

Bilateral Internal Carotid Artery Occlusions in a Young Patient with Nephrotic Syndrome

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Received December 8 1994; accepted March 15 1995

Summary. Hypercoagulable states resulting from nephrotic syndrome are focused on as factors of arterial thrombosis. We report on a 29-year-old woman with nephrotic syndrome presenting two episodes of cerebral infarction due to recurrent internal carotid artery occlusions. As she had no clinical evidence of other underlying conditions such as cardioembolism, arteriosclerosis or arteritis, the presence of nephrotic syndrome was speculated to be a significant factor in the onset of arterial occlusions. Nephrotic syndrome, which often complicates a hypercoagulable state, should be noted as a factor of cerebral infarction, especially in young patients.

Key words—cerebral infarction, nephrotic syndrome, carotid arteries, arterial occlusive diseases.

INTRODUCTION

Hypercoagulable states, which are recognized as predisposable factors to arterial thrombosis, result from many conditions.¹⁾ The nephrotic syndrome is one of the underlying conditions associated with secondary hypercoagulable states.²⁾ We here describe two episodes of internal carotid artery occlusions in a young female patient with nephrotic syndrome.

CASE REPORT

A 29-year-old woman was admitted to Toho University Hospital with a left-sided weakness and an inability to talk. She had suffered proteinuria until she

was nine years old, and was diagnosed at fourteen as having nephrotic syndrome due to a membranoproliferative glomerulonephritis. She was given prednisolone from the age of fourteen to twenty-five. She had a history of mild hypertension and hypercholesterolemia following the diagnosis of nephrotic syndrome. She did not have a history of diabetes mellitus, cardiac disease, cigarette smoking, use of contraceptives, or a family history of stroke. She was naturally left-handed. She experienced a transient weakness of the right arm lasting for a few days and had been diagnosed in another hospital as having cerebral infarction seven months previously. After the former episode, she had no remaining neurological deficit and was not given any anti-coagulant therapy.

On admission she had a motor dominant aphasia, left hemiparesis, and decreased sensory perception on the left. She did not have any consciousness disturbance or evidence of systemic embolism. Cardiac examination results were normal. The ocular fundus did not show any hypertensive or sclerotic change.

Brain computed tomography and magnetic resonance imaging demonstrated recent infarctions in the right basal ganglia, temporal cortex and watershed zone in the territory of the right middle and anterior cerebral arteries, and an old, small infarction in the left frontal paraventricule white matter (Fig. 1). Single photon emission computed tomography of the brain using ^{99m}Tc-PAO showed decreased radio-isotope uptake in the right hemisphere and the left frontal cortex. A chest roentgenogram, electrocardiogram, ambulatory monitoring, and transthoracic and transesophageal echocardiograms results were all normal. B-mode carotid ultrasonography did not show any sclerotic change of the intima of the proximal carotid arteries. Cerebral angiography revealed complete occlusions

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Fig. 1. T2-weighted magnetic resonance imaging axial views (TR, 2000 ms; TE, 90 ms) showing hyperintense area in the right basal ganglia, temporal cortex, and left frontal paraventricular white matter (left half), and in the watershed zone in the territories of the right middle and anterior cerebral arteries (right half).

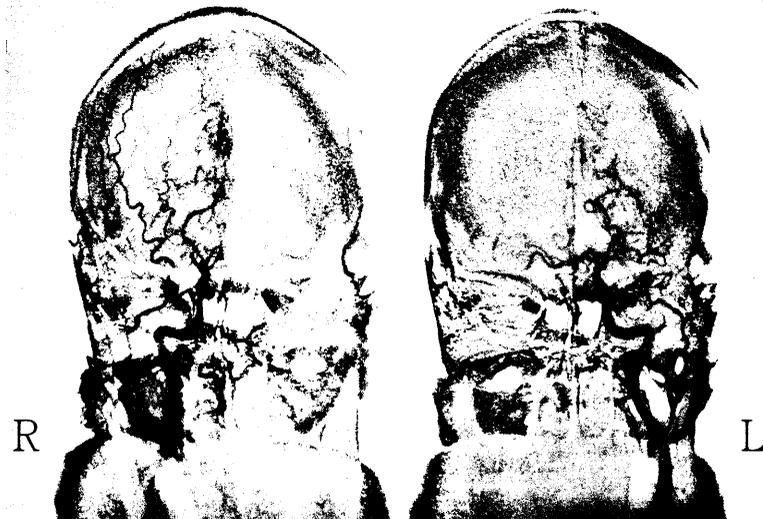


Fig. 2. Anteroposterior views of bilateral cerebral angiogram revealing complete occlusion at the cavernous segment of the right (left half) and the left (right half) internal carotid arteries, all without any arteriosclerotic change.

in the cavernous segment of the bilateral internal carotid arteries and retrograde filling of the branches of the bilateral middle and anterior cerebral arteries from posterior cerebral arteries via leptomeningeal anastomoses. There were no sclerotic changes in the arterial wall or narrowing of the lumen in any arteries including the proximal carotid arteries (Fig. 2).

Laboratory studies included a normal, complete blood count, normal concentrations of electrolytes and blood sugar, and normal serum chemistries for renal and hepatic functions. The total serum protein concentration was 5.8 g/dl, and the serum albumin concentration was 3.2 g/dl. The serum concentrations of total cholesterol, triglyceride, and HDL-cholesterol

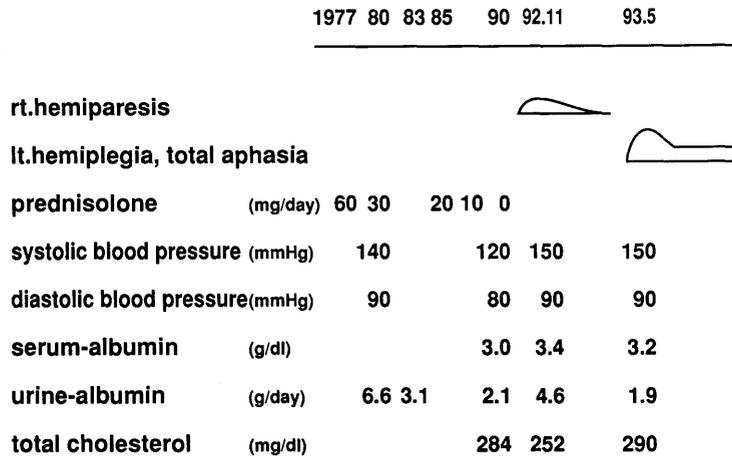


Fig. 3. Clinical course of the patient.

were 290, 222, and 27 mg/dl, respectively. Urinalysis showed 3+ protein and negative sugar, and urine protein content was elevated at 2.2 g/day. Prothrombin time and activated partial thromboplastin time were normal. Fibrinogen concentration was increased to 617 (normal range: 200-400) mg/dl. She had normal antithrombin-III, alpha-2 plasmin inhibitor complex, protein-S, and protein-C concentrations. Plasma levels of factors II, V, VII and XI were normal, but levels of factors VIII and X were increased to 282% and 162% (normal range: 50-150% and 56-138%), respectively. Thrombin-antithrombin-III complex concentration was 4.1 (normal value: <3.0) microgram/ml.

These findings suggestive of a hypercoagulable state had also been observed after the first ischemic attack in the former hospital seven months previously. Other studies included negative assays for anti-nuclear antibodies, anti-DNA antibodies, and anticardiolipin antibodies.

She was treated with warfarin. Although she has residual left hemiparesis and motor dominant aphasia, her clinical condition is gradually improving with rehabilitation.

DISCUSSION

Our patient suffering from nephrotic syndrome had two episodes of neurological deficit. These were diagnosed as cerebral infarctions resulting from recurrent internal carotid artery occlusions in the course of nephrosis (Fig. 3).

Her plasma levels of fibrinogen, thrombin-anti-thrombin-III complex, factors VIII and X were increased in the blood assay after the onset of the

second infarction. Normal cardiac examinations negated cardioembolism as a cause for arterial occlusions. Although she had mild hypertension and hyperlipidemia as complications of nephrotic syndrome, an examination of the ocular fundus, carotid ultrasonography, and cerebral angiogram did not show any arteriosclerotic change. In addition, there was no evidence of arteritis, Moya-Moya syndrome, or fibromuscular dysplasia on angiographic findings. Administration of prednisolone was stopped several years ago, and her anti-cardiolipin antibody assay was negative. These reasons strongly suggested the presence of a hypercoagulable state revealed by blood assay as being a contributing factor in the onset of arterial occlusions, and the hypercoagulable state was assumed to be secondary to nephrotic syndrome.

Thrombosis in patients with nephrotic syndrome has been recognized as one of the most serious complications resulting from a hypercoagulable state associated with hypoproteinemia. Several authors previously reported cases with cerebral infarction.²⁻⁴⁾ However, our case is very unusual because the subject had experienced recurrent thrombosis of the bilateral carotid arteries, and the results of examinations provided information sufficient to exclude other possible causes of infarction.

The mechanism by which nephrotic syndrome causes a hypercoagulable state has not been determined conclusively. Some reports in the literature describe abnormal levels of various clotting factors as resulting in a hypercoagulable state, including urinary excretion of protein such as plasminogen, antithrombin-III,^{5,6)} factor XII,⁷⁾ increased hepatic production of fibrinogen²⁾ and factor VIII.⁸⁾ Although plasma levels of protein C and protein S in nephrotic

syndrome are still controversial,^{8,9)} some authors propose a relationship between ischemic stroke and a deficiency in protein C or protein S.^{9,10)} While our patient had normal levels of antithrombin-III, protein C and protein S concentration, she had elevated levels of fibrinogen and factor VIII. Further, the increased plasma concentration of thrombin-antithrombin-III complex is assumed to reflect an activated coagulability.

When we encounter arterial thrombosis in a patient with nephrotic syndrome, we should consider anticoagulant therapy independently from other possible causes of infarction after making the differential diagnosis.

Acknowledgments. We wish to thank Dr. Sho Watanabe and Dr. Shuji Watanabe for their invaluable assistance.

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