

Editorial

How to Diagnose Behcet's Disease

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Behcet's Disease (BD) is classified among vasculitides [1], although some propose an auto inflammatory mechanism for it [2]. BD is rare, seen essentially along the silk road from Japan to Portugal [3], mainly in Turkey (370/100,000 inhabitants) and Iran (80/100,000). BD is characterized by oral and genital aphthous ulcers, skin manifestations (pseudo folliculitis, erythema nodosum, skin aphthous ulcers, pathergy phenomenon), and ocular manifestations as uveitis and retinal vasculitis [4]. There are no pathognomonic laboratory tests, imaging techniques, or other paraclinical procedures for the diagnosis of BD. Therefore, the diagnosis is mainly clinical, and in this context, the use of classification/Diagnosis criteria may be useful.

It is interesting to note that no disease has ever seen so many Classification or diagnosis criteria as Behcet's Disease [5]. The first was created by Curth in 1946. The most used criteria set was the International Study Group criteria (ISG criteria), created by 7 countries (France, Iran, Japan, Tunisia, Turkey, UK, and USA) in 1990 [6]. The last, the sixteenth set of criteria, was created by the collaboration of 27 countries (Austria, Azerbaijan, China, Egypt, France, Germany, Greece, India, Iran, Iraq, Israel, Italy, Japan, Jordan, Libya, Morocco, Pakistan, Portugal, Russia, Saudi Arabia, Singapore, Spain, Taiwan, Thailand, Tunisia, Turkey, and USA) in 2006, under the name of International Criteria for Behcet's Disease, known as ICBD criteria [7]. The criteria set were revised in 2013, becoming the 17th set of classification/diagnosis criteria for Behcet's Disease, still under the name of ICBD [8].

The ISG criteria works as follows. The presence of oral aphthosis was mandatory. Then, the presence of two of the following manifestations was leading to the diagnosis. They were genital aphthosis, skin manifestations (pseudo-folliculitis, erythema nodosum), ophthalmic manifestations (anterior uveitis, posterior uveitis, retinal vasculitis), and the presence of a positive Pathergy phenomenon, detected by the pathergy test.

ICBD works as follows: Oral aphthosis, genital aphthosis, and ocular manifestations get each two points. Joint manifestations, vascular manifestations (arterial thrombosis or aneurysm, and venous thrombosis), and neurological manifestations (Central or Peripheral) get each one point. The presence of a positive Pathergy phenomenon, checked by the pathergy test, will get also one point. If a patient gets 4 points or more, the patient is classified (or diagnosed) as having Behcet's Disease.

The performance of ISG criteria versus ICBD original and ICBD revised criteria were checked in different cohort of patients (BD versus Control patients). These cohorts were: India (50 BD), Singapore (37 BD), Iran 2004 (4900 BD, 2020 controls), the cohort of International patients for the creation of ICBD (2556 BD/ 1163 controls), Germany (86 BD, 38 controls), China (322 BD, 118 controls), Iran 2010 (6128 BD, 3400 controls), and Iran 2013 (7011 BD, 5226 controls). The sensitivity of the ISG/ICBD/rICBD criteria in the cohort of India was 72% / 100% / 100%, in Singapore 46% / 86.5% / 86.5%, Iran-2004 82% / 97.5% / 95%, ICBD 82.4% / 96.1% / 96%, Germany 83.7% / 96.5% / ?, China 65.4% / 87% / ?, Iran-2010 78.1% / 98.2% / 96.4%, and Iran-2013 77.5% / 98.3% / 96.8%. The specificity in the cohort of Iran-2004 was 98% / 93.6% / 95.7%, ICBD 96% / 88.7% / 91.2%, Germany 89.5% / 73.7% / ?, China 99.2% / 94.1% / ?, Iran-2010 98.8% / 95.6% / 97.1%, Iran-2013 99.2% / 96.2% / 97.2%. The Accuracy in the cohort of Iran-2004 was 87.1% / 97% / 96.1%, ICBD 86.7% / 93.8% / 94.5%, Germany 85.5% / 89.5% / ?, China 74.2% / 88.9% / ?, Iran-2010 85.5% / 97.3% / 97.4%, Iran-2013 86.8% / 97.4% / 97%.

The diagnosis may become easy, by using good classification/Diagnosis criteria, especially for a non-expert. Unfortunately, in Behcet's Disease, some of the clinical manifestations of the criteria, are also seen frequently in the normal population (oral aphthous ulcers), or may be seen in other diseases too (Erythema nodosum, ocular manifestations). Therefore, diagnostic errors may become frequent by non-experts. To avoid misdiagnosis, it is customary to say that when a patient fulfills the criteria, the diagnosis can be made if no other disease can explain their presence. A good example of criteria misdiagnosis may be a traumatic uveitis in a person with Recurrent Aphthous Stomatitis (RAS).

Another cause of misdiagnosis, especially by non-experts, is the misinterpretation of symptoms. This happens rather frequently for aphthous ulcers (oral and genital), which are the most frequent manifestations of Behcet's Disease. Oral aphthosis is seen, worldwide, in more than 95% or more and genital aphthosis in 2/3rd or more of the patients [3]. The most frequent errors that we see in our Behcet's Disease Unit are pemphigus vulgaris, lichen planus, herpes simplex, Crohn's Disease, and systemic lupus erythematosus, mistakenly taken for an aphthous ulcer. Therefore, to avoid errors, and subsequent misdiagnosis, one must pay attention to the clinical description of aphthous ulcers. Oral aphthosis is a round or oval ulcer, with a white yellowish necrotic base, surrounded by a red inflammatory areola. It may be from 1 to 20 millimeter wide, and last usually from one to two weeks sequelae are exceptional, except for giant aphthous ulcers. Genital aphthous ulcers resemble the oral aphthous ulcers, but they are usually larger, last longer, and produce Sequelae more frequently [3]. It is important to remember that not every oral or genital ulcer is an aphthous ulcer. Only an aphthous ulcer can be used as a diagnostic criterion. In case of doubtful lesions, a Dermatology consult is advised.

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