EVALUATION OF TRANSCRANIAL DOPPLER IN NEURO-BEHCET’S DISEASE PATIENTS
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KEY WORDS: TRANSCRANIAL DOPPLER, VASCULAR CHANGES IN BEHCET’S DISEASE.

ABSTRACT

Objective: to study the value of transcranial Doppler (TCD) in patients with neuro-Behcet's disease (Neuro-BD) and to correlate the findings with the MRI results.

Methodology: This study included 15 patients fulfilling the diagnostic criteria of international study group for Behcet's disease. MRI brain was done and evaluated for the presence of parenchymal lesions. Bilateral transcranial Doppler ultrasound of the middle (MCA), anterior (ACA) and posterior (PCA) cerebral arteries were performed in patient and control groups. TCD parameters were compared between 15 patients and age and sex matched control subjects.

Results: We found 12 (80%) patients had single or multiple brain lesions on MRI. Most of these lesions were of high signal intensity on T2-weighted images and located in the brainstem, basal ganglia and deep white matter region. TCD findings were abnormal in 5 (33.3%) patients. Pulsatility and resistivity indices of the MCA were significantly higher in patients than in normal control (p<0.001). The mean blood flow velocity of the MCA and ACA was marginally reduced in patients with neuro-BD than in healthy controls, but did not reach a statistical significance (p>0.05). No significant relation was found between abnormal MRI lesions and TCD parameters.

Conclusion: Cerebral hemodynamics might be affected in patients with Behcet’s disease compared with healthy
controls. TCD may be a useful tool in the evaluation of patients with neuro-Behcet's disease.

INTRODUCTION

Behcet’s disease (BD) is a chronic relapsing multisystem disease of unknown etiology. It was originally described by the Turkish dermatologist, Hulusi Behcet in 1937 (1). The disease commonly affects young adults and can involve the skin and mucous membranes, eyes, joints, vascular system, lungs, gastrointestinal tract, and nervous system.

Neurological involvement is one of the most devastating manifestations of Behcet’s disease (neuro-BD), with variable prevalence rates between 2.2% and 50%. This involvement may occur by primary neural parenchymal lesions or secondary to major vascular involvement (2-6).

Central nervous system involvement in Behçet’s disease is mainly caused by chronic, recurrent vasculitis affecting small vessels. Additionally, cerebral venous thrombosis is a major complication, and cerebral arterial thrombosis is infrequently observed in central nervous system involvement of BD (1, 7 and 8).

Previous studies have been performed to detect cerebral blood flow changes related to Behcet’s disease with or without neurological involvement using single photon emission computed tomography (SPECT). These studies showed decreased cerebral blood flow in patients with neuro-BD. The brainstem and parietal lobes were the most common areas with hypoperfusion lesions (9-11). Transcranial Doppler is an alternative non invasive and inexpensive technique for measuring blood flow velocities in the intracranial arteries. It provides additional information about the hemodynamic status of the intracranial circulation. Changes in blood flow velocity measured by TCD correlate well with changes in cerebral blood flow measured by single-photon emission computed tomography. However, only a few TCD studies have been performed in patients with BD (12, 13).

Aim of the work:

To investigate the value of transcranial Doppler ultrasonography in the evaluation of hemodynamic patterns in neuro-Behcet's disease and to correlate results with the MRI findings.
SUBJECTS AND METHODS

The study included 15 patients with neuro-Behcet's disease. Patients with Behcet's disease were diagnosed according to the criteria of the international study group for Behcet's disease, requiring the presence of oral ulceration plus any two of the following four criteria; genital ulceration, typical eye lesions, typical defined skin lesions and a positive pathergy test \(^{(14)}\). All the patients underwent neurological and general physical examination. Patients with neurological findings suggestive of involvement of the nervous system by the disease were regarded as cases of neuro- Behcet’s disease. Cranial magnetic resonance imaging was done in patients with neuro-Behcet’s disease and evaluated for the presence of parenchymal lesions.

TCD examinations were performed in all patients and control. The following arteries were examined by TCD on both sides: Middle, anterior and posterior cerebral. The following TCD parameters including, mean velocity (Vm), pulsatility index (PI) and resistivity index (RI) were measured bilaterally in all examined arteries.

Control group consists of 15 age and sex matched volunteers who had no neurological abnormalities. All control subjects were examined by TCD bilaterally. All TCD parameters were also measured in the same arteries.

Statistical analysis was performed using SPSS. Mann-Wittney U test and Fisher exact test were used for comparison between patients and control groups. p<0.05 was considered statistically significant.

RESULTS

We studied 15 patients with neuro-Behcet's disease with a mean age 38.7 years. The neurological features were recurrent headache (in all patient), epilepsy (one patient), hemiparesis or quadriparesis in 10 patients, transient left hemiparesis in two, paraparesis in two, radiculomyelitis in one and optic atrophy in one patient.

MRI showed single or multiple brain lesions in 12 of 15 patients with neuro-BD (80%). These lesions appear as high signal intensity on T2 weighted images and most of these lesions were located in the brainstem (Fig 1), basal ganglia extending to the diencephalic structures and white matter.

TCD was abnormal in 5 (33.3%) patients, 3 of them had abnormal MRI brain and 2 patients had normal MRI findings. MCA was the most
commonly affected artery in these patients. No significant correlation was found between TCD abnormalities and MRI findings of the brain in our study patients (P=0.242). Also there was no significant difference between right and left side regarding TCD parameters in all examined arteries in our patients group (Table 3).

TCD values for middle, anterior, and posterior cerebral arteries in both patients and control groups were shown in (Table 2). The results show that the blood flow velocities in middle and anterior cerebral arteries (Figure 2) in patients with neur-BD were marginally decreased in all patients compared with the normal control group, but this did not reach significance (p>0.05). We found a significant increase in PI (p<0.006) and RI (p<0.001) in the MCA, however, it was marginally increased in the ACA when compared with the control, but this did not reach significance (p>0.05)

Table (1): Baseline data of our studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Patients N = 15</th>
<th>Controls N = 15</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean±SD)</td>
<td>38.75 ± 9.7</td>
<td>37.40 ± 6.7</td>
<td>0.941</td>
</tr>
<tr>
<td>Sex (Male/Female)</td>
<td>11/4</td>
<td>10/5</td>
<td>0.695</td>
</tr>
<tr>
<td>Abnormal TCD</td>
<td>5 (33.3%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Abnormal MRI</td>
<td>12 (80%)</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Table (2): TCD parameters in neuro-Behcet's patients and controls.

<table>
<thead>
<tr>
<th>TCD parameters Bilateral cm/s</th>
<th>Patients N = 15</th>
<th>Controls N = 15</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vm</td>
<td>45.26 ± 11.07</td>
<td>48.57 ± 13.45</td>
<td>0.332</td>
</tr>
<tr>
<td>PI</td>
<td>0.91 ± 0.33</td>
<td>0.77 ± 0.17</td>
<td>0.006*</td>
</tr>
<tr>
<td>RI</td>
<td>0.60 ± 0.13</td>
<td>0.51 ± 0.02</td>
<td>0.001*</td>
</tr>
<tr>
<td>ACA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vm</td>
<td>36.90 ± 11.49</td>
<td>41.36 ± 11.75</td>
<td>0.136</td>
</tr>
<tr>
<td>PI</td>
<td>1.26 ± 1.20</td>
<td>1.09 ± 0.55</td>
<td>0.821</td>
</tr>
<tr>
<td>RI</td>
<td>0.64 ± 0.16</td>
<td>0.61 ± 0.16</td>
<td>0.207</td>
</tr>
<tr>
<td>PCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vm</td>
<td>25.91 ± 10.34</td>
<td>23.76 ± 8.43</td>
<td>0.520</td>
</tr>
<tr>
<td>PI</td>
<td>1.41 ± 1.30</td>
<td>1.37 ± 0.78</td>
<td>0.929</td>
</tr>
<tr>
<td>RI</td>
<td>0.73 ± 0.17</td>
<td>0.74 ± 0.18</td>
<td>0.623</td>
</tr>
</tbody>
</table>

Vm is the mean velocity, PI is the pulsatility index and RI is the resistivity index. Values are mean±SD, *p<0.05 is significant (Mann Wittney test).
Table (3): TCD parameters in neuro-Behcet's disease: Comparison between Right and Left sides.

<table>
<thead>
<tr>
<th>TCD parameters</th>
<th>Right side</th>
<th>Left side</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vm</td>
<td>46.40 ± 12.68</td>
<td>44.13 ± 9.51</td>
<td>0.567</td>
</tr>
<tr>
<td>PI</td>
<td>0.91 ± 0.43</td>
<td>0.92 ± 0.21</td>
<td>0.512</td>
</tr>
<tr>
<td>RI</td>
<td>0.62 ± 0.15</td>
<td>0.57 ± 0.02</td>
<td>0.618</td>
</tr>
<tr>
<td>ACA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vm</td>
<td>36.80 ± 10.56</td>
<td>37.0 ± 12.7</td>
<td>0.775</td>
</tr>
<tr>
<td>PI</td>
<td>0.99 ± 0.50</td>
<td>1.52 ± 1.58</td>
<td>0.102</td>
</tr>
<tr>
<td>RI</td>
<td>0.63 ± 0.19</td>
<td>0.65 ± 0.14</td>
<td>0.717</td>
</tr>
<tr>
<td>PCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vm</td>
<td>24.18 ± 11.85</td>
<td>27.50 ± 8.96</td>
<td>0.608</td>
</tr>
<tr>
<td>PI</td>
<td>1.69 ± 1.75</td>
<td>1.10 ± 0.38</td>
<td>0.654</td>
</tr>
<tr>
<td>RI</td>
<td>0.79 ± 0.13</td>
<td>0.67 ± 0.18</td>
<td>0.173</td>
</tr>
</tbody>
</table>

Vm is the mean velocity, PI is the pulsatility index and RI is the resistivity index. Values are mean±SD, *p<0.05 is significant (Mann Whitney test).

Fig. (1): Patient with brainstem involvement had parenchymal hyperintense lesion in the brain stem with abnormal PCA (Vm, PI and RI).
Fig. (2): TCD of the Rt. ACA with decreased flow velocity (A), normal flow velocity on the Lt. ACA (B) in neuro-BD patient with recurrent Lt. hemiparesis and has normal MRI and MRA brain and normal ACA blood flow in a control subject (C)
DISCUSSION

Behcet’s disease is a multisystemic inflammatory disorder with relapsing courses. Involvement of central nervous system is one of the most serious manifestations of BD, either by parenchymal or vascular involvement \(^{(2\text{-}3, 15)}\). The neuropathology of the parenchymal form is that of multifocal necrotizing lesions with marked inflammatory cell reactions, secondary to vasculitis. In patients with vascular BD, the visible lesions and clinical features usually correspond well to major vascular territories. However, the pathological process of the vascular system of patients with BD is not very clear \(^{(16)}\). The nature of parenchymal lesions in most of our patients was probably vasculitis because there were neither risk factors, findings of large or small artery disease nor evidence of meningoencephalitis.

In our study, 12 of 15 patients with neuro-BD (80\%) had brain lesions on MRI. Most of these lesions were of high signal intensity on T2 weighted image and were located in the brainstem, basal ganglia extending to the diencephalic structures and deep white matter. These findings are in accordance with the results of previous studies \(^{(16\text{-}18)}\). In vasculitic processes, location, extension, and distribution of vascular involvement might point to a specific diagnosis, such as Takayasu or temporal arteritis \(^{(19\text{-}21)}\). In neuro-BD, lesions therefore appear secondary to small vessel vasculitis and the anatomy of intraaxial structures explains the dominant involvement of the brain stem and diencephalic structures.

Previous reports have emphasized the high frequency of venous involvement and the rarity of arterial involvement \(^{(3, 7, 8, 22\text{ and }23)}\). However, study of Ko et al. \(^{(24)}\) reported a relatively equal incidence of venous (36\%), arterial (33\%) and combined arterial and venous (30\%) involvement in BD. The causes of this discrepancy are uncertain. In the present study, TCD showed arterial hemodynamic changes in 33.3\% of patients with neuro-BD.

BD is characterized by a prothrombotic state which contributes to the development of vascular occlusions affecting both the venous and the arterial system \(^{(19)}\). Although, the pathogenesis of thrombosis in BD is not completely understood, it is generally accepted as the endothelial dysfunction caused by vasculitis, coagulation abnormalities, deficiency of protein C and S, fibrinolytic system defects and hyperhomocysteinemia were shown to be risk factors for thrombosis in BD \(^{(25, 26)}\).

Previous SPECT studies have demonstrated hypoperfusion areas of the brain in patients with neuro-BD. The brainstem and parietal lobes were
the most common areas with hypoperfusion lesions \(^{(9-11)}\). According to our results, the middle cerebral artery was the most commonly affected artery. This finding suggests that the parietal lobe (the territory of the MCA) is at higher risk for cerebral vascular abnormalities in neuro-BD.

However, TCD does not measure actual blood flow, but flow velocity through the basal cranial arteries. Bishop et al. \(^{(27)}\) and Shigemori et al. \(^{(28)}\) showed that changes in flow velocity in the MCA correlated well with changes in hemispherical cerebral blood flow measured by single-photon emission computed tomography. In vasospasm, for instance, blood flow velocities are increased due to the constriction of vessels, whilst actual CBF is decreased. A decreased flow velocity can be due to low CBF secondary to low cardiac output, to a larger diameter of the insonated vessel, to a high vascular bed resistance, or to combination of these factors.

On the other hand, few studies have been performed using TCD in neuro-BD. Transcranial Doppler detection of microembolic signals have been reported in 29% of patients with BD \(^{(12)}\). The frequency of microembolic signals was higher in patients with neurological involvement than those without. Yilmaz et al. \(^{(13)}\) found ocular and cerebral hemodynamic changes including increased acceleration time of the MCA using color-coded duplex sonography in patients with Behcet's disease. In our study, TCD abnormalities were found in 5 (33.3%) of 15 patients with neuro-BD. These abnormalities include decreased cerebral blood flow velocity and increased pulsatility and resistivity indices mainly in the MCA.

The Gosling PI was originally designed to measure vascular resistance \(^{(29)}\). The increased PI and RI observed in the present study presumably represent enhanced cerebrovascular bed resistance in the cerebral circulation due to cerebral vasculitis in neuro-BD.

Conclusion:

Cerebral hemodynamics might be affected in patients with Behcet's disease compared with healthy controls. Transcranial Doppler may be a useful tool in the evaluation of hemodynamic patterns in patients with neuro-Behcet's disease and may allow the recognition of subset of patients at high risk for cerebral involvement.

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تقييم موجات دوبلر عبر الجمجمة في مرضى متلازمة بهجت ذوي الأعراض العصبية

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كلية طب جامعة الأزهر

الطريقة: إشتملت الدراسة على خمسة عشر مريضاً يعانون من متلازمة بهجت ذوي الأعراض العصبية. وقد تم فحص جميع المرضى إكلينيكياً مع عمل فحص بالرنين المغناطيسي على المخ. وفي بعض الحالات فحص بالرنين المغناطيسي على الأوعية الدموية المخية. وتشمل الدراسة على 15 من الأصحاء كمجموعة ضابطة. وتم الفحص بالدوبلر عبر الجمجمة على جميع المرضى والمجموعة الضابطة.

النتائج: وتبين أن الدراسة تتأثر 12 من المرضى بإصابة الأنسجة المخية عن طريق الرنين المغناطيسي. وأظهر الدوبلر نتائج غير طبيعية في 5 من المرضى مع تأثر تدفق الدم في الشرايين المخية.