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Case Report

Cerebral Venous Thrombosis in a Patient with Nephrotic Syndrome: A Case Report

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Abstract

Introduction: Nephrotic syndrome (NS) is the most frequent glomerular disease in childhood. Thromboembolic complications can occur. Cerebral venous thrombosis (CVT) diagnosis may be challenging since clinical signs are usually nonspecific. Acute phase treatment is anticoagulation.

Case Report: A previously healthy 3-year-old female child, presented with two days of irritability, prostration, and periorbital edema. Workup revealed nephrotic proteinuria, megaloblastic anemia, hypercholesterolemia, hypertriglyceridemia, hypoalbuminemia and elevated sedimentation rate. Remission occurred on the 8th day of steroid therapy.

About nine days after remission, she started with a headache, photophobia, nocturnal awakening, and morning vomiting. On examination, she was irritable, mildly dehydrated, but normotensive, with the normal neurologic and funduscopic examination. The head nano tomography showed an extensive venous thrombosis of the superior sagittal sinus. Antithrombotic therapy was started, with clinical and radiologic improvement.

Hereditary thrombophilia and dysfibrinogenemias study showed 675 4G/5G and -844A/G variants in the promoter region of the SERPINE1 gene. She remained on anticoagulant therapy for a year.

Conclusion: CVT although rare is an important complication of NS. The hyper coagulant state contributes to this phenomenon due to its multifactorial etiology. The high clinical suspicion with contrast-enhanced CT allowed the early institution of therapy, thus preventing the occurrence of post-thrombotic complications. In the absence of major intracranial hemorrhage anticoagulation is the gold standard of treatment.

Keywords: *Nephrotic Syndrome (NS); Cerebral Venous Thrombosis (CVT); Anticoagulant Therapy*

Introduction

Nephrotic syndrome (NS) is the most common glomerular disorder of childhood, affecting about 2 - 7 per 100,000 children [1]. This may be associated with thromboembolic complications, mostly of venous origin. The risk of thromboembolic events in the NS is esti-

mated at 1.8% to 5%. The incidence of cerebral venous thrombosis (CVT) in children is 0.67 per 100,000 children per year. NS confers a state of hypercoagulability caused by several mechanisms: urinary loss of anticoagulant proteins, especially anti-thrombin III, increased procoagulant activity, increased platelet aggregation, and thrombocytosis. Hyperlipidemia may also be an additional factor. Other factors include haemoconcentration, use of diuretics, severe hypoalbuminemia, and long-term catheters. Thrombosis in the NS is mostly due to these factors, but all children should be studied for hereditary causes [1].

The diagnosis of cerebral venous thrombosis is difficult as the clinic may be nonspecific [2,3]. Children may present with seizures, altered state of consciousness, papilledema, headaches, isolated intracranial hypertension, or focal neurological deficits. CVT is associated with a significant frequency of serious adverse effects that can be prevented through high clinical suspicion, diagnosis, and timely therapy [1]. The most common diagnostic test used in contrast-enhanced computed tomography with a pathognomonic cord sign represents thrombosis of a cortical vein [2].

Treatment with anticoagulation is safe and may be favorable for reducing mortality and long-term morbidity. The duration of the treatment depends if CVT is provoked or spontaneous. If it is provoked 3 to 6 months is a reasonable duration of treatment and if it is spontaneous 6 to 12 months [4,7].

Case Report

A previously healthy 3-year-old female child was admitted to the pediatric emergency department due to irritability, prostration and periorbital edema within 2 days of evolution. She also presented with a productive cough, rhinorrhea, and decreased appetite, without fever.

On observation, she was prostrate, with periorbital edema, but hydrated and normotensive. Resolution phase skin lesions compatible with the hand-foot-mouth disease were also present.

Laboratory workout showed nephrotic proteinuria, megaloblastic anemia (haemoglobin 10.8 g/dL), hypercholesterolemia (316 mg/dL), hypertriglyceridemia (409 g/dL) and hypoalbuminemia (15.3 mg/dL), normal C-reactive protein and high sedimentation rate were highlighted. Under the diagnosis of nephrotic syndrome, she was hospitalized and corticotherapy was started. She remained hemodynamically stable with progressive improvement of edema (loss of 4.2 kg from admission) and proteinuria (negative from the sixth day of admission the patient was discharged on the 12th day of hospitalization under corticotherapy and was referred to the Pediatric Nephrology follow-up.

Three days after being discharged she began intense headaches with associated photophobia, nocturnal awakening, and morning vomiting. On observation, she was normotensive, with a normal neurological examination, including fundoscopy. Considering the hypothesis of acute central venous thrombosis, a nano tomography (Figure 1) was performed, which showed extensive venous thrombosis of the superior sagittal sinus and extension to the transverse sinuses. She was admitted to pediatric intensive care and started subcutaneous Low Molecular Weight Heparin.

There was a progressive improvement in headache episodes, and she was asymptomatic after 3 days of antithrombotic therapy. On the 5th day of hospitalization, she started with enalapril due to her high blood pressure profile. A control head CT angiography was performed on the ninth day of anticoagulant therapy and showed improvement over baseline.

A genetic study for thrombophilia's and dysfibrinogenemia's showed 675 4G/5G and -844A/G variants in the promoter region of the SERPINE1 gene.

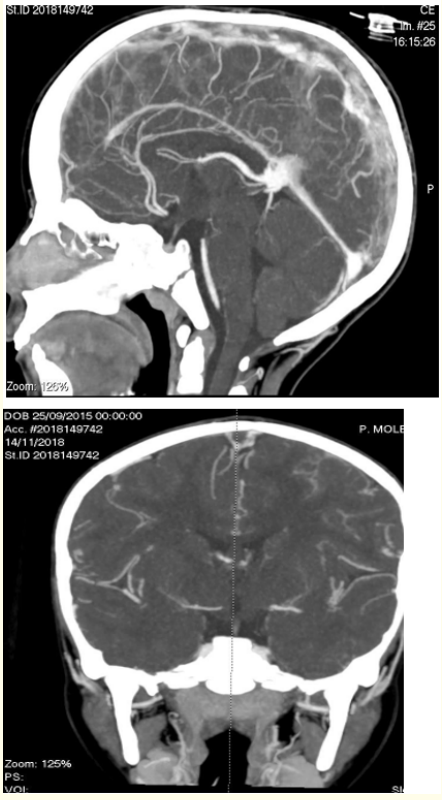

Figure 1: *A Nano tomography was performed, which showed extensive venous thrombosis of the superior sagittal sinus and extension to the transverse sinuses.*

She was clinically stable throughout the hospitalization period and was discharged on the 15th day treated with prednisolone, enoxaparin, and enalapril, with follow-up on paediatric nephrology and neuropediatric consultations.

She remained on anticoagulant therapy for a year and had the first relapse of nephrotic syndrome about 16 months after the inaugural episode.

Discussion and Conclusion

Cerebral venous thrombosis is a rare but challenging complication of the NS [1,5]. The hyper coagulant state contributes to this phenomenon and its multifactorial etiology [4]. The most frequently involved anatomical site is the superior sagittal sinus [6]. Analytical investigation and particularly proper imaging are required for a correct and timely diagnosis. In daily clinical practice, cranial computed tomography occupies a privileged place, but about 40% of cases may not be detected [7].

In this case, neurological symptoms were observed, namely, intense headache with nocturnal awakening and morning vomiting. The high clinical suspicion with contrast-enhanced CT allowed early initiation of therapy, thus preventing post-thrombotic complications. These complications tend to occur early in the disease, with a median time of 70.8 days from diagnosis to the occurrence of complications, with about 61% of cases occurring within the first 3 months. In the absence of apparent precipitating factors, the study of hereditary thrombophilia's is essential, in which case thrombophilia's and dysfibrinogenemia's including factor II G20210A, factor V Leiden R506Q, MTHFR C677T, and A1298C, SERPINE1/PAI1-675 4G/5G and -844A were studied. / G. Variants -675 4G/5G and -844A/G were detected in the promoter region of the SERPINE1 gene.

Some of the poor prognostic factors are an initial Glasgow coma scale of less than 12, hypoalbuminemia < 2 g/dL, age less than 2 years, fibrinogen > 6 g/L, non-vessel recanalization, and congenital thrombophilia. These factors increase the risk of recurrence and thus contribute to high morbidity [5].

Anticoagulation is the gold standard for the treatment of acute CVT, even in the presence of intracranial hemorrhage [7].

Our case highlights the importance of early clinical suspicion and diagnosis in patients with NS and any neurological symptoms. A careful objective examination, adequate imaging study, anticoagulation, and correct treatment of NS can reduce morbidity and prevent future complications.

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