BEHCET'S DISEASE: A STUDY DONE AT KING HUSSEIN MEDICAL CENTER, AMMAN – JORDAN

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ABSTRACT

Behçet's disease (BD) is a chronic, inflammatory, multisystem disorder. Pathogenesis is not exactly known. The aim of this study was to analyze the clinical and laboratory data for patients with Behcet's disease seen at King Hussein Medical Centre.

Forty four patients were diagnosed to have BD between 2013 and 2016. The diagnosis was made on the basis of the clinical criteria of the international study group for BD. Clinical and laboratory information was retrieved and analyzed from the clinical records of all patients at Princess Eman Center for Research and Laboratory Science, King Hussein Medical Center / Royal Medical Services, Amman – Jordan.

Forty-four patients (23 males, 21 females), mean age of 31 years were diagnosed with BD. 100% of the patients had oral ulcers. 79% patients had genital ulcers. 70% of the patients in this study sample were HLA-B51 carriers.

As there were no single specific manifestations or specific diagnostic tests, diagnosis relied on clinical features. However, with the diversity of signs and symptoms, immunological studies especially detection of HLA-B51 was considered a major supportive measure for the diagnosis of Behcet's disease.

Key Words: *Behcet's disease, Immunological studies, HLA-B51 detection.*

INTRODUCTION

Behçet's disease (BD) is a rare chronic, inflammatory, multisystem disorder.[1] It is a chronic vasculitis of arteries and veins of all sizes characterized by recurrent oral ulcers (OU), genital ulcers (GU), ocular and skin involvement, and other multisystemic features, such as articular, vascular, intestinal, pulmonary, and neurological systems. Despite a worldwide distribution, it predominantly affects populations of Asia, Middle Eastern to the Mediterranean areas.[2]

Although the pathogenesis is not exactly known, it is believed to be triggered by microbial or environmental factors, with a genetic predisposition.[3] Over the last 20 years, a substantial body of knowledge has accumulated supporting a strong genetic underpinning in Behceet's disease of the MHC-related gene HLA-B5, which was later more specifically linked to its predominant suballele HLA-B51.[4]

Laboratory findings are nonspecific and reflect the inflammatory state; C-reactive protein levels, erythrocyte sedimentation rate (ESR), leukocyte count, complement components, and acute-phase reactants may all be elevated during an acute attack. More specific immunological studies can be performed to confirm the diagnosis including Anticardiolipin antibodies test. Carriers of HLA-B51/HLA-B5 have an increased risk of developing Behçet's disease.[5]

In this retrospective clinicopathological study we collected and analyzed our Clinical and laboratory data for patients with Behcet's disease at Princess Eman Center for Research and Laboratory Science, King Hussein Medical Center (KHMC)/ Royal Medical Services.

METHODOLOGY

Forty four patients were diagnosed to have BD at KHMC between 2013 and 2016. The diagnosis of BD

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Received for Publication: March 18, 2017
Revised: April 22, 2017
Approved: April 23, 2017

was performed according to the clinical criteria of the international study group for BD, 1990, revised in 2013, (Table 1). Pathergy test was performed for all patients by dermatologists and evaluated at 24 and 48 hours. Other systemic signs and symptoms were evaluated by Rheumatologists.

Venous blood was obtained from each patient for immunological studies. Anticardiolipin antibody (ACLA) and Antineutrophil cytoplasmic antibody (ANCA) serology tests were performed. DNA was isolated from the samples collected using a high quality DNA extraction kit, QIAamp DNA Blood Mini blood kit (QIAGEN). All patients were typed for the HLA-B51 antigen using molecular methods. HLA-B51 and the subtypes were determined by PCR using sequence-specific primers (PCR-SSP).

Clinical and laboratory information was retrieved and analysed from the clinical records of all patients at Princess Eman Center for Research and Laboratory Science, King Hussein Medical Center/ Royal Medical Services, Amman – Jordan. Descriptive statistical analysis was performed for the clinical and laboratory data.

RESULTS

The database for 44 patients (23 males, 21 females), mean age of 31 years, diagnosed to have BD were reviewed retrospectively in this study. The clinical characteristics of patients in present sample showed that 100% of the patients had oral ulcers. 79% of the patients had genital ulcers. Ocular lesions (uveitis) were found in 41% of patients. Skin lesions were diagnosed in 73% of patients with positive pathergy test in 75%. Other systemic manifestations such as articular, vascular, intestinal, pulmonary, and neurological signs and symptoms were found in 34% of patients in our sample (Table 2).

TABLE 1: INTERNATIONAL CLINICAL CRITERIA FOR BEHCET'S DISEASE

- Recurrent oral ulcerations (apthous or herpetiform) at least three times in one year.

Additionally, patients must present any two of the following:

- Recurrent genital ulcerations
- Eye lesions (uveitis or retinal vasculitis) observed by an opthalmologist
- Skin lesions (erythema nodosum, pseudofolliculitis, papulopustular lesions, acneiform nodules) found in adult patients not being treated with corticosteroids
- Positive "pathergy test" read by a physician within 24-48 hours of testing.

TABLE 2: CLINICAL CHARACTERISTICS FOR THE PATIENTS

Clinical feature	No. of cases	Percentage
Oral Ulcers (OU)	44	100%
Genital Ulcers (GU)	35	79%
Uveitis	18	41%
Skin lesions	32	73%
Other systemic features	15	34%
Pathergy test	33	75%

TABLE 3: IMMUNOLOGICAL LABORATORY STUDIES

Immunological test	No. of cases	Percentage
Anticardiolipin antibody (ACLA)	14	32%
Antineutrophil cytoplasmic antibody (ANCA)	19	43%
HLA-B51	31	70%

The results of immunological laboratory studies are shown in Table 3. Anticardiolipin antibody (ACLA) was positive in 32% and Antineutrophil cytoplasmic antibody (ANCA) was positive in 43% of the patient's sample. 70% of the patients in this sample were HLA-B51 carriers.

DISCUSSION

The etiology of BD is still not exactly known and both microbial, mostly viral, and environmental factors have been proposed as triggering factors for the autoimmune mechanism. Certain immune abnormalities such as the functional T-cell subsets and mild over activity of B-cells with the presence of autoantibodies such as anti-endothelial cell antibodies and anti-cardiolipin antibodies have been reported in BD. These antibodies may contribute to the development of vascular damage and neutrophils are implicated in the pathogenesis of BD.[5]

There is no specific laboratory investigation for BD, and the diagnosis is usually based on clinical criteria. A number of classifications have been formulated, each with its own list of clinical features. The International Study Group Classification criteria, adopted in 1990 and revised in 2013 is the most widely used.[3] This classification was applied in the present study for the diagnosis of individual BD patients.

The genetic locus most widely studied in Behcet's disease is the human leukocyte antigen (HLA) complex on chromosome 6p21. Disease susceptibility has consistently been associated with many subtypes of HLA-B gene, particularly HLA-B51.1 This has been confirmed in all ethnic groups, although the association is stronger in Turkish and Japanese patients than in

Caucasians. HLA-B51 has at least 34 allelic variants: the association has been refined to the most common molecular subtypes, HLA-B5101 and HLA-B5108. HLA-B57 has recently also been associated with disease susceptibility in Caucasians, in whom it carried a relative risk of disease equivalent to that of HLA-B516. In this study, HLA-B51 positivity was found to be 70%, which was compatible with other studies.

Immunological studies are a supportive aids for diagnosis of BD. Anti-neutrophil cytoplasmic antibodies (ANCA) are strongly associated with some vasculitic disorders. In systemic vasculitis, interactions between neutrophils and ANCA may initiate endothelial and vascular injury. The presence of ANCA has been established as serological marker vasculitis such as Wegener granulomatosis, Churg-Strauss syndrome, and renal–limited glomerulonephritis as well as BD7. ANCA was positive in 43% of patients in present sample. However many researches revealed that ANCAassiciation with BD is not statistically significant.

Al-Dalaan et al studied 44 patients with Behçet's Disease (BD) to look for any correlation with anti-cardiolipin antibodies (ACLA). Twenty patients were positive for ACLA by MELISA method. They concluded that the association of ACLA with vascular thrombosis or CNS manifestation of Behçet's disease was statistically not significant.[8] In this sample only 32% were positive to ACLA which support the results of most studies in the literature.

CONCLUSION

Although the etiology of BD is not clearly identified, the pathogenesis of the disease is hypothesized as a profound vasculitis in response triggered by certain microbial or environmental factors in a genetically susceptible host. As there are no single specific manifestations or specific diagnostic tests, diagnosis relay on clinical features. However with the diversity of signs and symptoms, immunological studies especially detection of HLA-B51 are considered a major supportive measure for the diagnosis of BD.

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