Leukocyte Response in Patients Suffering From Acute Stroke

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The oxidation of adrenaline to adrenochrome has been shown to reflect the activation of leukocytes in vivo. We tested the in vivo activation of leukocytes by measuring plasma oxidation of adrenaline to adrenochrome in patients suffering from cerebral ischemia, cerebral hemorrhage, and transient ischemic attacks and in healthy subjects. Patients with cerebral ischemia and cerebral hemorrhage had significantly higher values than healthy subjects, while patients with transient ischemic attacks had values similar to those of healthy subjects. In some patients with cerebral ischemia, the test was repeated 4 and 15 days after the acute event, but the follow-up data did not differ from baseline values. Our study shows that leukocyte activation occurs in cerebral ischemia and cerebral hemorrhage. (Stroke 1988;19:1283-1284)

Infiltration by leukocytes is a constant morphologic feature of myocardial and cerebral ischemic tissues.1-3 Such leukocytic infiltration could induce unwanted effects, such as release of oxygen free radicals by activated leukocytes. Indeed, activated leukocytes are known to produce highly reactive oxygen radicals including superoxide anion and hydroxyl anion, both of which may further damage ischemic tissue by inactivating cellular membranes and enzymes and by inducing lipid peroxidation.4 Matthews and Campbell3 devised a simple method for evaluating activation of leukocytes in vivo, measuring plasma oxidation of adrenaline to adrenochrome, probably due to myeloperoxidases released by leukocytes. We report measurements of leukocyte activation among patients suffering from acute ischemic and hemorrhagic stroke.

Subjects and Methods

We studied 52 patients (37 men, 15 women; mean age 66 years) suffering from acute cerebral hemispheric ischemia (BI: 27 men, 13 women) or cerebral hemorrhage (BH: 10 men, two women). The lesion was right-sided in 23 and left-sided in 29 patients and was confirmed by computed tomography.

All patients were observed in the Intensive Care Stroke Unit between November 1985 and December 1986, and those with any proven acute or chronic inflammatory process were excluded. All instrumental and laboratory analyses were performed immediately after hospitalization and within a mean of 31 (range 20-48) hours after the acute episode. No patient was treated with antioxidant agents or drugs such as steroids that could potentially interfere with leukocyte function. Routine investigations included estimations of blood glucose, urea, and creatinine concentrations and erythrocyte and leukocyte counts.

The in vivo activation of leukocytes was evaluated by the oxidant activity of plasma following methods described by Matthews and Campbell.3 Heparinized blood was withdrawn from each patient after he or she had fasted for 12 hours. The blood was centrifuged at 2,000g for 10 minutes; the plasma was mixed with distilled water (1:1), and samples were incubated at 37°C for 2 hours with and without 1 mmol/ml adrenaline. Samples were then centrifuged for 2 minutes at 10,000g and read at 480 nm. The oxidant activity of plasma was quantified by measuring the oxidation of adrenaline to adrenochrome (Σadm = 4,020 mol⁻¹ cm⁻¹) in units per liter where 1 unit is 1 μmol of adrenaline converted to adrenochrome.

In vivo activation of leukocytes was also evaluated in two control groups, 22 healthy subjects (HS: 12 men, 10 women; mean age 59 years) and 12 patients suffering from transient ischemic attacks (TIAs) of presumed carotid origin (eight men, four women; mean age 60 years). In the TIA controls the...
plasma oxidant activity was studied ≤30 days after the acute transient episode.

Statistical analyses included evaluations of the mean, standard deviation (SD), and standard error of the mean (SEM). Groups were compared using Student’s t test and regression analyses.

Results

Plasma oxidant activities of BI and BH patients were significantly higher than those of age-matched HS (Figure 1). Activities of >62 units/L (mean ± 2SD of HS) were observed in 65% of BI patients compared with 50% of BH patients. Mean ± SD leukocyte counts in BI patients were significantly higher than in HS (10,400 ± 3,100 and 6,000 ± 1,200, respectively; p<0.001). No significant correlations between plasma oxidant activity and leukocyte count were observed. Leukocyte count was normal in all but two BH patients.

TIA controls had plasma oxidant activities similar to those of HS; however, leukocyte activation might have occurred during the acute phase of TIA and could have stimulated lipid peroxidation (which occurs after cerebral ischemia) and further contributed to damaging the surrounding tissue. Because this phenomenon is not likely to be counteracted by antioxidant enzymes, such as superoxide dismutase, present in cerebral tissue, there could be a reason to try the use of other antioxidant agents.

We conclude that leukocyte activation occurs among patients with ischemic and hemorrhagic stroke but that the relation between leukocyte activation and the clinical course has yet to be established.

Discussion

Infiltration of leukocytes into ischemic cerebral tissue has been demonstrated in experimental models and, more recently, in patients suffering from ischemic stroke. Relations between leukocyte activation, the release of oxygen free radicals, and further tissue damage has also been demonstrated in experimental models of myocardial ischemia.

We show that leukocyte activation occurs in acute cerebral ischemia and cerebral hemorrhage and that it persists for at least 2 weeks. Due to the short follow-up of plasma oxidant activity and the few patients, we could not establish any correlation of leukocyte activation with the clinical course.

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References


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