Nephrotic Syndrome May Be One of the Important Etiologies of Cerebral Venous Sinus Thrombosis

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Objective: Thrombosis is a common complication of nephrotic syndrome (NS). However, cerebral venous sinus thrombosis (CVST) secondary to NS is rarely reported. Here we report a case series study of 5 cases of CVST with NS, so as to make a better understanding and management of this disorder. *Methods:* A retrospective study was performed in 5 consecutive patients with CVST in combination with NS between 2009 and 2015. The clinical manifestations, laboratory and radiological findings, treatment, and clinical outcomes were analyzed. *Results:* This cohort of case series consists of 1 woman and 4 men, aged 16-49 years. All patients complained initially of an acute or subacute headache. CVST attacked during NS occurrence in 3 patients, and during NS recurrence in 2 patients. The median duration of signs and symptoms prior to clinical diagnosis and treatment was 12.80 ± 7.53 days. In all patients, it was magnetic resonance venography that detected the thrombosis in the cerebral venous sinus, with the most common site of CVST to be the superior sagittal sinus (5 of 5 patients). Two or more segments of sinus were involved simultaneously in 4 patients. The treatment of CVST in NS involved therapy of CVST in the general population. All the 5 patients had full recovery, and no one relapsed with a follow-up of 26.60 ± 29.75 months. *Conclusions:* NS may be one of the important etiologies of CVST. When patients with NS had progressing headache, seizure, or other unexplained neurological symptoms, CVST should be considered. **Key Words:** Cerebral venous thrombosis—nephrology—diagnosis—treatment—prognosis.

Introduction

Cerebral venous sinus thrombosis (CVST) characterized by obstruction of venous reflux, malabsorption of cerebrospinal fluid (CSF), and intracranial hypertension (intracranial pressure; ICP) is a special type of cerebrovascular insult, accounting for .5%-1% of all strokes.[1] Only 34% of these patients had an inherited or acquired prothrombotic condition,[2] including deficiency of anticoagulant protein, positive antiphospholipid antibodies (APL), pregnancy, use of oral contraceptives, cancer, and so on. Other uncommon predisposing causes include infection, hematologic disorders, systemic diseases, and mechanical precipitants.[3]

Nephrotic syndrome (NS) is a clinical syndrome of proteinuria, hypoalbuminemia, edema, and/or hyperlipidemia. Thrombosis is a common and life-threatening

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Received March 4, 2016; revision received May 28, 2016; accepted June 8, 2016.

Study funding: This study was sponsored by the 12th Five science and technology support program (No. 2013BAI07B01).

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1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2016.06.013

complication of NS that usually occurs early in the NS disease course.[4] The incidence of thromboembolism was nearly 1.8%-5.0% in children and 20%-30% in adults with NS.[5] Most thromboembolism events occur within 3 months after NS diagnosis in children and within the first 6 months of diagnosis in adults.[4] Patients with advanced age, membranous nephropathy, or massive proteinuria have an increased risk of NS-associated thromboembolism development.[6] Renal thrombosis, pulmonary embolism, and deep vein thrombosis are the common types of thrombosis.[7] CVST, which is often misdiagnosed because it lacks specific clinical manifestations, is a relatively rare complication of NS.[8]

Here we report a case series study of 5 cases of CVST with NS for a better understanding and management of this disorder.

Methods

A retrospective study was performed in 5 consecutive patients with CVST with comorbid NS admitted to the Department of Neurology, Xuanwu Hospital, Beijing, China, between 2009 and 2015. The demographic data, background medical history, symptoms, signs, laboratory findings, radiological findings, treatment, and clinical prognosis were recorded.

Results

Clinical Features

This case series consists of 4 men and 1 woman, aged 16-49 years (mean 31.20 ± 14.41 years). All patients presented with acute or subacute headache. The most frequent signs were papilledema (3 of 5 patients) and meningeal irritation (2 of 5 patients). CVST occurred at the initial onset of NS in 3 patients, and during the relapse of NS in 2 patients. In NS relapse, both the 2 patients had received immunosuppressive therapy before developing CVST. The median duration of signs and symptoms prior to clinical diagnosis was 12.80 ± 7.53 days (Table 1).

Table 1. *Clinical features of NS patients with CVST*

Case number	1	2	3	4	5
Sex	Female	Male	Male	Male	Male
Age at developing CVST	41	51	22	26	16
The interval between onset of symptoms and diagnosis of CVST (days)	5	10	10	14	25
Clinical course of NS at developing CVST	Initial onset of NS	Initial onset of NS	Initial onset of NS	Relapse of NS	Relapse of NS
Past history	Portal vein thrombosis	Healthy	Healthy	NS for 2 years	NS for 9 years
Clinical symptom of CVST	Headache, nausea, and vomiting	Headache, nausea, vomiting, and visual field defect	Headache, nausea, vomiting, and blurred vision	Headache, fatigue	Headache, nausea, and vomiting
Clinical sign of CVST	Negative	Papilledema, hemianopia	Papilledema	Hemiparesis of the left upper limb, papilledema, meningeal irritation sign	Abducens paralysis, meningeal irritation sign
Kidney pathology	None	None	None	Minimal change disease	None

Abbreviations: CVST, cerebral venous sinus thrombosis; NS, nephrotic syndrome.

Laboratory Manifestations

Laboratory findings on admission are presented in Table 2. The median values of urine protein, albumin, cholesterol, low-density lipoprotein, activated partial thromboplastin time (APTT), fibrinogen, and D-dimer were 6.52 ± 6.68 g/24 h (0-0.15), 20.84 ± 8.46 g/l (35.0-55.0), 7.70 ± 2.35 mmol/l (3.24-5.70), 5.14 ± 3.39 mmol/l (2.08-3.12), 42.46 ± 9.20 seconds (25.0-43.50), 6.83 ± 2.43 g/l (2.0-4.0), and 1.06 ± 1.15 μg/ml (.01-0.50), respectively. Prolonged APTT was found in 3 patients. The level of fibrinogen was elevated in 4 patients. Plasma deficiency of antithrombin III (ATIII) was detected in 1 patient and the level of protein C and protein S decreased in 2 patients. The titer of anti-beta 2 glycoprotein I antibody was high