Basic Science Controversy

Regulatory T Cells in Ischemic Stroke
Helpful or Hazardous?

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Research in the cerebrovascular field has focused recently on stroke-associated inflammatory processes. These studies produced important results and demonstrated, for instance, that stroke-associated infections are a substantial risk factor for a stroke to occur. In addition, the stroke itself was associated with an immunodeficiency-like syndrome. This immunodeficient constellation is currently thought to act as a potential inducer for poststroke infections, such as pneumonia, and to influence the final neurological outcome. Consequently, early clinical trials tested the hypothesis of improving outcome preventing infections by a prophylactic antibiotic treatment. These studies indeed revealed reduced infection rates. Disappointingly, the neurological status was unaltered, indicating that the concept of infection prevention to improve outcomes in ischemic stroke may fall short. Although potential reasons for these negative trial results could be explained in the study design and the patient selection criteria, the idea of an antibacterial treatment itself might be a too simple approach. Intense research is currently ongoing to uncover the complex biology behind poststroke immunodepression and other pathophysiological processes driven by the immune system. Within this approach, the role of T-lymphocytes in neurodegeneration and particularly ischemic stroke is increasingly recognized.

Although the harmful role of T lymphocytes during the early phase of cerebral ischemia is well accepted, much more unclear are the contributions of the different T cell subsets. Recent studies suggest that regulatory T cells (Tregs) exert an ambiguous effect during the course of cerebral ischemia: deleterious effects of Tregs were found by Kleinschnitz et al who implemented a sophisticated genetic mouse model in which Tregs were ablated. These findings are contrasted by the brain protective and outcome improving effects of Tregs described by Li et al using poststroke Treg cell therapy. Although some of the discrepancies between these 2 studies may be explained by different experimental settings and Treg kinetics that are discussed in the controversy below, these conflicting data clearly underline that we are far away from understanding how the immune system poststroke is regulated, during or after an ischemic insult. This is further illustrated by our changing knowledge of well-known old friends, the neutrophils. Thought to act in a deleterious manner attributable to micovascular plugging a decade ago, treatments causing a massive increase in circulating neutrophil counts were shown to be highly neuroprotective, whereas newer findings generally question a major pathophysiological role of neutrophils in stroke at all.

The editors of Stroke as the leading cerebrovascular journal have decided to initiate discussions of this and other highly relevant topics related to experimental cerebrovascular research in our new section Basic Science Controversies.

Disclosures

None.

References


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