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Lipid Profile and Anticardiolipin Antibodies in Behcet's Disease

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Background. Behcet's disease (BD) is a multisystem disorder characterized by a relapsing inflammatory process of unknown etiology. It is well known that atherothrombosis in systemic inflammatory disorders is closely related to coagulation and lipid metabolism abnormalities. The purpose of this study was to investigate some parameters of lipid metabolism, lipoprotein (a) [Lp(a)] and anticardiolipin antibody (ACA) levels and the relationship of these parameters with the clinical activity of BD.

Methods. Thirty three patients with BD (15 active, 18 inactive cases) and 20 healthy controls participated in the study. After performing a detailed physical exam, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very-low-density lipoprotein cholesterol (VLDL-C), apoprotein A and B (apo-A, apo-B), Lp(a), and ACA levels (ACA-IgG and IgM) were measured in all participants.

Results. Patients with active BD had higher ESR, CRP and Lp(a) levels, and lower apo-A and HDL-C levels compared with the patients with inactive BD and healthy controls. ACA-IgG and IgM levels were higher in patients with active BD than healthy controls but not higher than patients with inactive BD. On the other hand, ACA-IgG level was higher in active and inactive cases with vascular involvement than in those of active and inactive cases without vascular involvement. In the analyses of correlation, in active BD patients we found a positive correlation between CRP and Lp(a) levels.

Conclusions. Our findings suggest that Lp(a) behaves as an acute phase reactant and ACA levels are increased in patients with active BD. Data from patients with active BD may be compatible with the serum profile, which is accepted as a risk for the development of atherothrombosis.

Key Words: Behcet's disease, Lipoprotein, Anticardiolipin antibodies.

Introduction

Behcet's disease (BD) is a multisystem disorder characterized by a relapsing inflammatory process of unknown etiology (1). In this disease, there are four major symptoms including recurrent oral aphthous ulcers, skin lesions, ocular lesions, and genital ulcers, in addition to minor symptoms such as articular symptoms, involvement of the digestive tract, epididymitis, vascular involvement and neuropsychiatric symptoms. In BD, venous involvement is common, whereas arterial involvement is rare (2). Both small- and large-sized vasculature may be subsequently involved in the course of the disease. Based on the findings that thrombotic episodes were common in BD as seen also in primary antiphospholipid syndrome, antiphospholipid antibody levels under this condition have been investigated by many researchers (3,4).

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It is well known that atherothrombosis in systemic inflammatory disorders is closely related to the abnormalities of coagulation and lipid metabolism abnormalities (5). Likewise, in many studies, it has already been shown that changes in lipid profile occur in inflammatory conditions (6,7) and relationship between acute phase reactants, which have effects on inflammation and lipid metabolism (8).

Although antiphospholipid antibodies and some lipid and lipoprotein levels in BD were investigated separately in many studies (3,4,9,10), we are not aware of any previous studies of antiphospholipid antibodies, lipoprotein (a) [Lp (a)], which is cholesterol-rich plasma lipoprotein (11), along with lipid and lipoprotein profile in BD. The purpose of this study was to investigate some parameters of lipid metabolism, such as total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very-low-density lipoprotein cholesterol (VLDL-C), apolipoprotein-A (apo-A), apolipoprotein-B (apo-B) and Lp(a) and anticardiolipin antibody (ACA) levels (ACA-IgG and IgM), and the relationship of these parameters with the clinical activity of BD.

Methods

Patients and controls. This study was carried out in patients followed up at the Internal Medicine Clinics. Patient group consisted of 33 (28 male, 5 female) patients with BD (15 active, 18 inactive), aged 21–52 years. The diagnosis of BD was made according to the criteria proposed by International Study Group for BD (12). The disease activity was defined clinically. Clinical features included oral and genital ulcerations, eye involvement (uveitis and/or retinal vasculitis), skin manifestations (papuler pustuler lesion and/or acneiform eruption), arthritis, vascular involvement (thrombophlebitis, deep vein thrombosis and thrombosis of superior vena cava) and positive pathergy test. No neurologic involvement was found in any patient with BD. Of the patients, 12 had vascular involvement (6 active, 6 inactive). Whereas two of six active cases with vascular involvement had thrombosis of the superior vena cava, the other active and inactive patients with vascular involvement had thrombophlebitis and/or deep vein thrombosis. Disease duration ranged from 0 to 11 years (median 4) and from 1 to 28 years (median 4.5) in active and inactive cases, respectively. Clinical and laboratory reviews were made at the time when blood samples were collected. Seventeen healthy male and three female volunteers, aged 21–48 years, constituted the control group. The study was approved by the Ethical Committee of Gulhane Military Medical Academy.

Inclusion criteria. Inclusion criteria for study patients and controls were as follows: 1) >20 years of age, 2) not taking any lipid-lowering medications, 3) no history or current evidence of primary disorders of lipid metabolism such as familial hyperlipidemias and hypolipidemias, 4) no history or current evidence of endocrinologic disease that affects lipid metabolism such as diabetes mellitus, Cushing's disease, and acromegaly, 5) normal liver and renal function tests, 6) no other reasons, except BD, for thrombotic complications and 7) age- and sex-matched healthy volunteers for controls.

Of 33 patients, 17 were already diagnosed and being treated with colchicine or non-steroidal antiinflammatory drugs or immunosuppressive treatment or anticoagulant agents (12 inactive, 5 active), whereas 11 newly diagnosed patients (6 inactive, 5 active) and the remaining 5 active cases received no systemic medication for at least 6 months prior to the study. These active patients discontinued therapy because of adverse drug effects or unwillingness to undergo therapy. After obtaining a clinical history and performing a detailed physical examination by an internist, all patients were also evaluated routinely in the following areas: ophthalmology, dermatology, vascular surgery, neurology and radiology to define ocular, dermal, vascular lesions and nervous system involvement.

Measurement of erythrocyte sedimentation rate (ESR) and serum parameters. Erythrocyte sedimentation rate (ESR) was measured by using Westergreen's method and expressed in mm/h (13). C-reactive protein (CRP) levels were measured by turbidimetric method using a photometer (Biosystems S.A., Barcelona, Spain) and a level <6 mg/L was accepted as normal. Serum cholesterol and triglyceride levels were measured with an autoanalyzer (Technicon Dax-48, Miles Inc., Tarrytown, NY). Apo-A and apo-B levels were measured by a commercial kit using immunoturbidimetric method (Sigma, UK). HDL-C level was measured in the supernatant, which was separated from VLDL and LDL-C by adding dextran sulfate and $MgCl_2$ (14). LDL-C level was estimated by Friedewald formula [LDL-C=TC-(HDL-C+TG/5); this formula was only valid under conditions that TG levels did not exceed 400 mg/dL] (15). Lp(a) levels (Boehringer Mannheim, Germany) and ACA-IgG and IgM levels (Clark Laboratories, Jamestown, NY) were measured by ELISA method. For Lp(a), values <30 mg/dL were accepted as normal. In the measurement of ACAs, 12 GPL-units and 13 MPL-units were accepted as cut-off values for ACA-IgG and IgM, respectively. Whereas the ACA levels were tested only once in healthy controls, patients already diagnosed with BD were tested at least twice in an 8-week period. However, the final measurements of ACAs were included the study.

Statistical analyses. Statistical analyses were performed by using SPSS (SPSS 11.0, SPSS Inc., Chicago, IL) statistical package. For multiple groups, we used Kruskal-Wallis test. Differences between the two groups were evaluated by Mann-Whitney U test or χ^2 test, whichever was appropriate. To investigate relationships among the variables, we used