

Missed symptoms of Behcet's disease

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Abstract:

Background: Behçet's disease is a systemic chronic pro inflammatory vascular disease.

Objectives: To describe new criteria for the diagnosis of patients with Behçet's disease in Iraq.

Patients and Methods: Any patient suspected or diagnosed with Behçet's disease attending the Center of Dermatology/Behçet's Unit was enrolled in this study during December 2017- June 2018. A full history was taken followed by a clinical examination.

Results: A total of 47 patients were assessed with full history and examination, 37 were females and 10 were males. The age range of patients was 11-68 years. Pethargy test was negative in 13 patients, positive in 15 and was not done in 19. Twenty-one patients had a negative family history, nine had a positive one and 17 were not sure. In 20 patients, symptoms started since childhood.

The patients complained of malaise, oral ulcers, genital ulcers, unexplained fever, decreased hearing, eye complaints, dysphagia, dyspnea, headache, memory problems, depression, muscle contraction, peripheral paresthesia, joint complains, sleep disturbances, and renal problems.

Conclusion: unexplained fever, headache, depression, malaise, sleep disturbances, memory defects, and muscle contractions are important missed criteria that may help in the early diagnosis of BD.

Keywords: Behçet's, Symptoms, Blindness

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Introduction:

Behçet's disease (BD) is a systemic chronic pro inflammatory vascular disease (1, 2) with unknown etiopathogenesis (3), which can affect any tissue (4). Recurrent mucocutaneous lesions, ocular findings, and a positive pathergy (PP) test constitute common clinical findings of BD (5-7). The estimated prevalence of 1.7 BD patients per 10,000 Iraqis is more or less similar to the prevalence in other Mediterranean and Far East countries, excluding Turkey (8). With a lack of a pathognomonic test, BD diagnosis is based on clinical criteria. Oral aphthosis, genital aphthosis, cutaneous lesions, and a PP reaction as well as uveitis /retinitis have been used in several sets of diagnostic criteria. Rates of PP reaction vary widely in different populations, with a declining sensitivity over time (9). The International Study Group (ISG) criteria for BD were developed as a collaboration of scientists to bring international agreement on one set of diagnostic criteria (10). However, when evaluated in individual countries, it was found to have low sensitivity. ISG criteria did not allow for variations in the symptoms of BD, since oral aphthous was considered an obligatory manifestation for BD diagnosis (11). Early-onset BD tends to involve females more than males with a significant drop in

the male: female ratio as compared to previously reported in national and other Middle Eastern studies. The clinical characteristics are comparable to those reported from other countries with higher neurologic involvement as compared to previous national reports (12). BD activity has a significantly negative impact on the Health-related quality of life (HRQoL) which may suggest that treating activity of disease may improve HRQoL (13). Depression and anxiety are the most documented psychological conditions in BD and are found in similar levels in both Behçet's and neuro-Behçet's patients. Chronic disease burden, functional disability, and the impact of common treatment agents (e.g. corticosteroids) may be the driving factors for these mental health difficulties, rather than frank neurological changes (14,15). A further possible mechanism may be the inflammatory process that occurs in BD, as inflammation has been associated with increased rates of both depression and anxiety (16-20). Neurological compromise, in the form of cerebral lesions and abnormalities, appears to confer an additional burden to neurocognitive capacity, over and above other common BD factors (i.e. depression, anxiety, and corticosteroid treatment). Considering psychological and neurocognitive factors when working with BD patients is important, as evidence indicates that many will experience difficulties in one or both of these areas. It would be useful for screening of high prevalence psychological conditions, such as

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depression and anxiety, to be made routine in clinics that treat patients with BD. Referral pathways, for clinical psychology or psychiatry intervention, can then be provided to those who require assistance. Neurocognitive dysfunction should also be considered, particularly for neuro-Behcet's patients. Patients who show difficulties on cognitive screening measures, or report functional cognitive problems, should be referred for neuropsychological assessment and cognitive rehabilitation (21).

Patients and Methods:

Any patient with suspected or diagnosed BD, attending the Center of Dermatology/Behcet's Unit, who accepted to be included in the study with a written consent. This descriptive study was carried out in Behcet's Unit/ Center of Dermatology/ Medical City in Baghdad, during the period from December 2017- June 2018. A full history was taken and a complete physical examination was conducted, taking note of all signs and symptoms. The study was approved by the Arab Board of Dermatology and Venereology. We adhered to the Declaration of Helsinki, in addition to obtaining individual informed consent. The Statistical Package for Social Science (SPSS) version 26 was used for data entry and analysis. Tables and graphs were used to describe the data and suitable statistical tests were applied accordingly.

Results

A total of 47 patients with suspected or diagnosed BD who attend the Dermatology Center for consultation were enrolled in the study, 37 of whom were females and 10 were males, with a female: male ratio of 3.7: 1. The age range was 11-68 years with a mean and standard deviation of (37.3±13.13) years. Family history of BD was negative in 21 patients and positive in nine, while 17 patients didn't know if other family members had the disease. Pethargy test was conducted on 28 patients and was found to be negative in 13 patients, positive in 15 and 19 didn't do it. Table 1 shows the distribution of symptoms and complaints of the patients by systems. The table shows that most body systems were affected by BD. Unexplained fever, as a general symptom was reported by 20 patients (43%), oral and genital ulcers were reported by 22 and 16 patients respectively (47% and 34%). Neurological and psychological complaints were very prevalent ranging from 30% - 38% with the more serious ones being much less prevalent. Sensory organs were also commonly involved with eye involvement reaching a high of 40%. Involvement of the musculo-skeletal system was reported by up to 36% of the patients. Nine patients were diagnosed by a dermatologist, seven by an ophthalmologist, and three by a neurologist. Four patients reported that strong stress triggered the disease. Cases with a long history of various symptoms before diagnosis: -An 18-year-old female patient reported leg paresthesia after her first pregnancy with blurred vision and general paralysis from which she recovered. Two years later and with

her second pregnancy, she had a recurrence. Another patient developed blurred vision following head injury, and was then diagnosed with BD.

- A case with a history of an oral ulcer for 14 years with malaise. Four years later he had a red eye, dysphagia, headache, loss of memory for one day, involuntary movement of his hand, tremor, leg pain on standing, disturbed sleep, sudden arousal, and kidney stone. He was diagnosed as BD after six years.
- A patient with an oral ulcer and fever since childhood and was diagnosed after 21 years.
- A case with malaise, genital ulcer four years later, fever five years later, and after one year had oral ulcer, decreased hearing, and headache referred to the eye, then dyspnea after two years, and was diagnosed as BD after five years.
- A 22-year-old had blurred vision and was diagnosed after 18 years.
- A case at age 30 years had blurred vision then oral and genital ulcers after one year and was diagnosed after one year.

Table 1: Distribution of the cases by system involvement and complaints

System	Symptom	Number	%
General	Unexplained fever	20	43
	Dyspnea	9	19
Musculo-skeletal	Joint complains	17	36
	Muscle contraction	14	30
Dermatological	Foot fissure	2	4
	Hand fissure	1	2
	Scalp folliculitis	1	2
Sensory organs	Eye complaint	19	40
	Nose complaint	11	23
	Decreased hearing	8	17
	Ear pain	1	2
	Taste changes	1	2
Gastrointestinal complains	Oral ulcer	22	47
	General	9	19
	Dysphagia	8	17
Neurological / psychological	Headache	18	38
	Depression	15	32
	Memory problems	14	30
	Sleep disturbances	14	30
	Malaise	14	30
	Peripheral paresthesia	10	21
	Gait problem	1	2
Genito-urinary	Paralysis	1	2
	Genital ulcer	16	34
	Renal problems	12	26
	Genital infection	1	2
Childhood onset	Gynecological	1	2
		20	43

Discussion:

BD is a challenging condition for any doctor because of its permanent dangerous damage if not diagnosed and managed early. The diagnosis, however, is based on weak ISG criteria with no specific diagnostic tests. An International Team for the Revision of the International Criteria for BD met to reassess the sensitivity and specificity of the existing criteria, including ISG, from 27 countries (10). The present study identified interesting and important signs and symptoms, which were not mentioned clearly in previous studies, and they may help professionals in

the understanding of the variation in the presentation of the disease. Forty-seven patients with suspected or diagnosed BD were enrolled in the study within seven months which means that BD is not rare in Iraq. An Iraqi study by Alkazzaz et al, mentioned that both doctors' and patients' awareness of BD has increased in Iraq (12).

The sex distribution varies by country. In this study: female to male ratio: 3.7:1 which is similar to the results of other studies in the Middle East like; 3.8:1 (Israel), 5.3:1 (Egypt), and 3.4:1 (Turkey) (5,22,31). Alkazzaz et al from Iraq mentioned that early-onset BD tends to involve females more than males, which is different from previously reported results in national and other Middle-Eastern studies (12). Another Iraqi study by Faiq et al, found that the frequency of males was significantly higher than that of females, similar to the present study. The activity of BD disease was significantly higher in females than males, which suggests that sex influences the disease phenotype with the neurological, vascular, and gastrointestinal involvement being higher in males, while the joint affection and BD disease activity were increased in females (13).

The age range and mean of the patients in our series was close to the global results.

Pethargy test results varied from one study to another worldwide. It is not performed in all countries and the rate of PP varies in different populations (9).

In this study, 21 cases had a negative family history, nine had a positive family history, while the others did not have a definitive answer. In some other studies, BD was considered as a sporadic disease, but a familial aggregation is well known (24). More awareness should be encouraged among medical professionals on the history of oral ulcers, especially when associated with malaise, so the condition can be diagnosed at an early stage to prevent long suffering, permanent damage and complications. We need to alert doctors for early systemic management when signs and symptoms related to the eyes are suggestive of BD to prevent blindness. Many studies have reported that ocular disease has the greatest morbidity (32). Ocular presentations represent the first manifestation of disease in 10% of patients with BD but usually occur following oral ulceration (22). Fourteen of our cases had Malaise, which was not reported in other studies, 22 had an oral ulcer, 16 had a genital ulcer, and 20 had an unexplained fever. Up to our knowledge, this is the first study that mentions fever in BD. In 20 cases symptoms began during childhood, which may indicate that the disease begins at an early age but missed. Eight cases had poor hearing, which mandates early consultation of any suspected cases to prevent hearing loss, Diagnosis of BD delay have been documented (33). In an Iraqi study, they found neutrophil-lymphocyte ratio(NLR), platelet-lymphocyte ratio(PLR), and red blood cell distribution width(RDW) are significantly increased in BD patients. The PLR and NLR were the most valuable predictors of vascular activity (34) that may help in early diagnosis.

Conclusion:

Unexplained fever, headache, depression, malaise, sleep disturbances, memory defects, muscle contractions, renal defects, nasal complains, peripheral paresthesia, dyspnea, decreased hearing and dysphagia are important missed new criteria which may help doctors in the early diagnosis of BD to avoid permanent dangerous organs damage.

We recommend modifying the criteria for the diagnosis of BD to include nonspecific fever, malaise, headache, and nonspecific neurological signs like memory disturbances, decreased smelling, decreased tasting, decreased hearing, sleep disturbances, depression, and gastrointestinal complains. We also recommend a more holistic management with coordination between specialties to manage the cases.

Conflict of interest

The author declares no conflicts of interest.

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الأعراض المفقودة لمرض بهجت دراسة وصفية للأعراض المفقودة لمرض بهجت

د لمي حسني الطه

الخلاصة:

خلفية الدراسة: مرض بهجت هو مرض وعائي مزمن ومسبب للالتهاب.

الأهداف: لوصف أعراض جديدة لتشخيص مرض بهجت في العراق.

المرضى وطرق العمل: تم إدخال أي مريض يشتبه في إصابته بمرض بهجت أو تم تشخيصه سابقاً من المراجعين لمركز الأمراض الجلدية / وحدة بهجت، خلال الفترة كانون الأول 2017- حزيران 2018، وتم أخذ التاريخ الكامل وإجراء الفحص السريري.

النتائج: كان العدد 47 مريضاً، 37 من الإناث و 10 من الذكور، تراوحت أعمارهم بين 11-63 سنة. كان اختبار البثارجي سلبياً في 13 مريضاً وكان إيجابياً في 15 مريضاً أما الباقين فلم يجر لهم الاختبار. كان التاريخ العائلي للمرض سلبياً في 21 مريضاً وإيجابياً في تسعة مرضى أما الباقين فكانوا غير متأكدين من الإجابة. وقد بدأت أعراض المرض عند 20 منهم منذ الطفولة. كان المرضى يشكون من تعب، قرح في الفم، قرح في الأعضاء التناسلية، حمى غير مفسرة، ضعف السمع، شكوى في العين، عسر البلع، ضيق التنفس، صداع، مشاكل في الذاكرة، اكتئاب، تقلص عضلي، تنمل طرفي، شكوى المفاصل، اضطرابات في النوم ومشاكل في الكلى.

الاستنتاج: الحمى غير المفسرة، الصداع، الكآبة، التعب، اضطراب النوم، مشاكل الذاكرة والتشنجات العضلية هي أعراض مفقودة قد تساعد الأطباء على التشخيص المبكر لمرض بهجت.

الكلمات الدالة: مرض بهجت، أعراض، العمى