

Stroke

American Stroke
AssociationSM

A Division of American
Heart Association



JOURNAL OF THE AMERICAN HEART ASSOCIATION

Congenital antithrombin III abnormality and cerebral arterial thrombosis

T Imamura, T Yoshida, A Yamadori and T Matsuo

Stroke 1991;22;1090

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214
Copyright © 1991 American Heart Association. All rights reserved. Print ISSN: 0039-2499. Online ISSN:
1524-4628

The online version of this article, along with updated information and services, is
located on the World Wide Web at:

<http://stroke.ahajournals.org>

Subscriptions: Information about subscribing to Stroke is online at
<http://stroke.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters
Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2436. Phone: 410-528-4050. Fax:
410-528-8550. E-mail:
journalpermissions@lww.com

Reprints: Information about reprints can be found online at
<http://www.lww.com/reprints>

- Harrison MJG, Weisblatt E: A sex difference in the effect of aspirin on "spontaneous" platelet aggregation in whole blood. *Thromb Haemost* 1983;50:773-774
- ISIS-2 Collaborative Group: Randomised trial of intravenous streptokinase, oral aspirin, both or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988; 2:349-360
- The Canadian Cooperative Study Group: A randomised trial of aspirin and sulfinpyrazone in threatened stroke. *N Engl J Med* 1978;299:53-59
- Dyken ML: Antiplatelet aggregating agents in transient ischaemic attacks and the relationship of risk factors, in Bredin K, Loew D, Uberla K, et al (eds): *Prophylaxis of Venous, Peripheral, Cardiac, and Cerebral Vascular Diseases With Acetylsalicylic Acid*. Stuttgart, F Schattauer, 1980, pp 141-148
- Spranger M, Aspey BS, Harrison MJG: Sex difference in antithrombotic effect of aspirin. *Stroke* 1989;20:34-37
- Harrison MJG, Pollock SS, Steiner M, Weisblatt E: Inhibitors of "spontaneous" platelet aggregation in whole blood. *Atherosclerosis* 1985;58:199-203
- Carter AJ, Heptinstall S: Platelet aggregation in whole blood: The role of thromboxane A2 and adenosine diphosphate. *Thromb Haemost* 1985;54:612-616

Congenital Antithrombin III Abnormality and Cerebral Arterial Thrombosis

To the Editor:

A recent review by Hart and Kanter¹ pointed out that a congenital abnormality of antithrombin III can be associated with both venous and arterial intracranial thrombosis. They indicated that antithrombin III abnormalities with cerebral arterial thrombosis preceded systemic venous thrombosis, with only one reported exception.² We report here another such exception.

A 23-year-old woman who had no previous heart disease, venous or arterial thrombosis, migraine, or contraceptive use developed sudden severe headache preceded by symptoms of an upper respiratory infection. It subsided in some minutes, followed by blurring of her left visual field. When examined 6 hours after onset, she had no heart murmur, irregular pulse, or signs of systemic venous thrombosis. Neurological and neuropsychological examinations revealed left homonymous hemianopsia, left unilateral spatial neglect, defective route finding, and prosopagnosia. No other motor, sensory, or cranial nerve signs were present. Routine laboratory findings were normal.

On the second hospital day, computed tomography of the head showed posterior medial temporal and medial occipital infarctions of the right hemisphere. Subsequently, angiogram revealed an occluded branch of the right posterior cerebral artery, but there were no angiographic signs of atherosclerotic change or intracranial venous thrombosis. Neurological signs rapidly improved and, 2 weeks after onset, only the visual defect at the periphery of the left homonymous field could be detected. Survey of her heart, including electrocardiogram, Holter monitoring, and echocardiogram, was normal. Blood cell count, liver and renal functions, prothrombin and activated partial prothrombin times, plasminogen and protein C activities, and fibrin degradation products were all within normal ranges. The antigen concentration of antithrombin III measured by single radial immunodiffusion method was 30.7 mg/dl (normals 21.0-34.0 mg/dl). However, antithrombin III activity, estimated as heparin cofactor antithrombin activity of her plasma measured with Coatest Antithrombin (Kabi, Stockholm,

Sweden), was 55% (normals 75-126%), with increased fibrinopeptide A to 22.1 ng/ml (normals 0.5-2.0 ng/ml).

These findings suggested excessive production of active thrombin due to low antithrombin III activity and prompted us to begin oral coumarin therapy. Two months after onset, the fibrinopeptide A was reduced to 7.7 ng/ml, but repeated analysis of antithrombin III showed constantly reduced heparin cofactor activity (49%), with normal antithrombin III antigen concentration (30.3 mg/dl). Progressive antithrombin activity of her plasma in the absence of heparin measured by the reported method³ was 115% (normals 80-120%). She continued oral coumarin and had no recurrence of arterial or venous thrombosis for 3 years, but heparin cofactor activity did not normalize (65% at 3 years after onset). We could not evaluate other members of her family because she was an orphan and had no children.

The reduced heparin cofactor activity of her plasma is attributed to abnormal antithrombin III. Dysfunction of heparin cofactor II, the second major thrombin inhibitor of human plasma, cannot explain the degree of reduction found in this patient because of its relative activity⁴ and antigen concentration.⁵ This sustained hypocoactivity without reduction of progressive antithrombin activity and antigen concentration, together with the normal liver and renal functions, suggests the heterozygous type III form of congenital antithrombin III abnormality,^{1,6} although her family history is uncertain. The homozygous form of this type is predominant in patients complicated by cerebral arterial thrombosis.¹ The cerebral arterial thrombosis was the only manifestation of her antithrombin III abnormality, which we emphasize as the rare but probable etiology of intracranial arterial occlusive disease in young adults, even if they have no past history of venous thrombosis.

Toru Imamura, MD

Takashi Yoshida, MD

Atsushi Yamadori, MD

Neurology Service

Hyogo Brain and Heart Center at Himeji

Takefumi Matsuo, MD

Department of Medicine

Awaji Prefectural Hospital

Hyogo, Japan

References

- Hart RG, Kanter MC: Hematologic disorders and ischemic stroke: A selective review. *Stroke* 1990;21:1111-1121
- Fischer AM, Cornu P, Sternberg C, Mériane F, Dautzenberg MD, Chafa O, Beguin S, Desnos M: Antithrombin III Alger: A new homozygous AT III variant. *Thromb Haemost* 1986;55: 218-221
- Matsuo T, Ohoki Y, Matsuo O: Discrepancy of biological antithrombins measured as progressive activity and heparin cofactor in a family with antithrombin deficiency. *Jpn J Clin Pathol* 1982;30:1033-1036
- Tollefsen DM, Pestka CA, Monafó WJ: Activation of heparin cofactor II by dermatan sulfate. *J Biol Chem* 1983;258: 6713-6716
- Sie P, Dupouy D, Pichon J, Boneu B: Constitutional heparin cofactor II deficiency associated with recurrent thrombosis. *Lancet* 1985;2:414-416
- Hultin MB, McKay J, Abildgaard U: Antithrombin Oslo: Type Ib classification of the first reported antithrombin-deficient family, with a review of hereditary antithrombin variants. *Thromb Haemost* 1988;59:468-473