European Journal of Radiology 58 (2006) 102–109

EJR
EUROPEAN JOURNAL OF RADIOLOGY

www.elsevier.com/locate/ejrad

Changes in cerebral and ocular hemodynamics in Behçet's disease assessed by color-coded duplex sonography

Sevda Yilmaz [a,*], Cengiz Akarsu [b]

[a] *Department of Radiology, School of Medicine, University of Kirikkale, Kirikkale, Turkey*
[b] *Department of Ophthalmology, School of Medicine, University of Kirikkale, Kirikkale, Turkezy*

Received 25 July 2005; received in revised form 28 November 2005; accepted 3 January 2006

Abstract

Aim: To quantify the cerebral and retrobulbar hemodynamics in Behçet's disease with and without ocular involvement and compared with that of healthy controls.
Materials and methods: Of 51 people studied, 17 had Behçet's disease with ocular involvement, 17 had Behçet's disease without ocular involvement, and 17 were healthy controls. A single eye was examined in each patient. Peak systolic velocity (PSV), end-diastolic velocity (EDV), time-averaged maximum velocity (Tamax), and resistance index (RI) were evaluated in the ophthalmic (OA), posterior ciliary (PCA), central retinal (CRA) and middle cerebral artery (MCA). Additionally, the average blood flow velocities in the central retinal vein (CRV), and acceleration time (AT) and pulsatility index (PI) in the MCA were calculated.
Results: The mean EDV in the PCA was 25% lower and RI was higher in patients with ocular involvement of BD than in patients without involvement ($p = 0.006$ and $p = 0.005$, respectively) and in healthy controls ($p = 0.003$ and $p = 0.004$, respectively). Differences were smaller in comparisons of the CRA and absent on comparisons of the OA and MCA. The acceleration time of the MCA was significantly higher in patients with Behçet's disease than in healthy controls ($p = 0.03$).
Conclusion: This study suggests that the flow hemodynamics in retrobulbar circulation has more altered Behçet's disease with ocular involvement than without ocular involvement and healthy control. Additionally, the cerebral hemodynamic might be affected in patients with Behçet's disease compared with healthy controls.

Keywords: Behçet's disease; Color Doppler imaging; Transcranial Doppler sonography; Retrobulbar hemodynamic; Cerebral hemodynamic; Acceleration time

1. Introduction

Behçet's disease (BD) was firstly defined by Professor Hulusi Behçet in 1937 as an illness characterized by recurrent oral and genital ulcers and uveitis [1]. BD has been observed all over the world, but the largest numbers of cases have been reported from Japan, the Middle East, and Mediterranean countries [2,3]. It is considered as a chronic multisystem disorder with vasculitis, which is probably caused by abnormal circulating immune complexes [4]. Nonspecific vasculitis may affect any arteries or veins [5,6]. The most frequent and serious complication of BD is ocular involvement that has been reported as 60–90% [7,8]. BD is also associated with other systemic manifestations such as central nervous system (CNS), cardiovascular system, pulmonary and gastrointestinal tract, large vessels, joints, ear, and vestibular involvement due to large and small vessel involvement both in the arterial and venous sides [9–11]. CNS involvement, neuro-Behcet syndrome, is one of the most serious manifestations of BD and occurs in about 10–25% of patients [12,13]. Cerebral angio-Behçet's syndrome is rare but important complication of BD characterized by occlusive panarteritis of some medium-sized pial branches of the middle cerebral artery (MCA), small infarctions, and patchy or confluent demyelinated foci in the brain [14]. Although vascular lesions are

* Corresponding author at: İvedik cad. Ümit sok. 100, Yıl sitesi, A Blok 8/38, Yenimahalle-Ankara O6170, Turkey. Tel.: +90 312 3442833; fax: +90 318 2252819.
E-mail address: dryilmazsevda@yahoo.com (S. Yilmaz).

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doi:10.1016/j.ejrad.2006.01.001

not listed among the criteria for the diagnosis of BD, up to 25–30% of patients develop complications during follow-up in large vessels [15].

Both transcranial color-coded duplex sonography (TCCS) for the measurement of intracranial arterial blood flow velocities and color Doppler imaging (CDI) for the evaluation of retrobulbar hemodynamics are noninvasive, painless and highly reproducible imaging techniques [16–18]. CDI has been used to detect vascular disorders of the orbit and optic nerve in different diseases such as diabetes mellitus [21], glaucoma [22], tumors [23], and cigarette smokers [24]. TCCS permits visualization of intracranial blood vessels and direction of blood flow detecting intracranial vascular pathology [10,19,20]. Transcranial Doppler ultrasonography has been used in many central nervous system disorders to allow insight into cerebrovascular function. A limited number of CDI investigations of ocular hemodynamics in BD have been studied [25–32], but to the best of our knowledge, TCCS of cerebral hemodynamic changes has not been research previously in the literature.

Although vascular involvement is a well-known manifestation of BD and may affect systemic and regional circulation, little information is available for the extent of vascular involvement in patients with BD who are free of vascular sign and symptoms. Thus, we examined the retrobulbar blood flow velocities in patients with or without ocular involvement. As well as, we evaluated the cerebral hemodynamic alterations occurred in patients with Behçet's disease who are free of cerebrovascular symptoms and neurological involvement.

2. Patients and methods

2.1. Patients

Forty-one patients with known Behçet's disease and 17 healthy volunteers were enrolled in this prospective study. All participants gave informed consent to the study and the tenets of the Declaration of Helsinki were followed. According to the ethical standards of our institution, written informed consent was obtained from each patient and healthy control before they enrolled in present study.

The diagnosis of BD was based on the previously published diagnostic criteria of the International Study Group for Behçet's disease [33].

Each subject underwent a complete ophthalmologic, neurological and general physical examination. All healthy controls had a visual acuity of 20/20 or better and had normal ophthalmologic examination findings. The patients with Behçet's disease had no signs or symptoms of cerebrovascular and neurological involvement.

All subjects had no history of neurological disorders, arterial hypertension, hypercholesterolemia, ischemic heart disease, atrial fibrillation, cardiac valve prosthesis, cigarette smoking, diabetes mellitus, polistemia, and migraine. Excluded from this study were subjects with a history of incisional ocular surgery, acute ocular aggravation of Behçet's disease within last 3 months, oral contraceptive usage, and hormonal therapy. The ocular involvement was diagnosed on the basis of the presence of one or more following findings: keratic precipitates, posterior synechiae, retinal vascular sheathing and attenuation, retinal neovascularization, retinal hemorrhages, cells in the vitreous, chorioretinal scarring, optic nerve or macular edema, and optic atrophy. Of 41 patients, 22 had previous ocular involvement at least in one eye and 19 had no signs or symptoms of ocular involvement. In Behçet's disease with ocular involvement group, two patients had arterial hypertension, two patients had ocular aggravation within 3 months and one patient was heavy smoker. Similarly, in Behçet's disease without ocular involvement group, one patient had arterial hypertension and one patient was heavy smoker. Therefore, they were excluded from the study. If both eyes of each subject were eligible, we randomly selected one eye of each subjects. So, 17 eyes of 17 patients with Behçet's disease with ocular involvement, 17 eyes of 17 patients with Behçet's without ocular involvement, and 17 eyes of 17 healthy controls were enrolled. Participants were instructed not to drink caffeine-containing beverage during the day of test. Intraocular pressure (IOP) by a Goldmann applanation tonometer, blood pressure (BP) by sphygmomanometer, and heart rate by palpation of radial pulse were measured in a masked manner after a 15-min rest.

2.2. Color-coded duplex sonography examination

We used a color Doppler unit (Logiq 9; GE Healthcare, Milwaukee, WI) with a 9–14-MHz linear transducer for the retrobulbar vessels, and a 2–4-MHz sector transducer for the MCA. First ocular and then MCA color Doppler examination were performed in a thermally controlled room by the same radiologist after a 20-min rest. To minimize the effects of diurnal variation, all measurements were recorded at about the same time of day (between 9:00 and 10:00 a.m.). During CDI, transmission gel was applied to the external surface of the eyelids, in a supine position. Care was taken to apply as little pressure as possible on the eye. First, a preliminary gray-scale ultrasonographic examination of the eyes was performed to identify any abnormalities. Then, CDI measurements were performed. The central retinal artery (CRA) and central retinal vein (CRV) were depicted within the optic nerve, approximately 2–4 mm posterior to the optic disc (Fig. 1). The spectrum of the CRA showed a venous overlap from the CRV. The ophthalmic artery (OA) was examined in the deeper part of the orbit, near the optic nerve medially, 10–15 mm behind the globe (Fig. 2). The network of posterior ciliary artery (PCA) was examined where its branches surrounding the globe, near the optic nerve laterally (Fig. 3). The axial or oblique scans were used according to parallel to the long axis of each vessel and to identify the precise direction of the orbital vessels. Examinations were performed in a low or medium flow setting to permit for optimal detection of Doppler frequency shifts of the slow-flowing blood