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Case Report

Cerebral Venous Thrombosis in Children: About 3 Cases

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Abstract

The cerebral venous system is an unusual site for thrombosis. It is a rare pathology in children, with a considerable risk of morbidity and mortality in the absence of specific treatment. The incidence has increased over the last few decades due to improvements in neuroradiological techniques. Clinical features range from seizures, headache and respiratory distress to threatening focal neurological deficits and comatose state. The risk factors are age-dependent, frequently multiple and different from those reported in adults. Infections are the most common predisposing factor both in neonates and older children, followed by hypercoagulable/hematological states, dehydration and various other conditions. In majority of cases, it results from combination of prothombotic risk factors with or without underlying clinical condition. The prognosis is favorable in most cases if the diagnosis is made quickly and treatment is initiated promptly, although acute complications or chronic disability still occur in a quarter of patients. The mainstay of treatment is anticoagulation, which is needed to stop the clot spreading and recanalize it. Endovascular procedures are reserved for patients with a particularly severe presentation or rapidly developing neurological symptoms despite appropriate anticoagulation, although data from clinical trials is lacking. The aim of this work is to study the clinical, etiological, therapeutic and evolutionary characteristics of cerebral venous thrombosis (CVT) in the pediatric population.

Keywords

Thrombosis, Cerebral, Venous, Imagery, Anticoagulation, Evolution

1. Introduction

Cerebral venous thrombosis (CVT) is a rare form of cerebrovascular event in children and represents 10% of childhood strokes.

It is the formation of a thrombus within a vein or an intracranial venous sinus occurring on a favorable ground or a triggering circumstance.

The clinical presentation is varied and the diagnosis is based on brain imaging.

It is a diagnostic and therapeutic emergency causing serious complications including intracranial hypertension and parenchymal lesions.

There are 3 cases of CVT reported in children collected at the pediatric neurology unit of the Abderrahim El Harrouchi mother and child hospital in Casablanca, over a period of 2 years (January 2022-February 2023) in order to determine the clinical and radiological characteristics, etiological and progressive as well as the methods of management of this condition. [1]

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2. Methods

This is a descriptive study of 3 cases of CVT, managed within the pediatric neurology unit of the Abderrahim El harrouchi hospital in Casablanca, during the period 2022-2023. The diagnosis of CVT was established on CT data (without and with injection of contrast product) and magnetic resonance imaging (MRI) associated with angiographic sequences. Several parameters were studied: age, sex, personal or family history of thrombophilia, initial symptomatology and mode of onset (acute < 2 days, subacute: 2 days to 1 month, chronic > 1 month), radiological characteristics and the topography of the lesions. The location of the thrombosis was classified as superficial or deep, single or extensive, and parenchymal lesions were systematically searched for. The etiological investigation systematically included a complete infectious assessment, an oto-laryngological and ophthalmological examination, the study of hemostasis and thrombophilia and other assessments depending on the etiological orientation. The treatment modalities and the functional and vital prognosis were also evaluated.

3. Cases Presentation

3.1. Observation #1

Young girl aged 13, with no particular pathological history, hospitalized for intracranial hypertension syndrome associated with convulsions. Clinically, she presented with generalized tonic-clonic convulsive seizures with heaviness of the left hemibody associated with headaches and a decline in visual acuity lasting for 20 days.

On ophthalmological examination: papilledema stage 1 to 2. There was no edematous syndrome, the urine dipstick was negative; without proteinuria or hematuria.

Paraclinically: Brain scan with injection: normal; Brain MRI: Non-obstructive partial venous thrombosis of the superior longitudinal sinus. The lumbar puncture with pressure measurement was elevated to 55 cm of water.

The thrombophilia assessment was normal, namely protein S level at 80%, protein C at 70%, anti thrombin at 90%, homocysteine: 5.5 umol/l (<15umol/l) mutation of factor II and V de leyden: absence of mutation. Normal autoimmune assessment: C3 normal to C4: 0.40, anti-nuclear antibodies, anti-DNA and anti-phospholipid syndrome assessment were negative. Hemoglobin electrophoresis: normal. Cardiac ultrasound was normal, HLA B5 normal.

The patient was put on Acetazolamide (diamox) and LMWH at a rate of 100 IU/kg/12h.

The evolution was marked by the improvement of the clinical symptoms and the regression of the papilledema. Repermeabilization of the superior longitudinal sinus. Hence the cessation of treatment after 3 months.

3.2. Observation #2

Infant aged 13 and a half months, with no particular pathological history. Admitted for generalized tonic-clonic seizure with postictal coma and Gh hemiparesis evolving 10 days before hospitalization. On clinical examination: hypotonia, bulging anterior fontanelle, macrocrania (PC: 49 cm +3DS). On ophthalmiological examination: bilateral stage 1 papilledema.

Cerebral CT angiography showed cerebral venous thrombosis of the cerebral sinuses extending to the jugular veins complicated by bilateral supratensorial ischemia. Clinically no edematous syndrome, urine dipstick was normal without proteinuria or hematuria, blood pressure was normal at 9/5 and serum albumin normal at 35 g/L.

The entire etiological assessment was without abnormalities, namely: cerebral CT angiography, hemoglobin electrophoresis, echocardiography and assessment of anti-phospholipid syndrome (negative IgM and positive IgG cardiolipin antibodies, anti b2 glycoprotein IgM antibodies and negative IgG). The Thrombophilia assessment showed: Protein S was collapsed at 44%, protein C at 91%, antithrombin at 140%, normal homocysteine at 7.9 umol/l, absence of factor II AND V mutation,

The patient was placed on LMWH at a dose of 100IU/kg/12h.

Evolution: After 2 and a half months, the patient presented with convulsive status without change in the clinical examination. The brain scan revealed subacute bilateral subdural hematomas with cerebral thrombophlebitis of the superior sagittal sinus extending to the confluence and the right transverse sinus. The patient benefited from drainage with maintenance of the LMWH. The thrombosis of the right, upper longitudinal sinus had partially persisted, which motivated the maintenance of treatment with LMWH for a period of 6 months.

3.3. Observation #3

Child aged 6, admitted for headaches, vomiting and impaired consciousness lasting 3 days. The ophthalmological examination was normal.

Paraclinically: Brain CT showed a subarachnoid hemorrhage classified Fisher II, brain MRI showed thrombophlebitis of the right transverse and sagittal sinus. The patient was placed on LMWH.

Etiological assessment including: cardiac ultrasound, hemoglobin electrophoresis, anti-phospholipid syndrome assessment, thrombophilia assessment; came back normal.

On the evolutionary level, the control angioscan showed the persistence in the right sinus, the superior sagittal sinus and the right transverse sinus of a hypodense material filling the lumen. Hence the continuation of the treatment for 6 months.

4. Discussion

Cerebral venous thrombosis is rare in children but has serious consequences; it represents approximately 10% of childhood strokes. It is a diagnostic and therapeutic emergency due to intracranial hypertension and parenchymal lesions. [2]

It is the constitution of a thrombus within a vein or at the level of an intracranial venous sinus, they occur exceptionally spontaneously outside the neonatal period, and are generally linked to risk factors under -most often acquired and transient: central venous catheter, cancer, acute pro-inflammatory context, nephrotic syndrome, sickle cell anemia, etc [3].

The clinical presentation of CVT in children is very varied; clinical manifestations are linked to the type of vessel affected (vein or artery) and the location of the clot (thrombus) within the blood network. [4]

The circumstances of discovery in children are the signs of intracranial hypertension (the headaches are subacute intense, permanent), psychomotor slowing, ophthalmology, convulsions, focal motor deficit, disorders of vigilance or fortuitous discovery in imaging. [5]

In infants, the symptoms are dominated by unusual crying, asthenia, bulging of the anterior fontanelle.

There are also unusual aspects that sometimes make the diagnosis difficult to make: transient symptoms such as an isolated seizure; psychiatric disorders; symptoms mimicking a migraine with or without aura; isolated headaches. [6]

The diagnosis of CVT is urgent in order to begin the appropriate treatment, and is based on imaging which allows the positive diagnosis as well as the diagnosis of severity and sometimes the identification of the etiology or an associated pathology. The brain scan is the examination carried out urgently without iodinated contrast; it may show spontaneous hyperdensity along the path of a venous sinus and then disappearance. Facing the thrombus, the sinus wall may lose its physiological concavity and appears globular and convex with iodine contrast; the wall of the sinus or vein is enhanced while the thrombus does not take up the contrast, this only parietal enhancement explains the delta sign. [7]

It is associated with non-specific anomalies which are the consequences of obstruction of the venous sinus such as cerebral edema with disappearance of the cortical furrows and crushing of the ventricular system or a venous infarction appearing in the form of hypodensity or a hemorrhagic lesion. more or less extensive visible in the form of hyperdensity.

MRI remains superior to CT for cortical venous thrombosis and parenchymal lesions. T1, T2 and Flair weighted acquisitions make it easy to diagnose thrombus in a sinus: frank T2 hypo intensity whose diameter appears greater than that of the normal venous structure then hyper intense after a week then iso or even hypo intense. MRI angiography is also essential for the diagnosis and assessment of venous thrombosis. Although it does not visualize the signal changes of the thrombus, it shows the absence of opacification of the venous structures. In addition, it allows precise assessment of lesion extension and recanalization. [8]

A gadolinium injection is often necessary and shows the delta sign. Study of the brain parenchyma: vasogenic/cytotoxic edema, hemorrhagic venous infarction lesions (with T2 hypointensity often in the form of multinodular and subcortical flaky areas, lobar hematoma +/- commitment.

The etiological assessment is based on the search for an underlying pathology favoring:

The numerous conditions favoring the occurrence of cerebral venous thrombosis include the known causes of occurrence of deep thrombosis of the lower limbs in surgical contexts, or secondary to a medical pathology, they are also represented by locoregional infectious causes or by non-infectious events such as as head trauma, local compressive tumor processes. (Table 1) [9]

Table 1. *Causes and contributing factors involved in cerebral venous thrombosis.*

Infectious		**Non-infectious**	
Local	**General**	**Local**	**General**
1. Trauma 2. Septic cranial 3. Cranial infectious process: Abscess, empyema, neighboring infection: otitis, mastoiditis	1. Bacterial: 2. Sepsis, endocarditis, tbk 3. Viral: encephalitis, measles 4. Parasites: malaria	1. Head trauma 2. Tumor 3. Intracranial malformation: arachnoid cyst 4. Vascular Malformation	1. Autoimmune and inflammatory diseases: antiphospholipid syndrome, SLE 2. Neoplasia: lymphoma, leukemia 3. Hemoglobinopathies: sickle cell disease 4. Coagulation abnormalities: anti-thrombin III, protein S or protein C deficiency 5. Leiden factor II and V mutation DIC 6. Heparin-induced thrombocytopenia, plasminogen deficiency

Treatment is urgent with the aim of limiting the extension of the thrombus and promoting its disintegration in order to accelerate recanalization and is based on 3 aspects:

1. *Symptomatic treatment*: mainly aims to combat intracranial hypertension. It includes diuretics, hyperosmolar solutions (mannitol), fluid restriction, subtractive lumbar punctures.
2. *Etiological treatment:* consists of treating the disease causing venous thrombosis. To be started urgently, particularly in cases of septic cerebral venous thrombosis.
3. *Anti-thrombotic treatment*: it is started as soon as CVT is diagnosed, in the absence of contraindication. Local cerebral hemorrhagic suffusions complicating venous hyperpressure linked to thrombosis are not a contraindication to anticoagulant treatment.
   a) Low molecular weight heparins (LMWH: Enoxaparin or Tinzaparin) used as first-line treatment, a switch to vitamin K antagonists (AVK) can be taken early.
   b) Initial treatment with unfractionated heparin is possible, particularly in the intensive care unit or intensive care unit.
   c) Dose: 150 IU/kg/12h if < 2 months and 100 IU/kg/12h if > 2 months.
   d) Duration: 3 months for provoked thromboses, 6 weeks if thromboses in an infectious context and 6 months for spontaneous ones.
4. *The follow up anticoagulant treatment*:
   1) Under UFH or LMWH:
      a) Monitor thrombocytopenia blood counts the first 2 to 3 weeks of treatment.
      b) Anti-Xa monitoring is not recommended throughout treatment, but at least at the start of treatment to avoid any overdose in children.
      c) The anti-Xa targets are 0.5 to 1 IU at a curative dose.
   2) Under AVK:
      a) Monitoring of INR throughout treatment to adapt the dosage.
      b) The INR goal is 2-3.

The prognosis of CVT essentially depends on the age of the child, the etiology and the location of the CVT. According to a study carried out on 12 patients; the outcome was fatal in 2 children, due to diffuse and deep damage in one child and a picture of severe dehydration with organic renal failure in the other. Specific mortality from CVT is less than 10%, but residual neurological deficits are reported in between 17% and 79% of cases. Irreversible after-effects were noted in 27% with a mortality rate of 18%. [10]

5. Conclusion

Cerebral venous thrombosis is an uncommon thrombotic vascular condition whose clinic is polymorphous both in its mode of onset and in its symptomatic expression at the state phase. Its diagnosis is based on the demonstration by MRI and angio-MRI of the thrombus within a cerebral venous structure, the disturbances of venous drainage and its consequences on the parenchymal level. Its diagnosis requires the emergency implementation of anticoagulant treatment at a curative dose as well as the carrying out of an exhaustive etiological assessment in search of a constitutional or acquired thrombopathy but also of an infectious or non-infectious locoregional cause.

Abbreviations

CVT	Cerebral Veinous Thrombosis
MRI	Magnetic Resonance Imaging
CT	Cerebral Thrombosis
HLA	Human Leucoyte Antigen
LMWH	Low Molecular Weight Heparin
PC	Head Circumference
IgG	Immunoglobulin G
IgM	Immunoglobulin M
INR	International Normalized Ratio
DS	Standard Deviation
UFH	Unfractionatd Heparin

Author Contributions

Imane Menjel: Conceptualization, Formal Analysis, Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing – review & editing

Conflicts of Interest

The authors declare no conflicts of interest.

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