Letters to the Editor

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Stroke-Induced Immunodepression Is a Marker of Severe Brain Damage

To the Editor:

In the last years, several groups, including ours, have described the main traits and clinical implications of a stroke-induced immunodepression syndrome.1,2 This syndrome has raised the attention of the scientific community because it opens a field to assay newer diagnostic and therapeutic avenues for stroke. In a recent article in Stroke,3 Hug et al confirm many of the descriptions made in previous works and conclude that the main determinant of the immune changes that follow stroke and of the risk of stroke-associated infection is infarct volume. Indeed, this conclusion is reassuring because we have repeatedly described that stroke-associated infection is a marker of the severity of the disease.4,5 We have shown that some of the immune changes induced by stroke are directly related not only to the clinical severity of the stroke, but also to infarct volume and that stroke severity is the main predictor of the risk of infection.4,5 In agreement with us,4 Hug et al found a good correlation between the clinical severity measured by the National Institutes of Health Stroke Scale and infarct volume. Therefore, it is not surprising that these authors found that infarct volume was the main determinant of the risk of subsequent infection. However, the clinical scale was assessed within 12 hours from stroke onset, whereas the radiological quantification was obtained between 24 and 36 hours after admission. Hence, the National Institutes of Health Stroke Scale was able to predict a great number of infections at least 24 hours before infarct size was known. The sooner predictive value of the National Institutes of Health Stroke Scale score propagates the installment of earlier antibiotic therapy in patients who develop the infections within 24 hours. Expectedly, these patients would develop larger lesions at later brain imaging. The National Institutes of Health Stroke Scale has also other practical advantages such as simplicity and widespread use. For these reasons, we recommend use of the National Institutes of Health Stroke Scale score to predict at the bedside the risk of incident infections.

Hug et al also suggest that although patients with stroke-associated infection have lower HLA-DR expression in monocytes, its predictive value is lost in multivariate models once infarct size is accounted for. This observation was already published in Stroke; after accounting for stroke severity, monocyte HLA-DR measurement was not independently associated with the risk of infections any more. As opposed to HLA-DR, other markers of monocyte activity such as tumor necrosis factor-α production retained their independent predictive value.

Hug et al propose that infarct volume may be associated with monocyte deactivation rather than monocyte counts. Although they may be correct, this statement does not acknowledge the complexity of human monocytes. Monocytes are a heterogeneous population of cells and infarct volume is directly related to changes of specific monocyte subtypes such as CD14<sup>high</sup>/CD16<sup>+</sup> and CD14<sup>dim</sup>/CD16<sup>+</sup> monocytes.7 Moreover, monocyte subsets differ in their phenotype, function, and clinical meaning. Accordingly, the study of total monocyte numbers is not sensitive to draw conclusions about the role of monocytes in patients with stroke.

Overall, we feel that Hug et al confirm to a great extent previous observations by various groups. This and previous studies highlight the existence of a stroke-induced immunodepression syndrome that is associated with infectious complications and is mainly dependent on the severity of the brain injury. Future studies will be required to refine the details of the immune changes that follow acute stroke, their practical value at the bedside to predict complications, and the potential therapeutic benefits of modulating immunity in stroke.

Disclosures

None.

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