Cerebral Infarction in Young Men With Nephrotic Syndrome

J.L. Fuh, M.M.H. Teng, W.C. Yang, and H.C. Liu

Background and Purpose: Thrombosis is one of the main complications of nephrotic syndrome; however, cerebral infarction associated with nephrotic syndrome has been rarely reported.

Summary of Report: We describe acute cerebral infarction in two young men with nephrotic syndrome. Both had a hypercoagulable state based on hemostatic studies. By retrospectively reviewing the medical records of the past 10 years at our hospital, we found an additional five cases of cerebral infarction with nephrotic syndrome. Two of the patients were found to have nephrotic syndrome during admission for stroke.

Conclusions: Hypercoagulability may be the major contributing factor of cerebral infarction in patients with nephrotic syndrome. (Stroke 1992;23:295-297)

Thrombotic phenomena are a well-recognized complication of nephrotic syndrome. Recent studies have shown the incidence of renal vein thrombosis to be 5-62% and that of pulmonary embolism 8%. Cerebral infarction associated with nephrotic syndrome has been rarely reported, however. The tendency of nephrotic patients to have thrombotic episodes has been attributed to a hypercoagulable state. We present two young male patients with acute cerebral infarction, probably due to a hypercoagulable state secondary to nephrotic syndrome. Retrospectively reviewing the medical records for the past 10 years, we found five more cases of nephrotic syndrome with cerebral infarction at our hospital.

Case Reports

Case 1

A 21-year-old man was admitted in January 1991 because of the sudden onset of weakness of the right limbs and headache. A diagnosis of nephrotic syndrome had been made in 1989, and he had received steroid therapy. Renal biopsy showed minimal change lesion. He had no history of hypertension or diabetes. He smoked half a pack of cigarettes a day for >3 years, but drank no alcohol and used no illicit drugs. On admission, he had a right hemiparesis, right homonymous hemianopsia, and decreased sensory perception on the right side. Cardiac examination was normal. He had no evidence of systemic embolization, peripheral edema, or deep-vein thrombosis.

Initial computed tomographic (CT) scan of the brain was normal, but a second scan 2 weeks later demonstrated a focal low-density area in the basal ganglia and internal capsule with marginal irregular enhancement. A cerebral digital subtraction arteriogram demonstrated occlusion of the left internal carotid artery just above the bifurcation with inadequate collateral circulation from the right side. The patient's chest roentgenogram, electrocardiogram, and transthoracic echocardiogram were normal. His blood count and electrolytes were within normal limits; however, blood urea nitrogen and creatinine levels were mildly elevated to 47 mg/dl and 1.6 mg/dl, respectively. Serum albumin concentration was 1.5 g/dl, cholesterol 683 mg/dl, and triglycerides 458 mg/dl. Urinalysis revealed 3+ protein. A 24-hour urine protein content was 5.62 g. Prothrombin time was normal. Activated partial thromboplastin time was increased 4 days after stroke, but returned to normal 10 days later. The 1:1 mixed activated partial thromboplastin time of patient and normal serum was normal. The patient's chest roentgenogram, electrocardiogram, and transthoracic echocardiogram were normal. His blood count and electrolytes were within normal limits; however, blood urea nitrogen and creatinine levels were mildly elevated to 47 mg/dl and 1.6 mg/dl, respectively. Serum albumin concentration was 1.5 g/dl, cholesterol 683 mg/dl, and triglycerides 458 mg/dl. Urinalysis revealed 3+ protein. A 24-hour urine protein content was 5.62 g. Prothrombin time was normal. Activated partial thromboplastin time was increased 4 days after stroke, but returned to normal 10 days later. The 1:1 mixed activated partial thromboplastin time of patient and normal serum was normal. Thrombin time was mildly prolonged to 27 seconds (normal value <22 seconds). Fibrinogen concentration was normal. Antithrombin III level was 59% (normal 80-120%). The concentration of protein C was <12.5% (normal 70-140%). Assay of coagulation factors revealed the following values: factor V >100%, factor VII 30%, factor VIII >100%, factor IX >100%, factor XII 20%. Platelet aggregation tests were normal. The anticardiolipin antibody was negative.

The patient received antiplatelet therapy and gradually improved, but had a residual right hemiparesis at discharge 1 month later.
concentration was increased to 550 mg/dl. Anti-nu-

Cerebral angiography demonstrated narrowing of the 

other thrombotic disorders.

360-790. Blood count, prothrombin time, and acti-

level was 840 mg/dl and triglycerides 259 mg/dl.

albumin concentration of 1.6 g/dl. Serum cholesterol 

total serum protein concentration of 3.8 g/dl and an 

impairment of fluency and comprehension, but with 

Examination of the patient on admission included 

and there was no evidence of peripheral emboli, 

syndrome due to membranous glomerulonephritis 

and had no further thromboembolic complications 

and had previously been reported in only six cases.3-7

clear antibodies were negative, and C3 and C4 

concentrations were normal. Urinalysis demonstrated 

4+ protein, and 24-hour urine protein content was 

7.85 g. The patient received anticoagulant therapy 

and had no further thromboembolic complications 

during 6 months of follow-up.

Apart from these two cases, we also retrospectively 

reviewed the medical records of patients with cere-

bral infarction and nephrotic syndrome at our hospi-

tal in the past 10 years. An additional five cases were 

found. Table 1 summarizes the characteristics, symp-

toms, and brain CT scans of all seven patients, 

including the two cases presented in this report. Four 

of the seven were <35 years of age. Unfortunately, 

complete hemostatic studies and cerebral angiog-

rams were not performed in the earlier cases. In two 

cases, the diagnosis of nephrotic syndrome was made 

during admission for stroke, similar to diagnoses in 

the two cases reported by Marsh et al.5

Discussion

Thrombotic complications in patients with nep-

hrotic syndrome occur in both venous and arterial 

systems. Whereas in adults the majority of throm-

boses are venous, arterial thromboses are more com-

mon in children.2 A hypercoagulable state is thought 

to be the major contributing factor.

Cerebral infarction in nephrotic syndrome is rare 

and has previously been reported in only six cases.3-7

Marsh et al5 described two adult patients, 34 and 36 

years of age, who presented with acute cerebral 

infarction and were found to have a hypercoagulable 

state due to nephrotic syndrome. Both patients had 

increased fibrinogen concentration. One patient had 

a deficiency of free protein S, and the other had a 

pulmonary embolus 4 months after the stroke. Al-

though it is not clear why nephrotic syndrome causes 

a hypercoagulable state, there have been many the-

ories for its mechanism, such as urinary loss of 

Reference

Table 1. Characteristics of Seven Patients with Nephrotic Syndrome and Cerebral Infarction

As a result, the patient was considered to have 

thrombosis, or peripheral edema. He was 

mural thrombus. Cerebral angiography demonstrated narrowing of the 

left A1 segment of the anterior carotid artery and the 

knee of the left middle cerebral artery.

Serum chemistry studies were normal except for a 
total serum protein concentration of 3.8 g/dl and an 
albumin concentration of 1.6 g/dl. Serum cholesterol 
level was 840 mg/dl and triglycerides 259 mg/dl. Total lipid content was 2,160 mg/dl (normal range 
360-790). Blood count, prothrombin time, and activated partial thromboplastin time were normal. 
Erythrocyte sedimentation rate was 107 mm/hr. Anti-
thrombin III level was 65% (normal 80-120%). The 
concentration of protein C was normal. Fibrinogen 
concentration was increased to 550 mg/dl. Antinu-

Case 2

A 28-year-old man was admitted in January 1979 
because of loss of consciousness, lasting for about 30 
minutes, followed by incoherent speech. Nephrotic 
syndrome due to membranous glomerulonephritis 
proven by biopsy had been diagnosed 6 years previ-
ously, and he had been treated with steroids since 
then. In 1977, he developed occlusion of the abdom-
inal aorta and had an endarterectomy with bypass 
graft from the abdominal aorta to both common 
femoral arteries. He smoked half a pack of cigarettes 
a day. He did not abuse alcohol or illicit drugs. There 
was no family history of stroke, heart disease, or 
other thrombotic disorders.

Examination of the patient on admission included 
normal vital signs and a normal cardiac examination, 
and there was no evidence of peripheral emboli, 

Deep-vein thrombosis, or peripheral edema. He was 

awake, but sleepy at times. He had a mild right 

hemiapresis. Language examination showed partial 

Determined from brain computed tomographic scan.

Cases presented in this report.

Nephrotic syndrome diagnosed during admission for stroke.

MCL, minimal change lesion; MGN, membranous glomerulonephritis; L, left; R, right.

left Al segment of the anterior carotid artery and the 

capillary areas of infarction. Both patients had 

syndrome due to nephrotic syndrome. Both patients had 

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a deficiency of free protein S, and the other had a 
Pulmonary embolus 4 months after the stroke. Al-

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Table 1. Characteristics of Seven Patients with Nephrotic Syndrome and Cerebral Infarction

| Case | Sex/age | Hypertension | Duration of syndrome (yr) | Cholesterol (mg%) | Renal biopsy | Areas of infarction*
|------|---------|--------------|--------------------------|------------------|-------------|----------------
| 1†   | M/21    | No           | 1.5                      | 683              | MCL         | L basal ganglia and internal capsule
| 2†   | M/28    | No           | 6                        | 842              | MGN         | L middle cerebral artery territory
| 3    | F/73    | Yes          | ‡                        | 261              | ...         | R parieto-occipital area
| 4    | M/22    | No           | 2                        | 230              | MCL         | ...
| 5    | M/62    | Yes          | ‡                        | 525              | MCL         | R deep frontal area
| 6    | M/64    | Yes          | 1                        | 306              | MGN         | R internal capsule
| 7    | M/33    | No           | 2                        | 424              | MGN         | R occipital area

* Determined from brain computed tomographic scan.
† Cases presented in this report.
‡ Nephrotic syndrome diagnosed during admission for stroke.
MCL, minimal change lesion; MGN, membranous glomerulonephritis; L, left; R, right.

Brain CT scan demonstrated infarction in the 
distribution of left middle cerebral artery. Electro-
cardiogram showed an old anteroseptal myocardial 
infarction. M-mode and two-dimensional transtho-
racic echocardiograms demonstrated an aneurysm 
over the apical area with a 3-cm mural thrombus.
Cerebral angiography demonstrated narrowing of the 
left A1 segment of the anterior carotid artery and the 
knee of the left middle cerebral artery.

Serum chemistry studies were normal except for a 
total serum protein concentration of 3.8 g/dl and an 
albumin concentration of 1.6 g/dl. Serum cholesterol 
level was 840 mg/dl and triglycerides 259 mg/dl. Total lipid content was 2,160 mg/dl (normal range 
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thrombin III level was 65% (normal 80-120%). The 
concentration of protein C was normal. Fibrinogen 
concentration was increased to 550 mg/dl. Antinu-
Our two patients had a hypercoagulable state. The first patient had protein C deficiency and decreased level of antithrombin III. Assay of his coagulation factors revealed depressed factors VII and XII and increased factors V, VIII, and IX. The second patient had a decreased level of antithrombin III and an increased concentration of fibrinogen. Because our first patient had a head injury 6 months before admission, one could argue that occlusion of the right ICA was attributable to traumatic dissection rather than in situ thrombosis. Doppler color flow imaging of the internal carotid artery only suggested carotid dissection. One could also argue that cerebral infarction of the second patient was caused by cardiac emboli from the mural thrombus rather than by middle cerebral artery thrombosis. However, the angiogram favors thrombosis rather than embolism. Because a hypercoagulable state was clearly demonstrated in both patients, we believe that this was the major contributing factor in their cerebral infarctions.

Some studies described an increased incidence of thrombotic complications and hypercoagulation during steroid treatment. Hypercholesterolemia may be another contributing factor in cerebral ischemia in nephrotic patients. Five patients in our series were treated with corticosteroids, and all but one in our series had elevated levels of cholesterol.

Ischemic strokes in young adults are uncommon and have different etiologies or risk factors from those in the elderly. While the majority are caused by cardiogenic emboli and premature atherosclerosis, a small number may be due to a hypercoagulable state secondary to nephrotic syndrome.

References

Key Words • cerebral infarction • nephrotic syndrome • young adults
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