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Research Article

Venous and Cerebral Sinus Thrombosis in Newborns and Children

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Abstract

Analysis of a population of children with venous and cerebral sinus thrombosis. Cerebral venous sinus thrombosis (CVST) is a well-known, although underestimated, cause of stroke in childhood. Its diagnosis requires a high index of suspicion, a correct interpretation of neuroimaging studies and an interrelation between clinicians and radiologists. The clinical features, risk factors and neuroimaging of children under 15 years of age with CVST were analyzed.

Patients and methods: Multicenter, retrospective, descriptive, study of a consecutive series of cases of children under 15 years of age, who were admitted due to CVST between January 1st, 2010, and March 1st, 2022.

Results: The study included 51 patients: 39% with acute symptoms and 59% with subacute symptoms. Newborns predominantly presented encephalopathic symptoms and seizures, while children exhibited signs of intracranial hypertension (ICH). Risk factors were identified in 90% of the cases. Magnetic resonance with angiography in venous time confirmed the diagnosis in 80% of the patients, with the straight sinus being the most affected in newborns and the lateral sinus in children. Hemorrhagic complications were found in 30.5%, being more frequent in newborns. Anticoagulation was initiated in 82% without complications. Sequelae were present in 44.4% of newborns and 37.9% of children, being more frequent and severe in newborns.

Conclusions: To make an early diagnosis, it is essential to consider CVST in newborns with encephalopathic symptoms and/or seizures, and in children with signs of ICH in the presence of predisposing or triggering conditions.

Keywords: Cerebral venous thrombosis; Neuroimaging; Childhood

Introduction

SCVT is a type of cerebrovascular accident (CVA) that affects the cerebral venous, including venous sinuses and cortical and deep veins [1]. The Incidence varies (0.8-40/100,000 children per year), being more frequent in NB [1,2]. For diagnosis, magnetic resonance imaging with angiography (Angio-MRI) is the choice test [1,2]. Recently, available evidence has shown a favorable prognosis in those receiving anticoagulant therapy, leading to recommend it in most therapeutic guidelines [3-5].

The mortality is approximately 10%, and the sequelae affect half of the NBs and a third of older children, highlighting motor and cognitive abilities [3-5].

This condition is rare and underdiagnosed, due to the lack of symptoms and specific signs that depend on the location and underlying causes [1,2].

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Furthermore, the lack of interaction between the clinician and the radiologist makes it difficult to timely diagnosis [5].

Materials and Methods

Multicenter retrospective descriptive study of a consecutive series of cases of RN and children between 28 days of life and 15 years admitted to the Center Hospitalario Pereira Rossell (CHPR) and at the American Sanatorium in Montevideo- Uruguay, by TVSC between January 1, 2010 and March 1, 2022. In the analysis of ischemic and/or hemorrhagic lesions, those with a history of brain trauma (TBI) or brain surgery. For the follow-up and evaluation of sequelae, the PSOM score (Pediatric Stroke Outcome Measure). The study was approved by the Ethics Committee of the School of Medicine.

Results

51 patients were included, 28/51 men. Of the total, 11/51 belonged to the group of RN, while 40/51 were children, with an average age of 4 years and 6months. The most common form of presentation was acute and subacute, representing 98% of all cases.

A predominance of diffuse symptoms was observed. In the RN group, there was no reported focal symptoms, and all NBs presented diffuse symptoms, highlighting encephalopathic manifestations as the most common. On the other hand, in the group of children, focal symptoms were found in 13/40(32.5%), with oculomotor disorders and motor deficit being the most frequent. In this group, diffuse manifestations, such as CTEH symptoms, were the most described (67.5%). Seizures were also observed in 7/11 of the NBs and in 9/40 of the children (Table 1).

In 46/51 the existence of at least one risk factor was recorded

(Table 2). A risk factor, dystocic birth and asphyxia, was identified in all NBs. perinatal were the most frequent. In the group of children, 35/40 presented a risk factor, highlighting ECT as the most reported cause.

The diagnosis of the patients was carried out using different modalities of image. In 41/51 cases, Angio-MRI was used, in 7/51 arteriography and CT angiography (CTA) was used in 3/51.

Table 1: Clinical characteristics.

Parameters	Number of cases
Neonates	0/11
Focals Diffuse	0/11
Alteration of consciousness	0/11
Vomiting	5/11
Hypotonia	4/11
Irritability	3/11
Poor suction	3/11
Seizures	1/11
Children:	7/11
Focals	13/40
Oculomotor disorder	5/40
Hemiparesis	4/40
Visual deficit	3/40
Speech deficit	1/40
Diffuse	27/40
Headache	16/40
Vomiting	11/40
Alteration of consciousness	9/40
Irritability	3/40
Papilla edema	3/40
Seizures	9/40

Table 2: Risk factors.

Risk factor	Number of cases
Neonates	11/11
Dystocic Birth	3/11
Asphyxiation	3/11
Dehydration	2/11
Prematurity	1/11
Gestational diabetes	1/11
Maternal infection	1/11
Children	35/40
TEC	15/40
Dehydration	7/40
Locoregional infection	6/40
Anemia	5/40
Prothrombotic factors	4/40

In relation to topography, in the RN group, greater involvement was observed of the deep venous system, the straight sinus being the most frequently affected in 4/11 cases (36.3%). On the other hand, in the group of children, it was found greater involvement of the superficial venous system, with the lateral sinus as the most affected in 17/40 cases (Table 3).

For the analysis of ischemic and/or hemorrhagic lesions, we excluded those with a history of ECT or brain surgery to avoid confusion in the injuries related to these events. 15 patients with such background. The lesions were divided into ischemic and hemorrhagic, and these latter were classified as intraparenchymal hematoma and hemorrhages intraventricular (IVH). Injury findings were found intraparenchymal in 27.3% (3/11) of the NB and in 32% (8/25) of the children. In addition, HIV were observed in 45.5% (5/11) of the NBs and in 8% (2/25) of the patients in the children's group. These results indicate a significantly higher frequency of HIV in newborns compared to children.

Table 3: Location of the Thrombus.

Affected Breast	Number of Cases
Neonates	
Superficial	
Lateral	3/11
Sagital	3/11
Sigmoides	2/11
Labbe	0/11
Deep	
Straight	4/11
Internal cerebral	2/11
Vein of Galen	1/11
Children	
Superficial	
Side	18/40
Sagittal	13/40
Sigmoid	10/40
Labbe	1/40
Deep	
Straight	7/40
Internal cerebral	4/40
Vein of Galen	1/40

42/51 was treated with low molecular weight heparin (LMWH) without experience complications. Within the RN group, 4/11 patients did not received treatment, while within the group of children, 5/40 did not received, due to the presence of significant bleeding or evidence of partial recanalization. No deaths or recurrences were recorded in none of the groups. 38/51 patients were followed up using the PSOM score. This analyzes neurological dimensions and classifies them into 4 levels. The final score results can indicate a good (mild impairment) or bad (moderate or severe impairment).

Of a total of 38 patients, 15 of them presented sequelae. Of these, 11 they belonged to the group of children and 4 were RNs. Within the RN group, 3/4 obtained a score of 1 and the other obtained a score of 1.5, placing them in the "Bad" category. In the group of children, 7/11 patients with sequelae obtained a score of 0.5, which classifies them in the "Good" category. 2 others obtained a score of 1, 1 patient obtained a score of 2 and 1 obtained a score of 5, placing them in the "Bad" category. Therefore, our results indicate that sequelae were more frequent and severe in the RN group compared with the kids.

Discussion

SCVT represents a diagnostic challenge due to the varied neurological manifestations related to the age of presentation, severity and location of the thrombus [6].

In this study, 55% of the patients were male. In the literature, the predominance of the male sex is associated with ECT. In our study, a total of 12 male patients presented as a risk of ECT compared to the 3 female patients with the same antecedent, coinciding with what is reported in the literature [7].

In various published series, RNs constituted between 30% and 50% of the patients with CVST [6,8,9]. In this series, 11 cases (21.5%) were identified during said period.

In the majority, at least one risk factor is identified, these are found in more than 80% of patients 1.90% of the cases in our series had risk factors for SCVT. Risk factors differ depending on age. In newborns, they are frequently associated with maternal diabetes, preeclampsia, chorioamnionitis, prematurity, asphyxia or after birth to infections, dehydration and polycythemia [5]. In our series, 100% of NBs had minus one. Locoregional infections predominate

in infants and children, ECT, dehydration, anemia, thrombophilias and/or prothrombotic factors, and pre-existing diseases such as nephrotic syndrome, lupus erythematosus systemic, inflammatory bowel disease and cyanotic congenital heart disease [5]. Dehydration, anemia, otomastoiditis, ECT and prothrombotic factors such as antiphospholipid syndrome (APS), lipoprotein deficiency associated with homozygosity for MTHFR and nephrotic syndrome were present in our series.

A Swiss study showed that mastoiditis and middle ear infections were the most relevant risk factor in 57% of patients under 16 years of age with TVSC [7,10]. In our study, 11.7% had this history.

Our series includes a patient with nephrotic syndrome who showed symptoms from HTEC. CSVT should be suspected in patients with nephrotic syndrome and neurological manifestations. These patients have hypercoagulability due to abnormalities in coagulation factors, platelet function and system fibrinolytic, which increases the risk of thromboembolic complications [11].

There are differences in clinical manifestations between newborns and children (Table 4). NBs usually show seizures, altered consciousness, vomiting or rejection of food. In older children, HTEC symptoms prevail, seizures and focal neurological signs [5,12]. These manifestations coincide with our series. It is important to suspect CSVT in newborns with risk factors. Prenatal or perinatal risk that manifest an acute condition of encephalopathy with or without seizures. On the other hand, in children with a history, mainly from ECT or localized infections, it should be suspected when present focal symptoms or elements of HTEC.

MRI angiography is considered the study of choice since it allows identifying directly the thrombus and secondary changes in the brain parenchyma. However, CTA can also establish the diagnosis in emergencies, that is a quick and effective method but it presents false negatives, although it can be identify pathological findings within 6 hours of the onset of symptoms, may be normal in the first 24 hours [13] (Figure 1). At our experience, 3 patients presented signs suggestive of SCVT on CTA initial, which were later confirmed by angio-MRI.

The neuroradiologist and clinician must have a high index of suspicion and evaluate direct and indirect signs to achieve an early diagnosis. In our study, although the diagnosis was confirmed in the majority of patients using MRI angiography in venous time, we had a considerable percentage of diagnoses through arteriography (13%), which were performed in the early years of our series and in cases of clinical suspicion with neuroimaging inconclusive. (Figures 2 and 3).

The topography varies according to the associated etiology, being the lateral sinus compromised in 70% of cases followed by the sagittal in 35%to 50% [14]. In our series, in the NB group, involvement of the venous system predominated. Deep, with the straight sinus the most affected, which differs from most of the reports [1,3,5,6,8,9]. On the other hand, in the group of children, the breasts most affected coincided with the literature with the lateral and sagittal being the most committed.

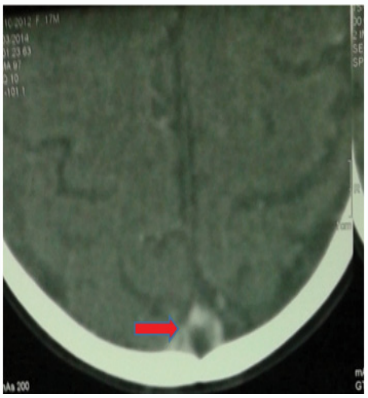

Figure 1: CT with contrast. Intraluminal filling defect in the posterior portion of the sinus sagittal "empty delta sign".

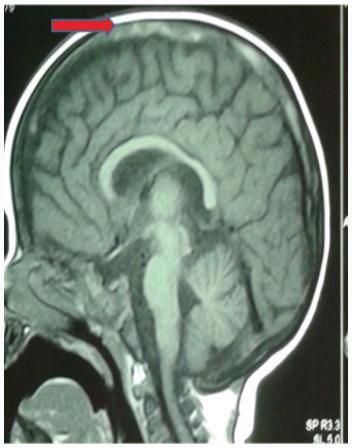

Figure 2: Sagittal MRI sequence T1 hyperintensity in sagittal sinus.

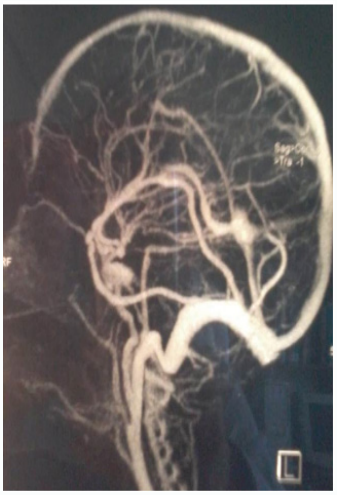

Figure 3: Angio MRI in venous time shows superior longitudinal sinus recanalization.

Table 4: Clinical manifestations according to age.

Age	Headache	Vomiting	Oculomotor Disorder	Seizures	Disorder awareness	Papilledema
Neonates	-	++	-	+++	+++	-
1m -12m	+ -	++	+ -	++	++	+ -
1-5 Years	++	++	+++	+	+	+++
>5 Years	+++	+++	+++	+	+	+++

One third of patients have venous infarctions, of which half they have a hemorrhagic component. Hemorrhage can also be primary and affect the parenchyma, intraventricular, subdural or subarachnoid system. The SCVT is one of the most common causes of intraventricular hemorrhage in Term RN [5,14]. In our series, 45.4% of the NBs presented HIV and 27.2% had intraparenchymal hemorrhages. On the other hand, in the group of children, the 6.4% had IVH and 25.8% had intraparenchymal hemorrhage. There are no pediatric studies comparing anticoagulants5. In children, it prefers unfractionated heparin (UFH) and LMWH for their good response and tolerance (Level E: 4) [6].

According to the American College of Chest Physicians 2012 guideline, in TVSC without significant hemorrhage, anticoagulants are recommended in newborns and children. Initially, UFH or LMWH, followed by LMWH or oral anticoagulants for minimum 6 weeks in RN and 3 months in older patients (Level E: 5). But there is complete recanalization or symptoms persist after 3 months, continue anticoagulation for 3 more months (Level E: 3). The presence of Minor bleeding does not contraindicate the use of anticoagulants, while Significant intracranial hemorrhage is considered a relative contraindication. It is recommended to carry out radiological surveillance for 5-7 days. In case of thrombus propagation, it is recommended to start anticoagulation (Level E: 3), in cases of recurrent risk such as nephrotic syndrome, it is recommended to consider prophylactic anticoagulation (Level E: 3) [15-17]. In the particular case of our patient with nephrotic syndrome, anticoagulation treatment was started without present recurrence.

This recommendation is supported by evidence that 25% to 30% of patients untreated will spread their thrombosis versus 5% of those who receive anticoagulation (Level E: 3) [18]. Of our patients they did not receive anticoagulation 9 (17.6%) due to the presence of significant bleeding or partial recanalization, while 42 (82.3%) received treatment with LMWH for three months or until evidence of thrombus recanalization.

Sequelae are common, mainly affecting motor function. Besides, children with SCVT show poorer performance on tests standardized neuropsychological tests [5,19].

In this series, no deaths were recorded despite the severity and risk, mortality (approximately 10%) [5]. Additionally, 44.5% of RNs and 38% of the older children evaluated presented sequelae, coinciding with what referred to in the literature.

Limitations

Our main limitations were follow-up, evaluation of sequelae and access to neuroimaging.

Conclusions

SCVT in pediatrics is an underdiagnosed entity that requires suspicion clinical presentation of neurological symptoms and predisposing factors. A diagnosis early treatment allows early treatment with anticoagulation. The delays are due to low incidence, variable clinical presentations and limited access to urgent neuroimaging. It is crucial to increase awareness about stroke in children among both doctors and caregivers.

Conflicts of Interest

None to declare.

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