

Internal Medicine
Section

Atypical Presentation of Nephrotic Syndrome and Cerebral Venous Sinus Thrombosis in Minimal Change Disease: A Case Report

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ABSTRACT

Minimal Change Disease (MCD) is a major cause of nephrotic syndrome in children and a minority in adults. MCD and primary Focal Segmental Glomerulosclerosis (FSGS) are both examples of pathogenic mechanisms that predominantly affect the podocytes. MCD has also been linked to thrombotic consequences. The term Cerebral Sino-Venous Thrombosis (CSVT) refers to a group of conditions that involve thrombosis of the cerebral venous system. The patient presented with a severe headache for seven days, accompanied by vomiting and he was diagnosed with Cerebral Sino-Venous Thrombosis (CSVT) with underlying MCD. There was no associated medical or surgical history. Laboratory examination showed serum hypoalbuminaemia, low protein levels, and an altered urine-protein creatine ratio. A follow-up magnetic resonance imaging showed chronic occlusion of the right transverse and sigmoid sinus with multiple flow voids adjacent to the right transverse and sigmoid sinus. The patient was managed with low molecular weight intravenous corticosteroids, which led to symptomatic relief, followed by a switch to oral steroids. This index case highlights that while MCD is typically a kidney disease, it can lead to severe and potentially overlooked thrombotic events in adults. The case underscores the link between nephrotic syndrome and a hypercoagulable state, which, although not definitively proven as a direct cause of thrombosis, is associated with profound clotting factor abnormalities.

Keywords: Corticosteroids, Heparin, Hypoalbuminaemia, Proteinuria, Sigmoid sinus

CASE REPORT

A 33-year-old male patient presented with a history of a sudden onset of severe headache for the last seven days. It was intensified on the final day, and the patient was admitted to the emergency room. Additionally, the patient reported experiencing five to six episodes of vomiting during the preceding two days, with no relief from antiemetics. The patient did not complain of any chest discomfort, syncope, palpitations, cold, cough, seizure activity, unconsciousness, orthopnoea, or dyspnoea. There was no associated medical or surgical history. There was no similar history in the family. The patient was a non-alcoholic, non-smoker and no other habits were present.

Vitals of the patients were noted as a heart rate of 88 beats/minute, a blood pressure of 130/80 mmHg, a respiratory rate of 20 breaths/minute, afebrile and bilateral pupils reactive to light. The patient did not exhibit any neurodeficit, including no loss of power from cranial nerve palsy, with a Glasgow Coma Scale (GCS)-15/15. Furthermore, there were no indications of meningeal irritation. Blood tests showed a normal complete blood count, normal kidney function, and an altered liver function test. Patient albumin was 2.1 g/dL, suggestive of hypoalbuminaemia as depicted in [Table/Fig-1]. The viral serologies were reported to be normal. On routine, the patient was advised to undergo ultrasound imaging of the abdomen and pelvis, which was found to be normal. Additionally, the patient underwent a brain Magnetic Resonance Imaging (MRI), which showed that there were several filling gaps in the brain's cerebral sinuses and showed occlusion of the right transverse and sigmoid sinuses with multiple flow [Table/Fig-2,3]. The patient was started on injection heparin 5000 IU QID for five days and proper hydration was maintained.

The patient was further screened for urinary protein analysis, which revealed elevated random urinary protein levels of 1563 mg/dL, whereas normal levels were less than 12 mg/dL, along with abnormal UPCR levels of urinary protein-279. Attributed to clinical presentations and a recent history of cerebral venous-

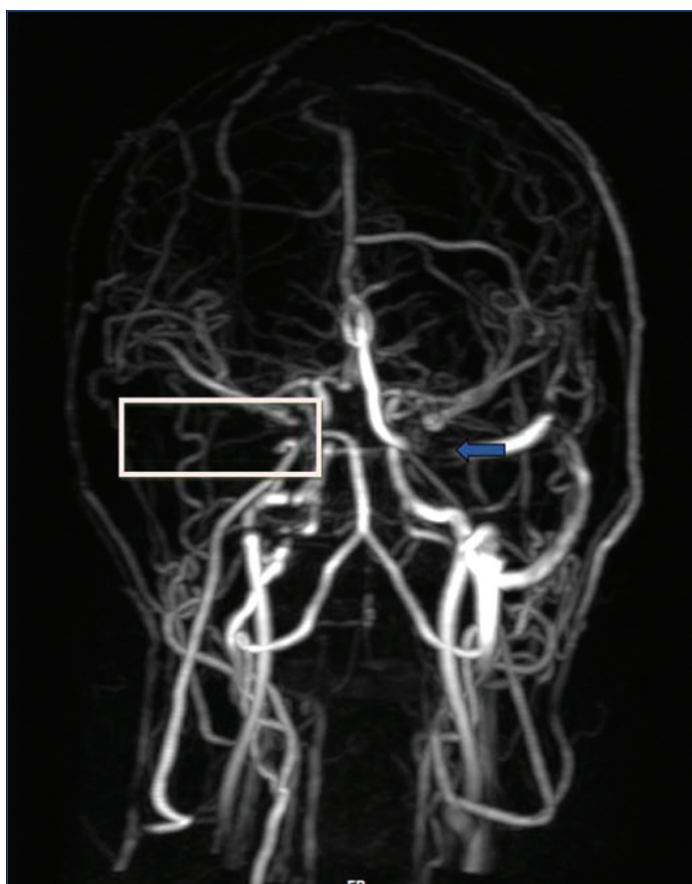
Laboratory investigations	Patient value	Normal range
Hb (gm%)	18.8	13-17
MCV (fL)	104.3	83-101
Platelets (lacs/cumm)	2.02	1.5-4.1
WBC (cells/cumm)	13500	4000-10,000
Urea (mg/dL)	31	19-43
Creatine	1.1	0.66-1.25
Sodium (mmol/L)	13.	137-145
Potassium (mmol/L)	5.1	3.5-5.1
Alkaline phosphatase (U/L)	87	38-126
Alanine transaminase (U/L)	24	<50
Aspartate transaminase (U/L)	87	17-59
Albumin (g/dL)	2.1	3.5-5
Total bilirubin (mg/dL)	1.1	0.2-1.3
INR	1.05	0.9-1.4
Prothrombin	12.5	11.9-13
Activated partial thromboplastin time	41.3	29.5-31.0
C3 complement component – 3 (mg/dL)	150	80-165
C3 complement component – 4 (mg/dL)	58.6	14-44
Homocysteine (µmol/ L)	23.67	4.7-2-12.6
Urinary protein (mg/dL)	1563	<12
Urinary creatinine (mg/dL)	70.1	20-275
UPCR (mg/molL)	279	<0.2

[Table/Fig-1]: Original table depicting the patients' laboratory values. MCV: Mean Corpuscular Volume; INR: International Normalised Ratio; UPCR: Urine Protein Creatinine Ratio

sinus thrombosis, a renal biopsy was performed, which showed that the foot processes of visceral epithelial cells were diffusely effaced, and there were no organised or electron-dense deposits on the mesangial portions of the Glomerular Basement membrane [Table/Fig-4]. These features were suggestive of 'MCD'. Provisional



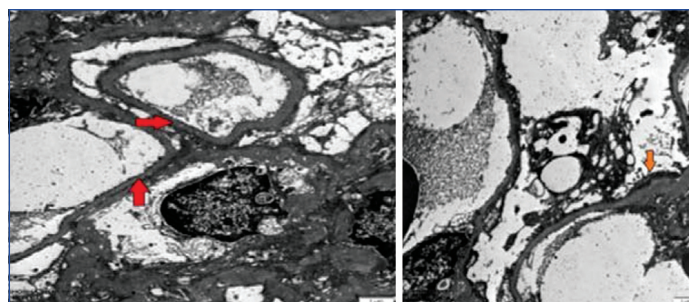
[Table/Fig-2]: MRI brain-sagittal section depicting empty sella sign (red arrow).



[Table/Fig-3]: Shows: i) occlusion of right transverse and sigmoid sinus with multiple flow; ii) Left transverse sinus hypoplasia.

diagnosis was Cerebral Sino-Venous Thrombosis (CSVT) under evaluation. Differential diagnoses considered were protein-losing nephropathy with (nephrotic range proteinuria due to MCD, FSGS, membranous nephropathy, rapidly progressive glomerulonephritis. However, based on the clinical presentation, MRI imaging and biopsy report, a final diagnosis of nephrotic syndrome MCD was confirmed.

Based on the diagnosis, the patient was managed by intravenous prednisolone (1 mg/kg/body weight) once per day during the hospital stay. The patient was later shifted to oral steroid therapy after the pedal oedema subsided by tablet methylprednisolone (60 mg, OD/16 weeks) and rosuvastatin (10 mg, OD/5 months) with a monthly follow-up for four months. Patient was symptomatically better.



[Table/Fig-4]: Electron microscopy of the kidney depicting the foot processes of visceral epithelial cells are diffusely effaced (red arrow) and there are no organised or electron-dense deposits on the mesangial portions of GBM, suggestive of Minimal Change Disease (MCD) (magnification: 6000x)

DISCUSSION

Nephrotic syndrome, per se, is defined as proteinuria of >3.5 g/24 hours, albuminaemia <3.0 gm, peripheral oedema, hyperlipidaemia, lipiduria, and elevated risk of thrombotic disorders. MCD is a type of nephrotic syndrome that is mostly seen in children (~90%) and a small percentage of adults (~10%) [1,2]. These pathogenic processes primarily impact the podocytes, also termed 'podocytopathies', including MCD and primary FSGS. Autoantibodies directed against the slit diaphragm component nephrin may play a role in the pathophysiology of MCD in a subgroup of patients [3]. IgA deposits and mild mesangial proliferation, suggesting the concurrence of IgA nephropathy and MCD [1,4]

The MCD typically causes nephrotic syndrome to develop suddenly. In adults, the abrupt start of nephrotic syndrome is not highly sensitive for MCD but is rather specific, where a kidney biopsy is recommended to confirm the diagnosis [5].

As CVT can be caused by a variety of predisposing factors and precipitants, it may be encountered by neurologists, neurosurgeons, ophthalmologists, obstetricians, oncologists, haematologists, rheumatologists, emergency clinicians, family practitioners, paediatricians, and specialists in the ears, nose, and throat [6,7]. Thrombosis in the sinuses or cerebral veins has rarely been linked to nephrotic syndrome. The deep veins in the lower limbs and the kidneys are most frequently affected by hypercoagulability and thrombotic consequences in nephrotic syndrome.

Prednisone is the primary treatment for steroid-sensitive types of cancer, but relapses may require second-line immunosuppression. 1 mg/kg daily or 2 mg/kg alternately is effective in adults [8,9]. An initial strategy for the management of this case was to initiate Prednisone daily and treat for up to 16 weeks [8-10]. A gentle Prednisone taper is started to finish a course of therapy lasting 4-6 months, if remission is achieved within 4-12 weeks, followed by a high dose for an additional 2-4 weeks as per the requirement [11].

CSVT is a symptom of MCD, highlighting the complexity of renal illnesses and the need for thorough diagnostics in adulthood [11]. Cerebral Venous Thrombosis (CVT) is uncommon in adults, but significantly more common than previously reported incidence in young adults, children, thrombophilia patients, pregnant females, females going through puberty, and women using oral contraceptives [4,12]. As CVT can be caused by a variety of predisposing factors and precipitants, it may be encountered by neurologists, neurosurgeons, ophthalmologists, obstetricians, oncologists, haematologists, rheumatologists, emergency clinicians, family practitioners, paediatricians, and specialists in the ears, nose, and throat [8,9,11].

Hypercoagulability is a theoretical concept that suggests pre-thrombotic alterations can be detected in the blood and these changes are crucial in the development of thromboembolic complications. However, there is recent evidence showing a relationship between a hypercoagulable state and nephrotic syndrome. There is a paucity of data explaining the increased incidence of thromboembolic complications due to a hypercoagulable state in nephrotic patients [1,12].

A patient experienced intense headache and vomiting, was hospitalised, and diagnosed with CSVT. Severe hypoalbuminaemia led to further investigation. Despite minimal nephrotic changes, the hypercoagulable state, known as CSVT in adults, is uncommon and missed daily [12].

A causal relationship between the hypercoagulable state and the subsequent development of thrombosis in the nephrotic syndrome has not been established, but profound clotting factor abnormalities have been observed in the nephrotic syndrome. A causal relationship between the hypercoagulable state and the subsequent development of thrombosis in the nephrotic syndrome has not been established, but profound clotting factor abnormalities have been observed in the nephrotic syndrome [13].

Our patient, who presented with a sudden severe headache and vomiting, was diagnosed with CSVT and managed accordingly. He also developed severe hypoalbuminemia, which led to a renal biopsy. The biopsy showed diffuse effacement of visceral epithelial cell foot processes, without electron-dense deposits. Our patient is diagnosed with MCD nephrotic disease, but presented with a complication of the disease as a hypercoagulable state, that is CSVT in adults, which is rare and missed out on a daily routine basis.

CONCLUSION(S)

This case highlights a rare but significant complication of nephrotic syndrome, particularly in adults, thrombotic events. While hypercoagulability is a theoretical concept, and a clear causal link between it and thrombosis in nephrotic syndrome has not been conclusively established, profound clotting factor abnormalities have been observed in this condition. The presentation of MCD as a hypercoagulable state, like CSVT, is uncommon and can be missed. This case underscores the importance of a comprehensive diagnostic workup for patients with CSVT to identify underlying

systemic disorders such as nephrotic syndrome, which guides effective long-term management.

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