxic and oxidative injury. This integration provides a coherent framework connecting TCM pathogenesis with cellular and molecular mechanisms, which can inform the design of combined therapeutic strategies [10].

4. TCM Interventions and Health Management Implications

Evidence indicates that TCM interventions exert multi-target, multi-pathway effects on inflammation and immunity. Heat-clearing and detoxifying herbs reduce pro-inflammatory cytokine release, mitigating fire-toxin effects. Blood circulation-promoting and stasis-resolving treatments improve microvascular perfusion, reducing tissue damage caused by stasis-toxin. Phlegm-dissolving and wind-extinguishing interventions stabilize the blood-brain barrier, reduce cerebral edema, and ameliorate neurological fluctuations associated with phlegm- and wind-toxin. In clinical practice, nursing and health management play a crucial role. Structured discharge education on medication adherence, scheduled follow-ups, and lifestyle modifications, combined with family and community support, enhance patient self-management and recovery. Integrating TCM interventions with modern rehabilitation strategies enables multidimensional approaches that optimize functional outcomes in acute stroke [11].

5. Discussion and Future Directions

From an integrative perspective, modern biomedical evidence on acute stroke inflammatory and immune mechanisms aligns closely with the TCM theory of “toxin damaging brain collaterals.” Microglial activation, cytokine storms, blood-brain barrier disruption, microcirculatory obstruction, and excitotoxic neuronal injury correspond to the conceptual categories of fire, stasis, phlegm, and wind toxins, respectively. TCM therapies, with holistic and multi-target regulatory properties, complement single-target biomedical interventions [12]. Future research should aim to quantify TCM pathological classifications using measurable biomarkers and imaging findings, investigate syndrome-specific inflammatory profiles to guide personalized interventions, and apply systems pharmacology to elucidate the network effects of TCM formulations [13]. Large-scale, multicenter clinical trials are necessary to validate the efficacy and safety of integrative interventions. Such approaches may provide actionable strategies for managing acute stroke in a holistic and evidence-informed manner [14].

6. Conclusions

Acute stroke elicits complex, multi-stage inflammatory and immune responses that correspond to TCM pathogenesis as described by the “toxin damaging brain collaterals” theory. TCM interventions regulate inflammation, protect brain tissue, and improve microcirculation, demonstrating holistic and multi-target advantages.

Integrating TCM with modern biomedical insights not only enhances mechanistic understanding but also provides a theoretical foundation for health interventions and nursing strategies, holding important clinical and research value.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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