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Case Report

An unusual presentation of congenital protein S deficiency: cerebral venous thrombosis with right atrial thrombi in an infant

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ABSTRACT

Cerebral venous thrombosis (CVT) is an uncommon but serious cause of pediatric stroke. In infants, it is most often related to dehydration, infection, or perinatal complications, while inherited thrombophilia is a rare underlying factor. Protein S deficiency, a congenital prothrombotic disorder, predisposes to severe thrombotic events from early life, though its presentation with intracardiac thrombosis is exceptional. We report the case of a six-month-old infant admitted with status epilepticus, in whom brain magnetic resonance imaging (MRI) demonstrated extensive CVT involving the superior sagittal, lateral, and straight sinuses. Echocardiography further revealed right atrial thrombi causing functional tricuspid stenosis, an atrial septal defect, and partial thrombosis of the superior vena cava. Etiological work-up confirmed congenital protein S deficiency. The association of CVT with right atrial thrombi in the absence of central venous catheters or structural heart disease is extremely rare. Functional obstruction of the tricuspid valve and the presence of an interatrial communication raised the possibility of paradoxical embolism as a contributing mechanism. The patient was successfully stabilized with anticoagulation alone. This case highlights the severity and unusual presentations of congenital protein S deficiency and underscores the importance of considering inherited thrombophilia in infants with extensive or multifocal thrombosis.

Keywords: Right atrial thrombus, Functional tricuspid stenosis, Atrial septal defect, Paradoxical embolism, Cerebral venous thrombosis, Protein S deficiency

INTRODUCTION

Cerebral venous thrombosis (CVT) is an uncommon but serious cause of neurological events in infants. While acquired factors such as dehydration or neonatal infections represent the most frequent causes, inherited coagulation disorders, including congenital thrombophilias, must also be considered in the etiological evaluation.[1]

Protein S deficiency is a rare congenital thrombophilia. As a cofactor of activated protein C, protein S plays a central role in the regulation of coagulation. Its deficiency, whether heterozygous or homozygous, predisposes to an increased risk of severe thrombotic events from early childhood, including deep vein thrombosis and CVT.[2]

Intracardiac thrombi are unusual in children, particularly in the right heart chambers, except in the presence of predisposing conditions such as central venous catheters or complex congenital heart disease. Their occurrence in the context of an inherited thrombophilia is therefore exceptional. The association with an atrial septal defect (ASD) and a functional tricuspid stenosis caused by the thrombus further raises the possibility of a paradoxical embolism mechanism.[3]

We report the case of a six-month-old infant who developed an extensive CVT associated with right atrial thrombi, complicated by functional tricuspid stenosis and partial thrombosis of the superior vena cava. Etiological work-up revealed congenital protein S deficiency.

Through this rare case, we discuss potential pathophysiological mechanisms as well as diagnostic and therapeutic challenges.

CASE REPORT

A 6-month-old female infant, born at term after an uncomplicated pregnancy and with no significant past medical history, was admitted to the pediatric emergency department for status epilepticus. She was managed in the intensive care unit for stabilization. Brain magnetic resonance imaging (MRI) demonstrated extensive cerebral venous thrombosis involving the superior sagittal sinus, the lateral sinuses, and the straight sinus (Figures 1 and 2). Electroencephalography showed a pattern consistent with left hemispheric dysfunction with epileptiform discharges.

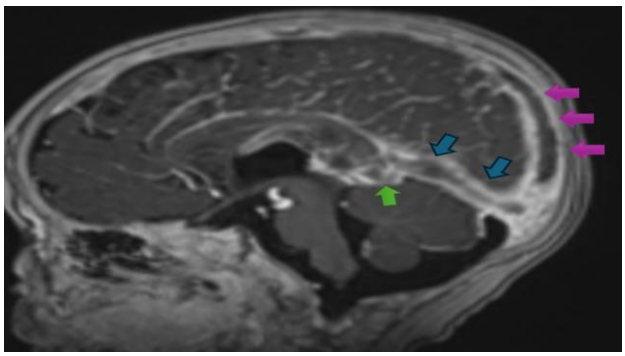

Figure 1: Sagittal T1-weighted brain MRI after gadolinium injection showing a lack of opacification of the superior sagittal sinus, straight sinus, and vein of galen, with visualization of intraluminal thrombi. Pink arrow: thrombus within the superior sagittal sinus; blue arrow: thrombus within the straight sinus; green arrow: thrombus within the vein of galen.

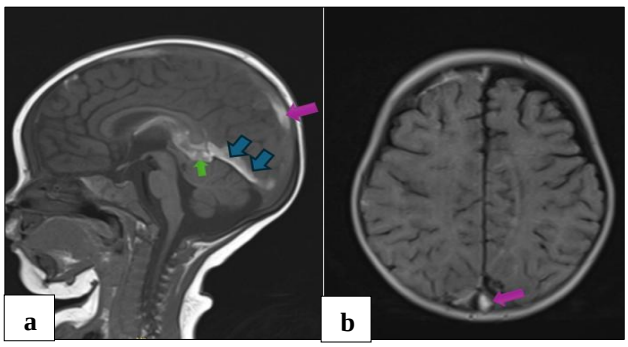

Figure 2: Brain MRI showing (a) sagittal T1-weighted image without gadolinium injection, and (b) axial FLAIR sequence, demonstrating hyperintense signal within the superior sagittal sinus (pink arrow), straight sinus (blue arrow), and vein of Galen (green arrow).

The infant was neurologically stabilized and started on anticoagulation (Sintrom (acenocoumarol)), then transferred to the pediatric ward for further management and etiological work-up. Transthoracic echocardiography (Figures 3-5) revealed an atrial masse adherent to the lateral wall of the right atrium measuring 16×11 mm; there was functional tricuspid stenosis, an interatrial communication, and a partially thrombosed superior vena cava. The patient's clinical condition was stable; he was discharged from the hospital and later reassessed for a thrombophilia workup, which revealed a protein S deficiency.

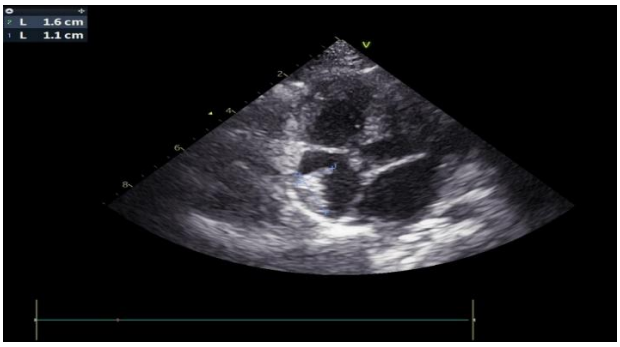

Figure 3: Transthoracic echocardiographic four-chamber views showing an atrial mass adherent to the lateral wall of the right atrium, measuring 16×11 mm.

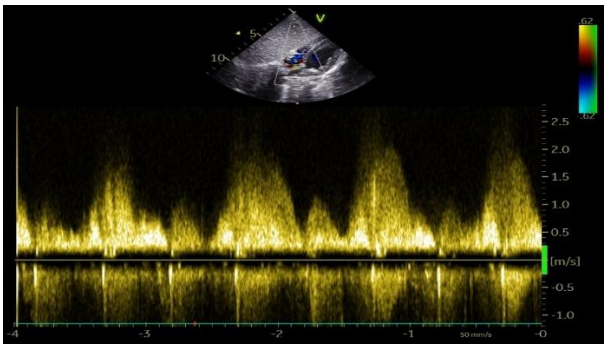

Figure 4: Doppler echocardiography demonstrating significant flow acceleration across the tricuspid stenosis.

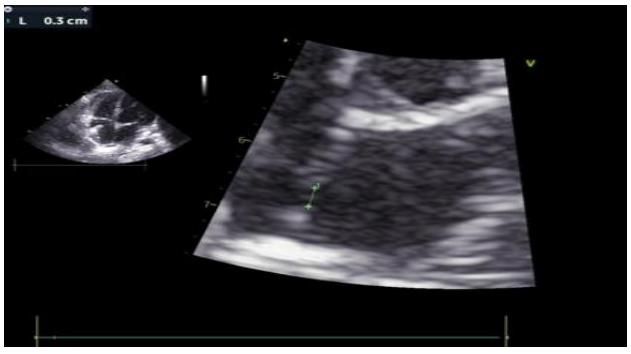

Figure 5: Transthoracic echocardiographic four-chamber view demonstrating an atrial septal defect.

DISCUSSION

CVT in infants is an uncommon condition but constitutes an important cause of pediatric stroke. Its reported

incidence is approximately 0.4–0.7 per 100,000 per year, with the highest risk occurring during the first year of life.[1,4] The clinical presentation is often subtle and non-specific. Many infants initially show signs such as seizures or unexplained irritability, which can delay diagnosis. Although MRI and venography have greatly improved detection, the condition still carries serious consequences, with a significant number of children later experiencing long-term complications, including epilepsy or developmental delays.[5]

The underlying causes of CVT are diverse. In infants, dehydration, infection, and perinatal complications are by far the most frequent.[6] Thrombophilia is less common but becomes relevant when thrombosis is extensive or unusual. Among inherited causes, protein S deficiency is particularly rare. it acts as a cofactor for activated protein C. When levels are low, clotting factors Va and VIIIa are not properly inactivated, resulting in a prothrombotic state.[7,8] Severe neonatal forms usually present with purpura fulminans. Heterozygous forms are often milder, but even then, infants may occasionally present with major venous thrombosis.[9]

Our case is noteworthy because the infant not only developed CVT but also had right atrial thrombi. In pediatrics, such findings are most commonly related to the presence of central venous catheters or underlying structural heart disease.[10] Neither was observed in our patient. Instead, we believe the systemic prothrombotic state created by protein S deficiency, combined with partial thrombosis of the superior vena cava and venous stasis, was the key factor.

An additional unusual feature was functional tricuspid stenosis due to obstructive atrial thrombi. Obstruction of the tricuspid valve by a mass is extremely rare in infants and has mainly been described with tumors or large vegetations.[10] In this child, the mechanical obstruction probably increased right atrial pressure and promoted right-to-left shunting through the atrial septal defect (ASD). This raises the possibility that some of the cerebral events could have been related not only to local thrombosis but also to paradoxical embolism.

Paradoxical embolism through an ASD is a well-recognized mechanism of arterial ischemic stroke in adults, but it has very rarely been reported in children and is almost never discussed in relation to cerebral venous thrombosis.

CVT is generally considered the result of local thrombosis rather than embolism. However, in our patient, the coexistence of right atrial thrombi, elevated right atrial pressure due to functional tricuspid stenosis, and an interatrial communication creates conditions in which venous-to-venous paradoxical embolism could theoretically occur. Although this mechanism cannot be proven, it remains a plausible explanation for the unusual association observed in this case.

Treatment in such situations is challenging. Anticoagulation remains the standard of care for CVT, even in the presence of intracranial hemorrhage.[12]

For intracardiac thrombi, anticoagulation is also the first step, with many cases resolving under medical therapy. Surgery or thrombolysis may be considered for massive or obstructive clots, but in small infants these options carry high risks.[13]

In our case, conservative management with anticoagulation alone led to clinical stabilization, which is reassuring.

Long-term outlook in protein S deficiency depends on severity of the defect, extent of thrombosis, and neurological outcome. These children need close hematology follow-up and sometimes prolonged anticoagulation. Family screening is recommended as well, since the disorder is inherited and may be silent in relatives.[2]

To our knowledge, very few cases have reported such a combination of extensive CVT and right atrial thrombi in an infant with protein S deficiency. The added presence of tricuspid stenosis and partial superior vena cava thrombosis illustrates the severity of the hypercoagulable state. This case underlines the importance of testing for inherited thrombophilia in infants with CVT, particularly when extracerebral thrombosis is found, and emphasizes the value of early anticoagulation and multidisciplinary care.

CONCLUSION

This case illustrates a rare and severe manifestation of congenital protein S deficiency in an infant, presenting with both cerebral venous thrombosis and right atrial thrombi. The unusual association of functional tricuspid stenosis emphasizes the need to consider inherited thrombophilia in infants with extensive or multifocal thrombosis. Early recognition, timely anticoagulation, and long-term follow-up are critical to optimize outcomes and to prevent recurrence.

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