Leukoaraiosis on CT and warfarin-related hemorrhage

The Smith et al. case-control study compared patients with warfarin-related intracerebral hemorrhage (ICH) and previous stroke vs age-matched poststroke patients on warfarin without ICH. The presence and severity of leukoaraiosis correlated strongly with ICH and was seen in 92% of ICH vs 48% of controls: odds ratio, 12.9.

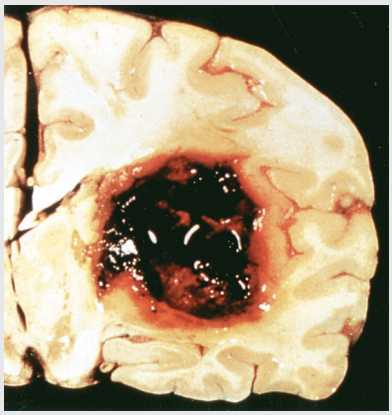
see following

Making anticoagulation safer

Commentary by Robert G. Hart, MD

Oral anticoagulation with vitamin K antagonists has been prescribed for stroke prevention for over 50 years, but only during the past decade have the benefits and risks been defined by adequate randomized clinical trials. Bleeding is the major toxicity, and most fatal bleeds are ICH. Some 5,000 to 10,000 warfarin-associated ICHs occur yearly in the United States.

Advanced patient age, anticoagulation intensity, and "cerebrovascular disease" are accepted risk factors for warfarin-associated ICH. Intensity of anticoagulation is the strongest, most consistent predictor, and targeting the lowest efficacious international normalized ratio is important. Recently, two novel predictors have been proposed in *Neurology*: *APOE* genotype (as a marker of cerebral amyloid angiopathy)[1] and "leukoaraiosis" evident on cranial CT scanning in noncardioembolic brain ischemia. (Smith et al. in this issue and Gorter[2]). Although these novel predictors offer pathogenetic clues, neither has been sufficiently validated for clinical use. Grading of leukoaraiosis suffers from substantial variability related to acquisition



techniques and interrater variability, and the positive and negative predictive values have not been defined. Further, the pathology underlying leukoaraiosis varies, and whether leukoaraiosis is predictive of ICH in anticoagulated patients with atrial fibrillation is unclear.

The surest way of avoiding anticoagulation-related ICH is not to use warfarin in patients for whom antiplatelet agents offer similar benefits for stroke prevention. Two recent randomized trials failed to show advantages of warfarin over aspirin for secondary prevention of noncardioembolic brain ischemia, testing the extremes of the therapeutic range of anticoagulation intensity.[3,4] Warfarin should be used sparingly (if at all) for patients with common causes of noncardioembolic brain ischemia, pending support from ongoing randomized trials.

References

1. Rosand J, Hylek EM, O'Donnel KC, Greenberg SM. Warfarin-associated hemorrhage and cerebral amyloid angiopathy: a genetic and pathological study. Neurology 2000:55:947–951.
2. Gorter JW. Major bleeding during anticoagulation after cerebral ischemia: patterns and risk factors. Neurology 1999;53:1319–1327.
3. Mohr JP, Thompson JLP, Lazar RM, et al, for the Warfarin-Aspirin Recurrent Stroke Study Group. A comparison of warfarin and aspirin for the prevention of recurrent ischemic stroke. N Engl J Med 2001;345;1444–1451.
4. Stroke Prevention in Reversible Ischemia (SPIRIT) Study Group. A randomized trial of anticoagulants versus aspirin after cerebral ischemia of presumed arterial origin. Ann Neurol 1997;42:857–865.

See the accompanying article by Smith et al., "Leukoaraiosis is associated with warfarin-related hemorrhage following ischemic stroke," page 193

continued on page 154

Hat, head, and brain size and cognition

Two papers and an editorial consider the relationship between brain volume and cognitive function. MacLullich et al. studied cognitive function, regional brain volumes, and intracranial capacity in healthy older men. Structural equation modeling suggested that positive correlations between regional brain volumes and cognitive function were best explained by a relationship between general cognitive ability and overall brain size.

see page 169

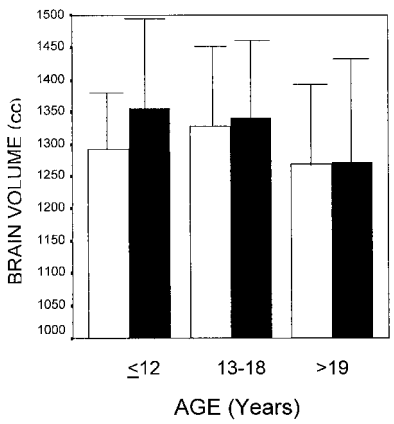
Edland et al. found that total intracranial volume was similar in AD patients and normal controls. This suggests there is no clinical value in determining head size when evaluating patients for Alzheimer's disease.

see page 272

The accompanying editorial by David Drachman introduces a consideration of these papers by noting the relationship between hat size and head circumference, and the generally poor correlation of head size or shape with intellect in many circumstances, including the failed science of phrenology. He points out that while larger head size and brain volume appear to have an association with intelligence, Edland et al. did not see a difference in volume in men or women who developed AD.

see page 156

Increased brain volume in autism



Autism (black bars) vs controls

Aylward et al. found increased brain volume in 8- to 12-year-old autistic children but no difference from controls in adolescents and adults. Brain development in autism follows an abnormal pattern, with accelerated growth early in life followed by a slight reduction in volume.

see page 175

Sparks et al. compared 3- to 4-year-olds with autism to 26 age-matched, typical-developing and 14 developmentally delayed children. The autistic sample had overall cerebral enlargement and proportional cerebellar, amygdalar, and hippocampal enlargement. A subgroup having strictly defined autism demonstrated disproportionate enlargement of the amygdalae.

see page 184

The accompanying editorial by Mink and McKinstry notes that while there is now consistent evidence for a slightly larger brain size in children with autism vs controls, brain size is still normal. They note that these observations have not yet given neurobiological insights into the disorder.

see page 158

Identifying language dominance with fMRI in partial epilepsy

Gaillard et al. used a reading and naming task to reliably identify language-processing areas in dominant frontal and temporal regions in 30 patients with partial epilepsy. They found excellent agreement between clinical visual interpretation, a quantitative region of interest approach, and the intracarotid amobarbital test.

see page 256

The accompanying editorial by Abou-Khalil and Schlaggar notes that fMRI is successful in establishing cerebral dominance for language. However, more work is needed to define its ability to localize memory in the temporal lobe sufficiently for fMRI to replace the Wada test.

see page 160

continued on page 155

Genetic association between MAOA and restless legs syndrome (RLS)

Desautels et al. investigated *MAOA* and *MAOB* genes in RLS, comparing 97 affected patients with 200 controls. They found that an excess of high-activity alleles of the *MAOA* gene may contribute to the genetic etiology of RLS in females. Moreover, this polymorphism seemed to influence the phenotypic expression of RLS symptoms.

see page 215

Longitundinal study of MCI

Studying Catholic clergy who had annual evaluation of cognition, Bennett et al. found that those with mild cognitive impairment (MCI) had a 70% increased risk of death and a threefold increased risk of AD compared to persons without cognitive impairment over 4.5 years of follow-up.

see page 198

Lamotrigine clearance during pregnancy

Tran et al. found a >65% increase in lamotrigine (LTG) clearance during pregnancy, necessitating dosage adjustment in 11/12 women to maintain therapeutic levels. Clearance returned to prepregnancy levels within 1 to 2 weeks postpartum, causing drug toxicity.

see page 251

Carbamazepine-induced hypertension

Jette et al. describe a patient with de novo hypertension following the initiation of carbamazepine, which resolved upon its discontinuation.

see page 275

Risk of mesothelioma in NF-2

Baser et al. reported an asbestos-exposed patient with NF-2 who developed malignant mesothelioma. They consider evidence that while NF-2 is not ordinarily associated with mesothelioma, it may increase the risk in such patients.

see page 290

Propofol sedation: MRI resembling SA hemorrhage

Stoner et al. report a 47-year old man in whom propofol sedation creating high T2 FLAIR signal simulating pathology such as subarachnoid blood. Similar MRI findings occur in propofol-treated children.

see page 292

July 23 Highlights

Neurology 2002;59;153-155
DOI 10.1212/WNL.59.2.153

This information is current as of July 23, 2002