Granulocytes, Platelet Activating Factor, and Stroke

To the Editor:
Saito et al1 reported increased leukotriene-like immunoreactivity (C4 and D4) in gerbil brain following bilateral common carotid occlusion and reduced leukotriene levels as a result of busulfan-induced granulocytopenia. Their results support the view that granulocytes may be involved in the pathogenesis of cerebral infarction.

In addition to being the source of leukotrienes, granulocytes, particularly basophils, produce platelet-activating factor (PAF, 1-0-alkyl-2-0-acetyl-sn-glyceryl-3-phosphorylcholine), which is a potent inducer of platelet activation, thrombosis, and ischemia. Apart from the platelet-mediated effects, PAF has been shown to cause direct neuronal damage, cerebral vasoconstriction, and cerebral hypoperfusion, vasoconstriction, and cerebral hypoperfusion, arterioles (vessel wall).

References

Pulsed Doppler Assessment of Arterial Obstructive Disease

To the Editor:
The article by Drs. Rautenberg and Hennerici in Stroke1 raised these questions for the authors in my mind:
1. How were the asymptomatic patients selected?
2. What were the features of the symptomatic transient ischemic attacks (TIAs)?
3. Were blood pressures obtained in both arms, and were there significant inequalities?
4. In those patients who received surgery to bypass the innominate obstruction, did the TIAs stop?
5. Finally, is it correct that some of the asymptomatic patients underwent surgery?

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Reference

The following is in reply:

To the Editor:
We appreciate the letter by Dr. Perron. His five questions are answered as follows:
1. The asymptomatic patients were investigated because of carotid bruits, risk factors for atherosclerosis, or coexisting peripheral arterial disease or coronary artery disease (cf. reference 1).

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Left atrial thrombi are often many weeks old, firm, and well-formed intracarotid thrombi. These recent reports suggest that the rate of cardioembolic (29%) versus noncardioembolic (75%) observed recanalization. While Mori et al. hypothesized that the hemorrhagic transformation was linked to presumed cardioembolic sources and the severity of initial deficit rather than to thromboembolic occlusion, intracarotid (n=\( \frac{56}{125} \)) infusion of fibrinolytic agents (<6 hours) showed hemorrhagic transformation in 45%.5

Hemorrhagic Transformation of Cardioembolic Stroke

To the Editor:

Two recent reports in Stroke provide interesting information and prompt further speculation about hemorrhagic transformation of cardioembolic stroke.1,2 Secondary hemorrhagic transformation of presumed cardioembolic stroke is usually not associated with recognized clinical worsening.3,4 Definition of the temporal window of hemorrhagic transformation has been based on retrospective case series in which computed tomography (CT) data were collected at nonstandard time intervals, perhaps in patients with late hemorrhagic transformation that was undetected and therefore not included.1,5 The single prospective study using serial CTs up to 3 weeks after stroke reported an extraordinarily high prevalence of hemorrhagic infarction (43% of all supratentorial infarcts, 61% of presumed cardioembolic infarcts).6

While initial case collections suggested that the great majority of spontaneous hemorrhagic transformation occurred within 2-4 days of cardioembolic stroke (Figure I),1,2,5 multiple case reports have since documented later occurrence.6-9 In short, the exact limits of the window of spontaneous secondary hemorrhagic transformation remain ill-defined. There is clearly a delay between stroke onset and the development of hemorrhagic transformation detected by CT. In the CT/autopsy series of Lodder et al., only 10% (2/21) of the infarcts had definitely transformed before 24 hours, and 43-90% transformed after 24 hours. Among 28 cases of autopsy-confirmed hemorrhagic infarction with reference to clinical spectrum of hemorrhagic infarction: A prospective study.10

The potential safety of acute fibrinolytic therapy in cardioembolic stroke may be influenced by this initial delay in hemorrhagic transformation. When Mori et al. infused intracarotid urokinase into patients with acute middle cerebral artery occlusion, hemorrhagic transformation was linked to presumed cardioembolic sources and the severity of initial deficit rather than to observed recanalization. While Mori et al. hypothesized that the volume of the embolus explained the differential recanalization rate of cardioembolic (29%) versus noncardioembolic (75%) middle cerebral artery occlusions (\( p < 0.048, \) Fisher’s exact test), the age of the embolic fragment may also affect recanalization.2,10 Left atrial thrombi are often many weeks old, firm, and well-organized and may be less susceptible to lysis than recently formed intracarotid thrombi. These recent reports suggest that while very early infusion of fibrinolytic agents (<6 hours) in cardioembolic stroke may safely precede the period of hemorrhagic transformation, recanalization may be less frequently achieved in thrombi of left atrial origin.

References

3. Cerebral Embolism Study Group: Immediate anticoagulation and prompt further speculation about hemorrhagic transformation, recanalization may be less frequently achieved in thrombi of left atrial origin.

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FIGURE 1. Timing of hemorrhagic transformation (HT) defined by computed tomography (n=34) or autopsy (n=14) from two combined case series.1,5 The area indicated as [?)HT reflects the interval between nonhemorrhagic CT [(+)HT] and diagnosis of hemorrhagic infarct [(+)HT] within which the exact time of HT is uncertain. For example, at 24 hours after stroke onset, at least 25% and possibly as many as 77% of patients had undergone HT.
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