Cerebral artery thrombi show similar structural composition regardless of etiology

Researchers from the David Geffen School of Medicine at the University of California, Los Angeles, have carried out a histopathological study of thromboemboli retrieved from the cerebral artery networks of patients with acute ischemic stroke. A mechanical retrieval device allowed the researchers to study emboli that would previously have been inaccessible.

Marder *et al.* removed thrombi from 25 patients shortly after the defined onset of stroke symptoms (mean delay between symptom onset and retrieval 6.2 ± 3.1 h). Most thromboemboli were retrieved in fragments, although removal as a single mass was achieved in 36% of cases. Only thromboemboli <3 mm wide reached the middle cerebral artery, whereas emboli extracted from the internal carotid artery reached a maximum width of 5 mm. Each thrombus sample had a unique histological appearance, despite the majority being composed of a complicated pattern of platelet and fibrin areas combined with deposits of nucleated cells and erythrocytes. This structural composition is consistent with clinical trial data indicating that both antiplatelet and anticoagulant agents are beneficial in stroke prevention. No relationship was found between thrombus histology and presumed cardiopathic or arteriopathic etiology or occlusion location, and no calcific deposits or cholesterol crystals were observed in any of the samples.

In addition to the 25 patients in whom thrombus extraction was successful, 29 patients underwent unsuccessful thrombus retrieval. The success of thrombus extraction was negatively correlated with patient age, but no relationship was found with sex, the timing of the retrieval procedure, stroke subtype or site of the thromboembolism.

Original article Marder VJ *et al.* (2006) Analysis of thrombi retrieved from cerebral arteries of patients with acute ischemic stroke. *Stroke* **37:** 2086–2093

Argatroban could improve recanalization in stroke patients

Argatroban is a thrombin inhibitor that, in combination with recombinant tissue plasminogen activator (rtPA), improves the speed and completeness of recanalization in animal stroke models. Sugg *et al.* conducted a phase I study of argatroban and rtPA in 15 patients (mean age 61 years) with occlusion of the middle cerebral artery. The primary outcome of the trial was incidence of intracerebral hemorrhage; the secondary outcome was complete recanalization at 2 h.

Symptomatic hemorrhage occurred in two patients, and one patient had an asymptomatic hemorrhage. Six patients had complete recanalization at 2 h; partial recanalization was achieved in a further four patients. Reocclusion occurred in three patients, one of whom had subsequent recanalization. One patient died, as a result of malignant cerebral edema. At 7 days, the median NIH stroke score had improved to 3.5, from 14 at baseline. The recanalization rate of 71% compared favorably with the 38% achieved with the control patients of the CLOTBUST study, who were treated with rtPA alone. Patient numbers, however, were insufficient to reach statistical significance for the comparison.

The authors conclude that argatroban combined with rtPA has the potential to bring about faster and more complete recanalization in stroke patients than does rtPA alone. Phase II of the study is ongoing.

Original article Sugg RM *et al.* (2006) Argatroban tPA Stroke Study: study design and results in the first treated cohort. *Arch Neurol* **63:** 1057–1062

High-dose cyclophosphamide can effectively treat severe refractory multiple sclerosis

High-dose cyclophosphamide chemotherapy is an effective treatment for a number of severe refractory immune-mediated conditions, but its efficacy for the treatment of severe refractory multiple sclerosis (MS) has been untested. Results of a recent study, however, indicate that the drug is well-tolerated in patients with MS, and can halt their disease progression.

Gladstone and colleagues recruited 13 patients (median age 41 years) with severe refractory MS, of whom 7 had secondary progressive disease. All patients had an Expanded Disability Status Scale (EDSS) score of ≥3.5 at baseline and had already received at least two FDA-approved treatments for MS. Baseline evaluation also included brain MRI scans and measurement of quality of life and fatigue levels. Patients were given 200 mg/kg

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