

CASE REPORT

Transverse and Sigmoid Venous Sinus Thrombosis Associated with Nephrotic Syndrome

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Abstract

A 6 years old female diagnosed with nephrotic syndrome developed, during her first admission in the hospital, sinus transvers thrombosis. At first it was considered a complication of the disease, but later it was proved that she had hereditary thrombophilia. The major symptom in this case was persistent headache.

Keywords: nephrotic syndrome, hereditary thrombophilia, anticoagulant, corticosteroid therapy.

Rezumat

Pacientă de sex feminin, în vârstă de 6 ani, diagnosticată cu sindrom nefrotic, a dezvoltat pe parcursul primei internări tromboză de sinus transvers. La început a fost considerată o complicație a sindromului nefrotic, ulterior s-a dovedit că pacienta asocia trombofilie ereditară. Simptomul major în tromboza de sinus transvers a fost persistența cefaleei.

Cuvinte cheie: sindrom nefrotic, trombofilie ereditară, anticoagulant, terapie corticosteroidă.

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INTRODUCTION

Nephrotic syndrome is one of the most interesting diseases encountered in pediatric patients, who has progressed a lot in terms of the therapeutic approach and improving quality life.

The diagnose of nephrotic syndrome is still based on the presence of nephrotic range proteinuria – urinary protein excretion $>50\text{mg/kg/day}$ or from the first morning urine, protein/creatinine ratio $\geq 2\text{mg/mg}$; hypoalbuminemia- serum albumin $<3\text{g/dL}$; edema and hyperlipidemia¹. For cases of steroid-resistant nephrotic syndrome, genetic testing and renal biopsy offer more answers on how to manage and treat these patients.

Steroid-sensitive nephrotic syndrome has the most favorable outcomes and usually patients attain remission in the first 4 weeks of steroid therapy. Also, we have to keep in mind that usually 80% of the patients will experience one or more relapses, especially children aged <6 years at onset^{2,3,4,5}.

The main complications in steroid nephrotic syndrome are: infections, venous thromboembolism and acute kidney injury due to severe edema and hypovolemia⁶.

CASE REPORT

A 6-year-old female started presenting 72h prior to admission in the hospital: periorbital edema in the morning, which disappeared during the day and after 48h progressed to generalized edema associated with dry cough, fever, an overweight of 2kg and normal urine output.

On examination: she had fever ($38,8^{\circ}\text{C}$), pale skin, periorbital edema associated with lower extremities edema, abdominal distention. The affected areas were soft, pitting and nonerythematous. Other symptoms were: dry cough with no pulmonary abnormalities, blood pressure= $100/71$ mmHg, normal urine output.

Based on the clinical exam we suspected nephrotic syndrome and performed specific laboratory testing to confirm the diagnose.

According to test results, the patient had the criteria for nephrotic syndrome: nephrotic range proteinuria, hypoalbuminemia, dyslipidemia (Table 1).

Table 1. Laboratory markers.

Parameters	Results	References
	Urine	
24h proteinuria	2,96 g/L	$<0,2$
Urine test- proteinuria	500 mg/dL	Negative
	Serum lipid profile	
Total Cholesterol	481 mg/dL	<170 mg/dL
Total lipids	1290 mg/dL	<150 mg/dL
Triglycerides	117,52 mg/dL	<150 mg/dL
	Others	
Serum Albumin	2,5 g/dL	3,8-5,4 g/dL
Serum Sodium	132 mmol/L	138-145 mmol/L
Serum Potassium	4,4 mmol/L	3,3- 5 mmol/L
Serum Calcium	7,8 mmol/L	8,8-10,8 mmol/L
Serum creatinine	0,21 mg/dL	$<0,59$ mg/dL
C3 level	1,8 g/dL	0,9-1,8g/dL
aPTT	26,3 sec	<40 sec
fibrinogen	760 mg/dL	140-360 mg/dL

After diagnosis was established, we started the patient on oral Prednisone (60mg/m^2) daily, intravenous albumin, diuretic: furosemide, enalapril, antibiotic: Ceftriaxone, low salt intake. Daily blood pressure, 24h urine output and 24h proteinuria was monitored daily.

Under the treatment the edema was reduced and disappeared in a few days, serum albumin was corrected after 1 administrations of albumin. The evolution was favorable seen in the graphic of daily 24h proteinuria (figure 1). Remission was achieved after 10 days on daily oral Prednisone.

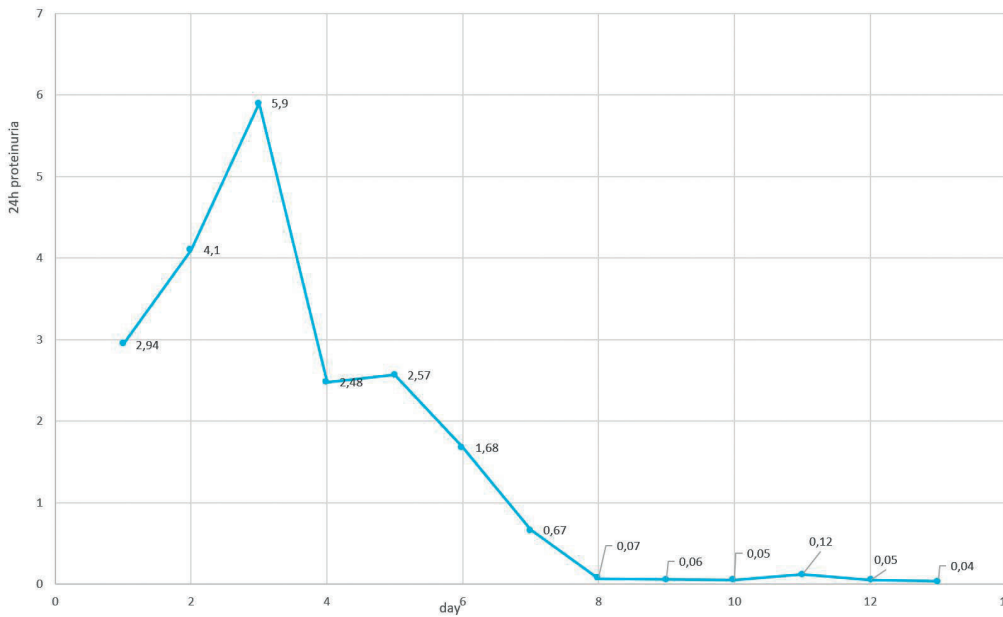


Figure 1. Proteinuria evolution during steroid therapy.

On the 10 day of admission the patient started presenting persistent headache, associated with intermittent photophobia, who responded to symptomatic treatment. Neurological, ophthalmological exam were normal but the head MRI was a surprise. The head

MRI described thrombosis of the right transverse and sigmoid venous sinus (figure 2). In this case MRI, which is evidence-based medicine with high-performance contrast imaging helped us with a precise positive diagnosis⁷.

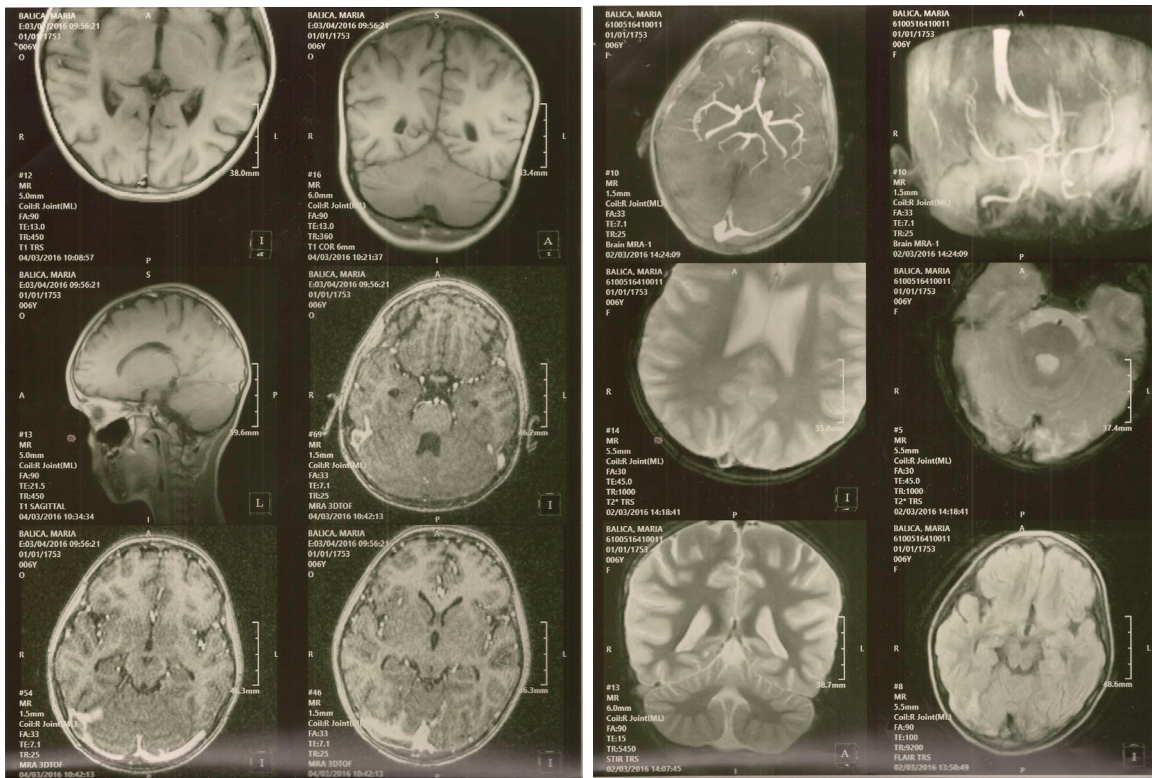


Figure 2. Head MRI- Thrombosis of the right transverse and sigmoid venous sinus

Blood tests suggestive for hypercoagulable state were collected: normal coagulation; high D-dimer (2,61µl/mL), normal protein S (82%); high protein C (282%), low antithrombin III (60%) and normal anti-cardiolipin.

Thrombosis is a complication in patient with nephrotic syndrome, but was unusual considering the evolution of the patient so we decided to test for genetic thrombophilia. The results were:

- *factor V Leiden H1299R(R2) mutation: positive heterozygous;*
- *MTHFR A1298C mutation: positive heterozygous;*
- *factor XIII V34L mutation: positive heterozygous;*
- *PAI-1 4G/5G mutation: genotype heterozygous 4G/5G;*
- *EPCR A4600G mutation: positive heterozygous;*
- *EPCR G4678C mutation: positive heterozygous.*

Anticoagulant treatment with Clexane was started. Later the patient continued with oral Sintrome (Acenocoumarol), dose adjusted according to the coagulation. After starting the treatment, the symptoms (photophobia and headache) stopped and no neurological sequelae were described.

Headache is one of the most common causes of thrombosis, followed by motor disfunction, seizures, papillary edema and alterations of the state of consciousness^{8,9}.

The patient was discharged with oral Prednisone daily until it reached 28 days of treatment and after that the dose was decreased at 40 mg/m² alternate-day for 4 weeks and continued with the decreasing dose. Sintrome was also continued. Since she was diagnosed in 2016 with steroid-sensitive nephrotic syndrome and genetic thrombophilia there were no relapses.

DISCUSSION

Steroid-sensitive nephrotic syndrome has a good outcome and as histological finding it's considered the patients have minimal changes disease. Important in

all patients with nephrotic syndrome is to prevent the possible complications like: infections, thromboembolism, acute kidney injury due to anasarca and hypovolemia.

The risk of thromboembolic complications in children with nephrotic syndrome is: hemoconcentration, infections, immobility, the presence of central venous catheter and an underlying genetic thrombophilic disorder¹⁰. In our case the risk was the underlying genetic thrombophilia.

The most frequent sites of thrombosis is described to be: renal vein, cerebral vein, pulmonary artery, inferior vena cava, deep legs veins, femoral or iliac artery. Rare sites are: cerebral artery, mesenteric and hepatic veins¹¹.

The patient responded to daily steroid therapy and obtained complete remission in the first 28 days and maintained remission in the next years with no relapse.

CONCLUSIONS

We present a case of idiopathic nephrotic syndrome, steroid-sensitive, complicated with thrombosis of the right transverse and sigmoid venous sinus, due to an underlying genetic thrombophilic disease.

In our case the thromboembolic symptoms appeared after 10 days of admission and after responding to steroid therapy. The symptoms were: headache and intermittent photophobia. The genetic thrombophilia is an additional risk factor, because patients with nephrotic syndrome are predisposed to hypercoagulation state, that can lead to thrombotic events.

Early anticoagulant therapy is important to prevent neurological sequelae.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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