Diagnosis Performance of Cerebral Venous Thrombosis with Magnetic Resonance Imaging and Magnetic Resonance Venography in Zahedan (Southeast of Iran): A Series of 57 Patients

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Abstract

BACKGROUND: Cerebral venous sinus thrombosis (CVST) is a scarce disease with poor prognosis and its diagnosis often challenges physicians due to nonspecific symptoms and widespread clinical manifestations.

AIM: To investigate the findings of magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) of patients with CVST diagnosis in Ali Ebne Abitaleb Hospital in Zahedan during 2013–2016 and to evaluate imaging pitfalls involving in late diagnosis, complications, and even death.

METHODS: This retrospective descriptive study was done on 57 patients confirmed CVST during 2013–2016 in Ali Ebne Abitaleb Hospital in Southeast of Iran (Zahedan). The MRI and MRV findings and related diagnostic pitfalls were evaluated. Twenty-one patients are pediatrics and 33 patients are adults.

RESULTS: Of 57 patients, evidences of cerebral edema were found in 33 patients, among whom 2 patients showed parenchymal edema (cerebral edema) without infarction, and 31 patients exhibited parenchymal edema with infarction. The frequency of involvement in descending order was as followed: transverse sinus (96.49%), sigmoid sinus (49.12%), superior sagittal sinus (29.82%), jugular vein (19.20%), internal cerebral veins (7.01%), straight sinus (5.2%), and cortical veins (5.2%). Diagnostic pitfalls were also found in 8 patients. Seven patients exhibited acute and subacute thrombosis mimicked normal sinus flow void in T2-weighted images. No filling defect was seen on gadolinium-enhanced T1-weighted image in the other patient due to the sub-acute phase of thrombosis.

CONCLUSION: The delayed diagnosis of CVST originating from nonspecific clinical features and diagnostic imaging pitfalls can result in poor outcomes in patients. To prevent the diagnostic pitfalls, the clinician should give a brief history and clinical data and radiologist(s) should interpret the findings in addition to the use of advanced MR sequences.

Introduction

Cerebral venous sinus thrombosis (CVST) is considered as a rare life-threatening condition, which is associated with 0.5% of all stroke types, and affects 5 people per million each year [1], [2]. The disease can occur at any age, but the young age group constitutes the main patient population, and women account for 75% of adult patients [1], [3]. This increased risk in women seems to be related due to oral contraceptive use and prenatal and postpartum periods [2], [3], [4]. It is believed that the disease is underdiagnosed, thus early diagnosis requires a high clinical suspicion and the use of imaging modalities [3], [4].

CVST diagnosis often challenges physicians due to nonspecific symptoms and widespread clinical manifestations [5]. Early treatment greatly enhances the disease’s prognosis, saves the lives of patients, improves their quality of life, and decreases family and social burden [6].

Overall, several factors such as severe dehydration, external injury, hematologic diseases, heart disease, pregnancy, infections, oral contraceptives, and immune disorders can be associated with CVST, whereas are not considered to be a susceptible cause in 20% of patients [7]. Imaging is of great importance in the diagnosis of CVST because of the nonspecific clinical picture and their variability [8].

The combination of magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) is capable of increasing the sensitivity of CVST diagnosis to 90%, and MRI in combination with MRV is the preferred method for diagnosis of CVST [9]. In MRI sequences, healthy dural sinuses are often seen in the form of no signal [10]. The main finding of CVST in the standard MRI protocol is the absence of a flow-void
signal in standard T1 and T2 sequences [5]. The diagnosis of sinus thrombosis is based on the presence of a hyperintense signal on T1 and hyperintense or isointense signal on T2 and lack of flow signal (filling defect) in the MRV [2]. The presence of an abnormal T2 signal in a venous sinus can be the most reliable confirmatory diagnosis of thrombosis in comparison with the corresponding absence of flow, since blood flow is very slow, and it may have a high signal in T1 images, even in the absence of any thrombosis [4].

It is worth noting that chemical products of blood breakdown in thrombosis veins and sinuses have been defined to be associated alteration of T1- and T2-weighted images over time. Therefore, the actual manifestation and intensity of the intraluminal thrombus signal can change over time, which will be considerably dependent on the paramagnetic effects of products resulting from the breakdown of hemoglobin [5].

Changes in CVST signal in T1- and T2-weighted images may not be clear or even completely hidden, so their diagnosis requires a high clinical suspicion [5]. Investigating potential pitfalls in interpreting images are very essential for proper detection and prevention of false-negative results. The thrombosis signal may be very hypointense on T2-weighted images, and may mistakenly lead to a commentary on the absence of normal flow in sinus. Thus, the use of contrast-enhanced MRV or computed tomography venography for diagnosis is needed at this stage [11].

This study aimed to investigate the findings of MRI and MRV in patients with CVST diagnosis in Ali Ibn Abi Talib Hospital in Zahedan during 2013–2016 and to evaluate imaging pitfalls involving in late diagnosis, complications, and even death.

Methods

Ethics approval was obtained from the institutional review board of Zahedan University of Medical Sciences, according to the Helsinki declaration. Written informed consent was signed by the parents of the pediatrics at study entry.

In this retrospective descriptive study, all patients who were treated with a diagnosis of CVST in Ali Ibn Abi Talib Hospital in Zahedan during 2013–2016 were enrolled. At the end of the study, 57 patients were diagnosed with CVST.

Inclusion criteria included

Patients diagnosed with CVST, who have their medical records, MRI, and MRV, were available at the hospital’s PACS archive and also CVST was confirmed by the clinical findings and the imaging methods used.

Exclusion criteria included

Missing MRI and MRV in the PACS system of the hospital were excluded from the study.

Data collection

Findings of magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) were assessed by the radiologist and their results were collected. Furthermore, to determine the diagnostic pitfalls in the imaging, a questionnaire containing all possible pitfalls was used.

Then, the frequency of various findings, including anatomical site involved (frontal, temporal, parietal, and occipital lobes, the thalamus, basal ganglia, internal capsule, cerebellum, and hippocampus), involved sinus (sinus caudal, transverse sinus, striate, sigmoid, deep vein of the brain, and jugular veins), hemorrhagic and non-hemorrhagic infarcts, intra-parenchymal hemorrhage, subacute hemorrhage, diffuse and localized cerebrospinal edema, midline shifts, evidence of infection (mastoiditis, abscess, and ethmoiditis meningitis), and brain herniation were determined in the images.

To evaluate possible diagnostic pitfalls, two radiologists were consulted that did not know the pathology of these patients. No other action was taken if each of these radiologists were able to easily diagnose CVST by examining the MRI and MRV of these patients. When MRI and MRV were reported to be a false negative, they were asked to complete a pre-made questionnaire. The questionnaire included a list of pitfalls that led to a false negative CVST diagnosis, which were extracted from similar studies. By assessing the data of these questionnaires, the most important reason for the lack of diagnosis of CVST in these patients was identified. Descriptive statistics, indexes, and tables were used for analyzing the data.

Statistical analysis

The data were analyzed using descriptive statistics and descriptive statistics. All statistical analysis was performed using statistical software (SAS version 9.1, SAS Institute Inc., Cary, North Carolina, USA).

Results

A total of 57 patients, who had been diagnosed with venous thrombosis, were enrolled in the study. Twenty-one patients belonged to the age group of infants and children and 36 patients were categorized into adult age group.
Of the 21 patients in the pediatric group, 9 patients were under the age of 1 month, followed by a range of 1 month to 5 years (8 patients), 5–20 years (4 patients). The age range of the adult patients was determined, ranging from 20 to 78 years old, and the mean age was 39.23 ± 13.47. Of the 36 adult patients, 25 were female (69.44%) and 11 (30.55%) male.

**Distribution of cerebral vein structures in patients with CVST**

The involvement of cerebral vein sinus is presented in the table (Tables 1 and 2).

**Table 1: Distribution of cerebral vein structures involvement in 57 patients understudy**

<table>
<thead>
<tr>
<th>Place of thrombosis</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transverse sinus</td>
<td>56 (96.49)</td>
</tr>
<tr>
<td>Sigmoid sinus</td>
<td>28 (49.12)</td>
</tr>
<tr>
<td>Upper sagittal sinus</td>
<td>17 (29.82)</td>
</tr>
<tr>
<td>Cortical veins</td>
<td>3 (5.2)</td>
</tr>
<tr>
<td>Deep venous system</td>
<td></td>
</tr>
<tr>
<td>Internal cerebral veins</td>
<td>4 (7.01)</td>
</tr>
<tr>
<td>Jugular vein</td>
<td>11 (19.29)</td>
</tr>
<tr>
<td>Straight sinus</td>
<td>3 (5.2)</td>
</tr>
</tbody>
</table>

**Brain parenchymal changes in the brain of patients with CVST**

Of 57 patients, 33 patients had evidence of edema in areas of the cerebral parenchyma, among which 2 patients showed parenchymal edema (cerebral edema) without infarction, and 31 patients exhibited parenchymal edema with infarction. Eight patients demonstrated cerebral edema in the focal region only in one lobe of the right or left hemisphere, and other patients in more than one lobe of a cerebral hemisphere or in parts of both cerebral hemispheres. Among 31 patients with venous infarction, 18 patients showed a hemorrhagic infarction and 13 non-hemorrhagic patients. In addition, hemorrhagic infarction was observed in two patients with subarachnoid hemorrhage (SAH) and in one patient with subarachnoid and intravenous hemorrhage.

**Table 2: Distribution of cerebral vein sinus involvement in 57 patients with diagnosis of CVST**

<table>
<thead>
<tr>
<th>Venous sinus involved</th>
<th>Number of patients (%)</th>
</tr>
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<tbody>
<tr>
<td>Unilateral transverse sinus involvement</td>
<td>13 (22.80)</td>
</tr>
<tr>
<td>Bilateral transverse sinus involvement</td>
<td>8 (14.03)</td>
</tr>
<tr>
<td>Unilateral transverse and sigmoid sinus</td>
<td>9 (15.78)</td>
</tr>
<tr>
<td>Unilateral transverse and sigmoid sinus and jugular vein involvement</td>
<td>7 (12.28)</td>
</tr>
<tr>
<td>Unilateral transverse and sigmoid sinus and jugular vein involvement + upper sagittal sinus</td>
<td>1 (0.175)</td>
</tr>
<tr>
<td>Unilateral transverse and sigmoid sinus and jugular vein involvement + upper sagittal sinus</td>
<td>6 (10.52)</td>
</tr>
<tr>
<td>Bilateral transverse sinus involvement and upper sagittal sinus</td>
<td>1 (0.175)</td>
</tr>
<tr>
<td>Bilateral transverse sinus involvement + unilateral sigmoid sinus</td>
<td>1 (0.175)</td>
</tr>
<tr>
<td>Bilateral transverse sinus involvement + jugular vein involvement + upper sagittal sinus</td>
<td>1 (0.175)</td>
</tr>
<tr>
<td>Internal cerebrovascular involvement together with involvement of other venous sinuses</td>
<td>4 (0.701)</td>
</tr>
<tr>
<td>Cortical veins involvement together with involvement of other venous sinuses</td>
<td>3 (0.0526)</td>
</tr>
<tr>
<td>Venous sinus involvement and jugular vein involvement + upper sagittal sinus</td>
<td>1 (0.175)</td>
</tr>
</tbody>
</table>

**Diagnostic pitfalls**

Based on the results obtained from the examination of patients' MRI by two radiologists, diagnostic pitfalls were showed in 8 patients of 57 patients. Plus, in 7 patients, venous sinuses detected in the conventional MRI, but in all of these patients, CVST was detected by MRV images. In addition, with or without gadolinium injection, thrombosis was observed in all patients by MRV and only in 19 patients was seen by conventional MRI.

**Discussion**

For diagnosis of patients with CVST, symptomatic patients and separate examination of sinuses in all brain MRI are of great importance [4], [10], [11]. The suspicious signs that require a closer look at the MRV are (1) failure of the signal void at the site of the venous sinuses (even vaguely and indeterminate), (2) observation of lateral and bilateral focal edema in the part of the brain with symmetrical or nonsymmetrical patterns, (3) observation of hemorrhagic or non-hemorrhagic infarction in part of brain parenchyma, (4) observation of hemorrhagic or non-hemorrhagic infarction in parts of the brain parenchyma that do not supply from an arterial trichotomy, (5) infarction or bleeding in brain parenchyma at infancy, childhood, and young age, especially in women of childbearing age and neonates, and (6) intravenous sinus dilatation site with a non-diagnostic signal [4], [8], [11].

The lesions have been frequently demonstrated in many regions, including the cerebellum, basal nuclei, thalamus as a mass of gray matter, cerebral cortex, hippocampus, brain stem, subcortical white matter, external capsule, and splenium as previously described at MRI results in the literature [12], [13], [14].

Our findings revealed anatomical site involved including frontal, temporal, parietal, occipital lobe, thalamus, basal ganglia, internal capsule, cerebellum, and hippocampus, involved sinus (caudal, transverse sinus, striate, sigmoid, deep vein of the brain, and jugular veins).

Thrombosis of cerebral veins and sinuses along with elevation of venous and capillary pressures is considered as one of pathophysiological mechanisms for the development of cerebral venous thrombosis (CVT). Another mechanism is associated with a reduction of absorption of cerebrospinal fluid due to cerebral sinuses obstruction; both mechanisms are capable of promoting inductively coupled plasma, and vasogenic and cytotoxic edema, as well as hemorrhage [15], [16], [17].

Parenchymal abnormalities, including hemorrhagic and non-hemorrhagic infarcts, intra-parenchymal hemorrhage, subacute hemorrhage, diffuse and localized cerebrospinal edema, midline shifts, evidence of infection (mastoiditis, abscess,
ethmoiditis meningitis), and brain herniation) were determined based on imaging techniques.

Based on findings in the present study, hemorrhagic and non-hemorrhagic infarcts, intraparenchymal hemorrhage, subacute hemorrhage, diffuse and localized cerebrospinal edema, midline shifts, evidence of infection (mastoiditis, abscess, and ethmoiditis meningitis), and brain herniation. Edema is mainly frequent among 33 patients, including parenchymal edema with infarction (31 subjects) and parenchymal edema without infarction (2 subjects). Furthermore, 8 patients demonstrated cerebral edema in the focal region only in one lobe and/or more than one lobe, or in parts of both cerebral hemispheres.

Diffusion-weighted MR imaging is capable of providing a classification of parenchymal abnormalities in two categories, including primarily vasogenic edema and primarily cytotoxic edema. The presence of hemorrhage can be observed with both kinds of edema and different patterns [11], [18], [19].

Among 31 patients with venous infarction, hemorrhagic infarction was identified in 18 patients with CVT, of which SAH and subarachnoid along with intraventricular hemorrhage were observed in 2 and 1 subjects, respectively, while 13 were non-hemorrhagic patients. It has been defined as intracerebral infarction, hemorrhage, and focal cerebral edema are among the most prevalent brain parenchymal lesions of CVT [20], [21].

Based on the findings in the literature, focal brain abnormalities and parenchymal lesions are more common in MR than CT findings [11], [22], [23], and also, focal edema without hemorrhage [18], [19], [24], [25].

Among the patients enrolled in this study, 8 patients revealed diagnostic pitfalls, among which 7 patients exhibited acute and subacute thrombosis mimicked normal sinus flow void in T2-weighted images, so they were neglected and not detected in the primary MRI.

These seven patients were young children and adults. Due to clinical symptoms, age, and clinical suspicion, MRV of patients showed thrombosis, except for one patient, where thrombosis was not observed in CE T1-weighted scan with contrast due to subclinical thrombosis; however, in mentioned patient, thrombosis was detected by combining data from contrast T1 and T2 sequences and sequences without contrast.

Empty delta sign has been found in sinus thrombosis at CE imaging. The presence of the empty delta sign has been previously found in 20% of subjects with sinus thrombosis by applying CECT. It can be also attributed a higher percentage when thin-section helical CT and volumetric MR images be used for diagnosis [11], [26]. On the other hand, normal findings of non-contrast head CT have been attributed to a percentage of 30% among patients with CVTs, with a high proportion of nonspecific abnormalities [27], [28], [29], [30], [31]. Of course, unenhanced MR imaging has been indicated to show high sensitivity for the diagnosis of venous thrombi, when compared with unenhanced CT [11].

A review study by Leach et al. showed that the superior sagittal sinus had the highest degree of involvement based on MRI images of 510 patients with CVST (61%), followed by transverse sinus involvement (57%), sigmoid sinus involvement (15%), and straight sinus involvement (15%). In addition, the frequency of other involvement areas is included in the following categories: Internal cerebral veins, jugular bulb, Galen vein, and cortical veins [11].

However, our findings demonstrated that the highest frequency of involvement was observed in the transverse sinus (96.49%), sigmoid (49.12%), superior sagittal sinus (29.82%), and jugular veins (19.29%), respectively, followed by internal cerebral veins (% 7.01), cortical veins (5.2%), and straight sinus (% 2/5) were followed. These results are more or less in agreement with Leach et al., 2006 [11].

Conclusion

Taken together, to avoid delays in diagnosis, radiologists need to be aware of the various imaging characteristics of patients with CVT that can be likely hidden. To prevent the diagnostic pitfalls, the clinician should give a brief history and clinical data and radiologist(s) should interpret the findings in addition to the use of advanced MR sequences.

Authors' Contributions

Authors equally contributed to the manuscript.

Ethical Publication Statement

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

References