Clinical and Radiological Patterns of Cerebral Venous Sinus Thrombosis in Children

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ABSTRACT

Background: Cerebral venous thrombosis is a rare disease in children, but it is considered an important cause of infarction due to its potential morbidity. Since magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) are widely used, the reports with confirmed diagnosis are increased. Objectives: To identify the common clinical presentations and radiological findings of cerebral venous sinus thrombosis (CVST) in pediatric age group, and to investigate thoroughly the underlying predisposing conditions. Methodology: This study included 13 children with CVST confirmed by MRI and MRV. Patients were submitted to complete general and neurological examination, Electroencephalography (EEG), and routine laboratory tests in addition to complete coagulation profiles including protein C, protein S, and Anti thrombin III, hemoglobin electrophoresis, Anticardiolipin autoantibodies, and antinuclear antibodies. Screening tests for homocystein, lactate, pyruvate and ammonia serum levels were done and Factor V Leiden was done for 5 cases only. Results: Headache was the main presenting clinical picture of cases, followed by nausea, vomiting, seizures and papilledema. MRI brain was done prior to MRV and most patients 12/13 (92.3%) showed loss of normal signal void pattern of involved sinuses. Ten patients (76.9%) showed cerebral parenchymal changes, and MRV showed that superior sagittal sinus (SSS) was the most common vessel to be involved (84.4%) either alone or in combination with other dural sinuses, followed by transverse and sigmoid sinuses either alone or in combination with SSS (53.8%). Ten cases (76.9%) had detectable identifiable factors which included dehydration, prothrombotic disorders either hereditary or acquired disorders, and we had one patient with recurrent CVST and Moya-Moya disease. Conclusion: MRI in conjunction with MRV are both sensitive and specific enough to provide the best non-invasive method of diagnosing CVST in pediatric patients, in whom hereditary or acquired prothrombotic risk factors should be tested carefully. (Egypt J. Neurol. Psychiat. Neurosurg., 2008, 45(2): 361-374)

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) in children is a rare but serious disorder that affects at least 0.67 per 100 000 children per year, and it accounts for less than 1% of all strokes¹. The increasing reports of this disorder had been described since the evolution of the magnetic resonance imaging (MRI)³ that helps in early and definite diagnosis and rapid intervention which can significantly improve the outcome³. Ideally, therapy should be started before the patient has developed significant edema and/or permanent cerebral insults, and though mortality figures range from 20% to 78% in different patients series, yet there is a trend of lowered rates with increased availability of MRI and early intervention⁴. The importance of inherited and acquired coagulation disorders and other thrombophilic factors has been emphasized in various series of pediatric CSVT as major risk factors²,⁵,⁶. Other prethrombotic conditions that can increase blood viscosity, such as polycythemia, chronic hypoxia, dehydration may predispose to cerebral venous thrombosis, and these factors could be present in 30% to 40% of cases with sino-venous thrombosis⁷. Anemia is another risk factor, possibly because of alteration in hemodynamics or imbalances in thrombotic pathways⁸, however, no etiology is found in 20 to 30% of the cases⁹.
Clinical diagnosis of CVST is frequently overlooked or delayed due to diverse presentations and wide spectrum of non-specific clinical symptoms that range from subtle manifestations to aggressive scenarios that are either life-threatening or causing long-term neurological deficits. The most frequently encountered symptoms are headaches, other symptoms of raised intracranial tension, seizures, presentation of pseudo-tumor cerebri and focal neurological deficits. De Veber et al. reported that 58% of those children had seizures, 76% had diffuse neurologic signs, and 42% had focal neurologic signs. The evaluation of children with suspected CVST has been made precisely and more easier by modern neuroimaging techniques. Unenhanced CT scans may detect signs of venous thrombosis as linear densities, and as the thrombus becomes less dense, contrast may demonstrate the “empty delta” sign, a filling defect, in the posterior part of the sagittal sinus. However, CT scan with contrast can miss the diagnosis of CVST in up to 40% of patients, then confirmatory diagnostic imaging should be performed with MRI, magnetic resonance venography (MRV) or diffusion and perfusion MRI.

Current therapeutic measures which are used in clinical practice include the use of anticoagulants either the dose-adjusted intravenous heparin or body weight-adjusted subcutaneous low-molecular-weight heparin, the use of thrombolysis, and symptomatic therapy including control of seizures and elevated intracranial pressure.

The aim of this work was to identify the common clinical presentations and radiological findings of CVST in pediatric age group and to investigate thoroughly the underlying predisposing conditions and risk factors.

SUBJECTS AND METHODS

Study Design and Enrollment Criteria

This was a prospective, descriptive study that included 13 Egyptian children with definite diagnosis of cerebral venous thrombosis based on MRI and MRV findings assessed by expert neuroradiologist. They were recruited from the Neurology and Pediatrics departments of Cairo University Hospitals. Their age ranged from 6.1 to 12 years with a mean age of 8.76±1.72 years. Patients were eligible for the current study if they had definite CVST with normal perinatal history, and having normal developmental history.

Exclusionary Criteria. (1) Patients with previous global delay, (2) a known epileptic patients, (3) patients who had diagnosed as CNS infection (meningitis or encephalitis), and (4) patients with positive history of drug intake which alter the coagulation status.

Patient Evaluation

All patients enrolled in this study were submitted to a conjoint assessment composed of a neurologist and a pediatrician to evaluate their general and neurological status. Any pre-existing medical conditions and predisposing factors were recorded.

Neurological Assessment

Neurological signs and symptoms (conscious level assessed by Glasgow coma scale, convulsions, hemiplegia and other focal neurologic deficits, signs of increased intracranial tension, and ophthalmological and funduscopic examination) were frequently rated, and functional outcome was evaluated by using the Glasgow Outcome Scale (GOS) at the time of discharge and during follow-up period.

Laboratory Profile

All included children were subjected to the following tests; CBC including platelets counts and ESR, liver and kidney functions tests, serum electrolytes, complete coagulation profile (prothrombin time and concentration, INR, Partial Thromboplastin Time (PTT), protein C, protein S, and Anti thrombin III), hemoglobin electrophoresis, anticardiolipin autoantibodies (IgG, and IgM), antinuclear antibodies, lupus anticoagulant, screening tests for Homocystein, lactate, pyruvate and ammonia serum levels, and Factor V Leiden was done for 5 cases out of 13.

Digital EEG

All patients had their EEG carried out at at Neuropediatrics Department in Children Hospital, or the Neuropsychiological Department of Kasr El-Aini Hospital. All EEGs were carried either under standard conditions or after sedative premedications as chloral hydrate in non-cooperative children or
those with irritability. Hyperventilation was used whenever possible and IPS was used for all patients. EEG electrodes were placed on the patient's head according to the international 10-20 system using a cap to which the electrodes are adherent. The EEG machine parameters were adjusted before the recording as follows; time constant: 0.3 seconds; drawing speed: 3.0 cm/sec; filter: 75 Hz for EEG; and gain: 70 µv/cm. The EEG tracing was analysed carefully as regards; background activity, presence of generalized or focal slowing and epileptogenic discharges. According to the classification applied by Elwan et al.\textsuperscript{17}; the recorded EEG findings were described as normal or abnormal; the abnormalities were described either epileptogenic activities or background abnormalities. The epileptogenic activities were either focal discharges (whether alone or with secondary generalization) or generalized discharges. Background abnormalities were either focal or generalized slowing and its form was either delta or theta activities.

Magnetic resonance imaging (MRI), and Magnetic resonance venography (MRV). Most of the patients had their MRI and MRV carried out at the Radiodiagnosis Department of Kasr El Eini Hospital on closed 1T unit and others in private center on 0.2 T open unit. All studies were carried out either under standard conditions or after sedative premedication in non cooperative or irritable children.

MR sequences. Sagittal and axial T1 spin echo, coronal or axial fluid–attenuation inversion recovery (FLAIR) and axial or coronal T2 fast spine echo sequences are routinely included in our studies. 2D time of flight MRV is the method used for the diagnosis of dural venous sinus thrombosis. Because 2D techniques are most sensitive to flow that is perpendicular to the plane of acquisition, the coronal plane, axial and coronal planes, or an oblique plane are often used for image acquisition and by using an inferior saturation slab to saturate arterial inflow. A close assessment of the source images is mandatory to accurately evaluate venous morphologic features and reduce the potential for diagnostic error, and no contrast agent was administered. Source images were reconstructed by using a maximum intensity projection (MIP) algorithm and viewed in multiple oblique and orthogonal projections.

Image analysis. Thrombosis may be identified on spin echo images as an absence of the normal flow void and presence of altered signal intensity in the sinus. On MRV, thrombosis manifests itself as lack of signal. Thrombus signal intensity differs on T1 and T2-weighted spin echo images and evolves with the phases of haemoglobin degradation. Focal brain edema, secondary venous infarctions and foci of hemorrhage can be seen with spin echo images.

Management. All patients included in the current study received maximum medical management which included the routine intensive care monitoring. Whenever diagnosis was established patients received anticoagulation using the standard regimen of dose-adjusted IV heparin till sufficient activated PTT level was reached, then followed by oral anticoagulation\textsuperscript{14,18}. Specific management for the identified predisposing factors and symptomatic management including control of fever, seizures and elevated intracranial pressure were adopted\textsuperscript{18} and mechanical ventilation was used whenever indicated.

Statistical Analysis:
Data analysis was carried out with the Statistical Package for Social Sciences (version 10.0, 1999; SPSS Inc. Chicago, IL, USA). We used descriptive statistics to measure the mean±SD, number and percentages.

RESULTS

Clinical Characteristics
This study included 13 patients with confirmed diagnosis of cerebral venous thrombosis who were hospitalized in Neurology and Pediatrics Departments of Cairo University Hospitals. The studied group comprised of 8 females and 5 males with a female to male ratio 1.6 : 1. Their ages ranged between 6.1 to 12 years with a mean age of 8.76±1.72 years. Basic clinical characteristics of included patients on hospital admission were shown in Table (1).

All of cases were previously normal in motor and mental development and none of them had evidence of acquired or congenital heart diseases.

EEG Findings
Ten cases developed seizures and 8 of them showed abnormal EEG findings (Table 2).
Focal epileptic discharges were represented as high amplitude, slow waves with sharpish contour. Subcortical activity showed generalized paroxysmal discharges of spike and wave complexes. All cases with normal MRI showed also normal EEG record.

**MR Findings**

Twelve patients (92.3%) out of 13 examined by MRI showed loss of the normal signal void pattern seen in the dural venous sinuses, the last case showed almost no abnormalities in their MRI images, but MRV proved dural venous sinus thrombosis by loss of normal venous signal in the left transverse sinus (Fig. 5). Ten cases (76.9%) out of 13 examined by MRI showed cerebral parenchymal changes. MRI and MRV findings are presented in tables (3, 4).

**Predisposing risk factors**

Among the studied populations, three (23.1%) patients had no identified etiologies; whereas, 10 (76.9%) had detectable factors which included dehydration, prothrombotic disorders either hereditary (Deficiency of protein S and mutation of Factor V Leiden) or acquired disorders (LA, ACA, TTP), and we had one patient with Moya moya disease (Table 5).

**Outcome Measures**

On discharge, 5 (38.5%) patients showed good recovery (grade 1 by GOS); as they can lead a full and independent life with minimal neurologic deficit, 5 (38.5%) were moderately disabled (grade 2 by GOS); as they had neurological impairment but still they were independent, 2 (15.4%) were severely disabled and totally dependant on their caregiver (grade 3 by GOS) and one (7.7%) patients died, the residual neurologic deficits at time of discharge are shown in table (6). The mean duration of hospital stay was (7±1.53) days with a range from 5 to 10 days.

**Follow up period.**

Seven patients were followed up from 6 months to 12 months with a mean of 8.36±2.14 months. At follow-up, only one patient had a recurrent attack after 5 months, while she was on oral anticoagulation with satisfactory INR ranged from 1.9 to 2.4 following the first attack. This patient was diagnosed as Moya Moya disease based on her clinical data (she had had an occlusive arterial disorder presented with right sided hemiparesis and right homonymous field defects 9 months before the diagnosis of venous thrombosis), her MRA was diagnostic (Fig. 8), then she had two attacks of venous sinus thrombosis with 5 months apart in form of hemiplegia, seizures, manifestations of increased intracranial pressure and third nerve palsy. Her MRV showed occlusion of left transverse and left sigmoid sinuses. Other patients showed a satisfactory gradual and constant trend of improvement during the follow up period.

**Table 1.** Baseline clinical characteristics of the study population.

<table>
<thead>
<tr>
<th>Clinical presentations</th>
<th>No of patients (%)</th>
</tr>
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<tbody>
<tr>
<td>Headache</td>
<td>13 (100%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>10 (76.9%)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>11 (84.6%)</td>
</tr>
<tr>
<td>Disturbed conscious level</td>
<td>7 (53.8%)</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>9 (69.2%)</td>
</tr>
<tr>
<td>Cortical blindness/hemianopia</td>
<td>4 (30.8%)</td>
</tr>
<tr>
<td>Third nerve palsy</td>
<td>2 (15.4%)</td>
</tr>
<tr>
<td>Papilledema</td>
<td>10 (76.9%)</td>
</tr>
<tr>
<td>Ataxia</td>
<td>5 (38.5%)</td>
</tr>
<tr>
<td>Chorea</td>
<td>4 (30.8%)</td>
</tr>
<tr>
<td>Sensory affection</td>
<td>4 (30.8%)</td>
</tr>
</tbody>
</table>
Table 2. Types of EEG abnormalities in studied population.

<table>
<thead>
<tr>
<th>EEG findings</th>
<th>No of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal discharges</td>
<td>4 (30.8%)</td>
</tr>
<tr>
<td>Multifocal activity</td>
<td>1 (7.7%)</td>
</tr>
<tr>
<td>Subcortical activity</td>
<td>3 (23.1%)</td>
</tr>
</tbody>
</table>

Table 3. MRI findings in studied population.

<table>
<thead>
<tr>
<th>MRI Findings</th>
<th>No of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of signal void in dural sinus only</td>
<td>2 (15.4%)</td>
</tr>
<tr>
<td>Loss of signal void and cerebral parenchymal change</td>
<td>10 (76.9%)</td>
</tr>
<tr>
<td>No MRI abnormality but abnormal MVR</td>
<td>1 (7.7%)</td>
</tr>
</tbody>
</table>

Table 4. MRV findings and extension of dural venous sinus thrombosis among studied population.

<table>
<thead>
<tr>
<th>MRV Findings</th>
<th>No of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior sagittal sinus thrombosis alone.</td>
<td>6 (46.2%)</td>
</tr>
<tr>
<td>Superior sagittal sinus thrombosis in combination with other sinuses.</td>
<td>5 (38.5)</td>
</tr>
<tr>
<td>Transverse or sigmoid sinus alone or in combination with each others</td>
<td>2 (15.4%)</td>
</tr>
</tbody>
</table>

Table 5. Identifiable predisposing factors in studied population.

<table>
<thead>
<tr>
<th>Predisposing factor</th>
<th>No of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dehydration</td>
<td>2 (15.4%)</td>
</tr>
<tr>
<td>LA</td>
<td>1 (7.7%)</td>
</tr>
<tr>
<td>ACA</td>
<td>2 (15.4%)</td>
</tr>
<tr>
<td>TTP</td>
<td>1 (7.7%)</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>2 (15.4%)</td>
</tr>
<tr>
<td>Deficiency of protein S</td>
<td>1 (7.7%)</td>
</tr>
<tr>
<td>Moya moya disease</td>
<td>1 (7.7%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10 (76.9%)</strong></td>
</tr>
</tbody>
</table>

Table 6. Residual neurologic deficits at time of hospital discharge.

<table>
<thead>
<tr>
<th>Residual neurologic deficit at discharge</th>
<th>No of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>3 (23.1%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>6 (46.2%)</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>7 (53.8%)</td>
</tr>
<tr>
<td>Cortical blindness/ hemianopia</td>
<td>2 (15.4%)</td>
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<td>Third nerve palsy</td>
<td>1 (7.7%)</td>
</tr>
<tr>
<td>Ataxia</td>
<td>2 (15.4%)</td>
</tr>
<tr>
<td>Sensory affection</td>
<td>2 (15.4%)</td>
</tr>
</tbody>
</table>
Figures from 1 to 9 showed representative cases in our study.

**Fig. (1):** Axial T1-weighted images (A) for 6.9 year old girl with positive anticardiolipin antibodies showed focal area of high signal in the anterior part of the SSS thrombus. Axial T2 (B) and coronal FLAIR weighted images (C) showed focal area of signal abnormality in the right parietal lobe with high signal intensity thrombus in the anterior part of SSS is noted. Sagittal MRV TOF (D) of the same patient proved segmental anterior SSS thrombosis.

**Fig. (2):** Sagittal oblique MRV TOF for 11.2 year old girl with positive anticardiolipin antibodies showed occlusion of the posterior part of SSS and both transverse sinuses.

**Fig. (3):** Axial T1 (A, B) and T2 (C) weighted images showed high signal thrombus in SSS and right transverse sinus in 9.8 year old girl with unremarkable definite diagnosis. Hemorrhagic parenchymal changes were noted for the same patient in the right temporal and right parietal lobes with evidence by high signal of subacute blood in T1-weighted images.
Fig. (4): Coronal, FLAIR weighted images (A, B) for 8 year old boy with mutation of Factor V Leiden showed loss of normal signal void pattern in superior sagittal, left transverse and left sigmoid sinuses with high signal thrombus noted within. Left high parietal, high signal parenchymal change is noted.

Fig. (5): Coronal MRV TOF for 7.3 year old boy with severe dehydration and hyper viscosity showed occlusion of left transverse sinus.

Fig. (6): Axial T1 (A, B) and T2 (C) images for 12 year old girl with positive Lupus anticoagulant showed high signal in SSS, right transverse and right sigmoid sinuses. Multiple focal areas of abnormal parenchymal signal in the right cerebral hemisphere and edema with subacute blood of high T1 signal noted within.
Fig. (7): Axial T1 (A), axial T2 (B), sagittal T1 (C) images for 7.5 year old girl patient with hypercoagubility state (deficiency of protein S) showed loss of signal void and presence of high signal thrombus in the posterior part of SSS. Associated bilateral parenchymal signal changes are seen in the parietal regions. Sagittal (D) and coronal (E) MRV TOF for the same patient showed thrombosis in the posterior part of superior sagittal sinus.

Fig. (8): 6.10 years old girl presented with hemiplegia, third nerve palsy, headache and seizures. Her MRA (A, B, C) and MRV (D), showed occlusion and attenuation of the vessels of the circle of Willis especially the A1 and M1 segments of the anterior and middle cerebral arteries respectively as well as the left posterior cerebral arteries with hypertrophied basilar and right posterior cerebral arteries together with presence of dilated external carotid artery branches. MRV showed occluded left transverse and left sigmoid sinuses. The case was diagnosed as moyo-moya disease with dural venous sinus thrombosis.
Fig. (9): Axial T1 (A), and Axial FLAIR (B) images for a boy, 9 years with mutation of Factor V Leiden showed loss of signal void and focal area of increased signal in SSS and straight sinus representing thrombus. An area of increased FLAIR signal is noted in the left cerebral peduncle. Sagittal T2 (C) weighted images showed thrombus in SSS and straight sinus as well as parenchymal changes in brain stem (The case was diagnosed as SSS and straight sinus thrombosis).

DISCUSSION

Although cerebral venous sinus thrombosis is rare in children, information on clinical characteristics, radiological findings and outcome is emerging. Thrombosis of the venous channels in the brain is an uncommon cause of cerebral infarction relative to arterial disease, but is an important consideration because of its potential morbidity. Hypercoagulable states via multiple mechanisms as well as a variety of medical and surgical comorbidities may confer increased risk of CVST, whilst single or multiple concomitant thrombophilic factors may increase the relative risk of CVST; its low prevalence makes it difficult to identify patients at high absolute risk who may benefit from prophylactic anticoagulation.

Cerebral venous thrombosis is believed to be more common in females than males, and in the study of Ameri and Bousser, the female to male ratio was 1.29:1, this was in agreement to our result that showed female to male ratio of 1.6:1, while the results of Carvalho et al. showed the reversal pattern as there were 21 males and 10 females; however, in this study was retrospective and 61% of included patients were neonates, an age group that was not addressed in our study.

Symptoms and signs of cerebral venous thrombosis may evolve over days. In neonates, it is characterized by diffuse neurologic signs and seizures, whereas focal neurologic signs are more prominent in older children. In the current study, headache was the most prominent symptoms that presented in all cases (100%). This finding was in concordant with that reported by Saneto et al. in 2000 who found that headache was the most frequent symptom in their patients with cerebral venous thrombosis. Other clinical presentations included in our study were nausea and vomiting in 84.6%, seizures in 76.9%, disturbed consciousness merging to coma in 53.8%, sings of pyramidal tract lesions in 69.2%, and papilledema in 76.9%. Other focal neurological deficits in the form of cortical blindness and hemianopia, third nerve palsy, ataxia, chorea, and sensory loss were present in a lower percentage.

The clinical presentations varied from one study to other depending on the age of patients included in each study. So, in the study of Buccino et al. in 2003 which included patients with younger age than our cases; the presenting features were seizures in 59%, headaches in 18%, disturbed consciousness in 50%, papilledema in 18% and cranial nerve palsy in 33%. While patients included in the study of Sebire et al. with a mean age close to
that of our series had anorexia, vomiting, headache, seizures and disturbed consciousness as the main presenting features.

Currently, the combination of T1- and T2-weighted spin echo magnetic resonance imaging (MRI) sequences with MR venography is considered the best diagnostic tool for diagnosing cerebral venous thrombosis. MR may identify both the intraluminal clot in the deep venous system, decreased flow-related enhancement within the dural venous sinuses and concomitant parenchymal findings that vary according to the stage of the process from normal to cerebral oedema and subcortical hyperintensities in T2 and FLAIR sequences and in more severe cases cerebral hemorrhages could be detected. In the involved veins, flow voids may be replaced by abnormal signals, and the specific appearance of the abnormalities varies according to the age of the thrombus and the imaging parameters used.

In the current study; MRI brain was done prior to MRV and most patients 12/13 (92.3%) showed loss of normal signal void pattern of involved sinuses and cerebral parenchymal changes were noted in 10/13 (76.9%) of our patients. These findings were in concordance with what was reported by Connor and Jarosz [2] that confirmatory diagnostic imaging should be performed with MRI and MRV when there is suspicious of CVST, where they found that MRI is 100% sensitive in detecting dural venous sinus thrombosis depending on the radiological sign of the loss of normal signal void and presence of abnormal signal in the affected sinus. Our only case that showed normal MRI was a case with severe dehydration complicated by transverse sinus thrombosis in which loss of signal void could not be detected and was not associated with notable parenchymal changes. Diagnosis was suspected on clinical background and was then confirmed by MRV (Fig. 5).

In view of the variable nature of the parenchymal abnormalities that may occur in CVST, the use of the term venous infract in reference to these lesions should be discouraged because that term implies irreversibility; but in contrast with arterial ischaemic states, many parenchymal abnormalities secondary to venous occlusion are reversible [23]. Other investigators found in their study by diffusion weighted MRI, cerebral parenchymal changes in 90% of their cases, which is relatively higher than our result and this could be due to the high sensitivity of the diffusion sequences that could detect early subtle parenchymal changes [25]. According to the MRV findings in the current study, the most common vessel involved in our cases was the superior sagittal sinus (SSS) that was detected in 11 cases (84.6%) either alone or in combination with other dural sinuses, while transverse sinuses involved in 7 cases (53.8%) also either alone or in combination with others. This finding was in agreement with the results of Suwonpanich and Laothamatas [27] in 2007 who showed that the commonest site of involvement was SSS followed by left and right transverse sinuses; on the other view, Sebire et al. [7] found that transverse sinus was as common as SSS in their cases, whereas, Wasay et al. [28] showed that in their patients; transverse sinus thrombosis was more common and represented (73%), while sagittal sinus thrombosis represented only (35%).

As regards the etiology that we aimed to identify, predisposing factors were detected in ten cases (76.9%) of our series. These included prothrombotic disorders either hereditary, as deficient regulatory protein S (7.7%) and heterozygous mutation of Factor V Leiden (15.4%); or acquired disorders with positive lupus anticoagulant (7.7%), antiphospholipid autoantibodies (15.4%), and thrombotic thrombocytopenic purpura (7.7%) cases. Dehydration was observed in 2 (15.4%) cases, and we recognized a case with Moya-moya disease. Metabolic disorders that may predispose to thrombotic disease as homocystinuria were not detected in this study. No etiology was found in 3 cases (23.1%) and this was in concordance with the result of Rosenstingl et al. [5], who reported that no etiology was found in up to 20-30% of cases of CVST, and in the same study, deficiency of protein S, mutation of factor V Leiden, presence of lupus anticoagulant and anticardiolipin antibodies were the main risk factors of their cases and all were in agreement to our results. In cohort of 163 patients with first time incident CVST who underwent comprehensive thrombophilia testing, Wysokinska et al. [5] found that 29% of their patients with abnormal test results; these included 17% with anticardiolipin antibodies and 10% with heterozygous factor V Leiden. It is noteworthy that none of our cases had prior discovered chronic
condition, and all are discovered with their etiology during their current illness.

In our patients series; the only case who had a recurrent attack of venous thrombosis following the first time was girl patient diagnosed as moy-a-moya disease. This patient was presented in every episode with hemiplegia, third nerve palsy, headache, papilledema, and seizures in the form of complex partial with secondary generalization. All her tests for coagulation deficit and metabolic screening were negative. Her diagnosis as Moya-moya disease with cerebral venous thrombosis (CVT) was based on MRA and MRV studies (figure 8), where the former showed occlusion and attenuation of the vessels of the circle of Willis especially at the A1 and M1 segments of the anterior and middle cerebral arteries respectively as well as the left posterior cerebral artery with hypertrophied basilar and right posterior cerebral arteries together with the presence of dilated external carotid artery branches. MRV of the same patients showed occluded left transverse and left sigmoid sinuses. The same finding was detected by Del – Rio Camacho et al.29, who reported a girl with Down’s syndrome and moy-a-moya disease that was associated with dural venous sinus thrombosis.

The two cases who presented with dehydration had had severe gastroenteritis before the onset of their neurologic deficits, their MRV showed thrombosis in the dural sinuses either transverse or sagittal sinuses (figure 5). This finding was in agreement with several studies showed that severe dehydration may result in thrombosis of superficial sagittal sinus or others due to hyper viscosity and slugging of blood31,32.

Hereditary prothrombotic disorders include several causes such as deficiency of regulatory protein C, protein S, Anti thrombin III, or synthesis of pro coagulant protein which is unable to be inhibited by its regulatory protein; Factor V Leiden were reported in 3 cases in the current study, 2 cases showed mutation of Factor V Leiden, and one case detected with protein S deficiency. This emphasized that children with this hereditary mutation have an increased frequency of venous thrombosis as reported previously by Male et al.31. Those patients showed picture of SSST in their MRV. These results were in concordance with the results of other investigators who found the most common vessel involved was sagittal sinus in association with risk factors that increasing blood hyperviscosity, and inhered coagulation disorders such as defect in protein C and S and mutation or deficit in Factor V Leiden7.

Lupus anticoagulant is a special case in which an apparent inhibitor of clotting causes a predisposition to thrombosis. In the laboratory, the lupus anticoagulant causes prolongation of Partial Thromboplastin Time (PTT). Although PTT is prolonged, the patient with an isolated lupus anticoagulant is usually not at increased risk for bleeding, paradoxically 5-20% of such individuals may develop arterial or venous thrombosis33 while thrombocytopenia may be associated. In the current study we had one girl with dural sinuses thrombosis associated with positive lupus anticoagulant which was associated with thrombocytopenia and prolonged PTT, but this was not a component of antiphospholipid syndrome or systemic lupus erythematosis. Her brain MRI showed high signal in SSS, right transverse and right sigmoid sinuses, with multiple focal areas of abnormal parenchymal signal in the right cerebral hemisphere and edema with subacute blood of high T1 signal were noted (Fig. 6). This case was matched with 2 cases reported by Alper et al.35, who presented with SSS thrombosis associated with thrombocytopenia and had positive lupus anticoagulant test. On other hand other studies showed an association of lupus anticoagulant with anticardiolipin autoantibodies in 12-50% of cases with venous sinus thrombosis34; in our series, we had 2 cases (15.4%) with SSS thrombosis with positive anticardiolipin antibodies in absence of systemic lupus erythematosis (Figs. 1 and 2). However, Saneto et al.36 emphasized that cerebral venous thrombosis in the presence of anticardiolipin antibodies and in the absence of systemic lupus erythematosis is a rare event.

Lastly thrombotic thrombocytopenic pupura which is rare pentad of fever, microangiopathic hemolytic anemia, thrombocytopenia abnormal renal function, and central nervous system changes, is also a rare cause for cerebral venous thrombosis. Microvascular thrombi within the central nervous system cause subtle neurologic signs, and the initial manifestations are often nonspecific35. One case in this study was diagnosed as thrombotic thrombocytopenic pupura with SSS thrombosis confirmed by MRV. This girl patient was manifested
mainly with headache, nausea, vomiting, and seizures. Disturbance of consciousness, pyramidal tract lesions and focal neurologic deficit were not detected. Laboratory findings were the clues for diagnosis by presence of hemolytic anemia documented by elevated reticulocytic count in association with thrombocytopenia and elevated blood urea nitrogen and creatinine levels, while her coagulation studies were not diagnostic.

Regarding the outcome measures of our patients, on hospital discharge there were 5 (38.5%) patients with good recovery (grade 1 by GOS), 7 (53.8%) patients were either moderately or severely disabled (grade 2 or 3 by GOS), and one (7.7%) patients died. Almost the same percentages were reported by Carvalho et al.

In conclusion, MRI in conjunction with MRV are both sensitive and specific enough to provide the best non-invasive method of diagnosing CVST in pediatric patients. As brain parenchymal alterations and venous thrombus formation are potentially reversible, early diagnosis and appropriate medical therapy is important. All children with cerebral venous thrombosis need thorough tests for either hereditary or acquired prothrombotic risk factors. Further studies should be followed to assess the outcome of different etiology and results of early therapeutic trials.

REFERENCES


الأنماط الإكلينيكية الإشعاعية لجلطات الأوردة المخية في الأطفال

يعتبر التجلط الوردي المخي مرضا نادرا في الأطفال ولكنه من الأسابيع الهامة لجلطات المخ نتيجة الأعراض المرضية التي تصاحبه. باستخدام التصوير بالرنين المغناطيسي للدماغ والأوردة المخية يصوص تشخيص هذا المرض أكثر انتشاراً.

يهدف هذا البحث تحديد الأعراض المرضية الشائعة المصاحبة لهذا المرض ونماذج المخيخ المختلفة التي تظهر بالرنين المغناطيسي. بالإضافة إلى تحديد أهم الأسباب المؤدية له. حيث هذه الدراسة على 13 مريضاً تأكد إصابتهم بجلطات الأوردة المخية باستخدام تصوير الرنين المغناطيسي للدماغ واوردة المخ ضمن مرصد الأمراض الداخلية لقسم الأعصاب والأطفال بمستشفى جامعة القاهرة. وقد تم فحص الحالات ضمناً إكلينيكياً وعصابياً دقيقاً وأجريت جمع المعامل الأساسية شاملة فحص للعوامل المؤدية للجلط مثل بروتين سي إس. انتهى ثلاثين الثالثة وتم بحث وجود العوامل المشابهة المناعية مثل الانتي كارديوباريب وفشل عضلة الأوموميا والكتات والهيموسينت في الدم. وقد أجري تحليل وجد حال في العامل الخاص لأطفالن نقص فقط من الحالات. كما تم إدراج جميع الحالات بعمل رسم حى كهرماني الرنين المغناطيسي للدم والأوردة المخية. وقد أظهرت النتائج أن الصداع عرض أساسي في جميع الحالات (100%) بينما القلق والغثيان في 84.6% وارتفاع الحسم البصري في 76.9%. أما نتائج تصوير الرنين المغناطيسي للدم في أظهرario أن الحصول بالرنين المغناطيسي لأوردة المخ فقد كانت إيجابية بنسبة 92.3%. وكان الحجم الوريدي الوعائي هو أكثر الحوامل انتشارا لحدث جلطة بعمل التصوير بالرنين المغناطيسي لأوردة المخ وذلك بنسبة 84.4% أما متفردة أو مصاحبة لجربو وريدي أخرى ويلي الحجم الوريدي المستعرض بنسبة 53.8% أيضاً مفردة أميرلي مصاحبة لجربو وريدي أخرى. أمّا بالنسبة للأسباب الأولية لهذا المرض فقد تم تأكيده من وجود أسباب عملية في 10 حالات بنسبة 76.9% بينما لم يجد أسباباً في 3 حالات. وقد كان وجود خلل بالعوامل المؤدية للجلط الأحيان تكون وراثية أو مكتسبة في 7 حالات بنسبة 53.8% مثل منخفض نقص البروتين إس. طفيرة في العامل الخاص لأطفالن. وجود العوامل المشابهة المناعية مثل الانتي كارديوباريب وفشل عضلة الأوموميا. وقد كان الشفاف شديد في حالتين وذلك نتيجة لزيادة نزوى الدم في هذه الحالات. كما تم تشخيص حالة موياميا مصاحبة بجلط وريدي المخ.

وقد على هذا فقد وجدنا أن التصوير بالرنين المغناطيسي المخى من أكثر الفحوصات حساسية قبل التأكد من التشخيص بالتصوير بالرنين المغناطيسي لأوردة المخ وانه يجب التشخيص مبكر حيث أن الجلطات الوردية أكثر استجابة للعلاج من لجلطات الأوعية الشريانية. كما يجب أن يتم فحص الحالات فحصاً دقيقاً للتأكد من اختماليات وجود خلل بالعوامل المؤدية للجلط التي قد تكون وراثية أو مكتسبة.

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