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.5-7 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).8 While initial case collections suggested that the great majority of spontaneous hemorrhagic transformation occurred within 2-4 days of cardioembolic stroke (Figure 1),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.,1 only 10% (221) of the infarcts had definitely transformed before 24 hours, and 43-90% transformed after 24 hours. Among 38 cases of hemorrhagic transformation collected by the Cerebral Embolism Study Group, CTs done before 6 hours (n=7) showed no cases of hemorrhagic transformation while those done between 6 and 18 hours (n=11) showed hemorrhagic transformation in 45%.5

The potential safety of acute fibrinolytic therapy in cardioembolic stroke may be influenced by this initial delay in hemorrhagic transformation. When Mori et al.2 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 lysin 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 thromb of left atrial origin.

Robert G. Hart, MD
Carla Putnam, PharmD
The University of Texas Health Science Center at San Antonio
San Antonio, Texas

References

FIGURE 1. Timing of hemorrhagic transformation (HT) defined by computed tomography (n=34) or autopsy (n=14) from two combined case series.1,3 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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R G Hart and C Putnam

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