2015 Persian Gulf Criteria for Early Diagnosis of Behcet’s Disease

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Abstract
Behcet’s disease (BD) is a chronic inflammatory multisystem disorder belongs to the vasculitides characterized by oral aphthosis, genital aphthosis, ocular inflammation, skin lesions and vascular involvement. Behcet’s disease typically affects young adults 20 to 40 years of age with no significant difference in gender. Oral aphthosis is classically recurrent and it can be multiple or major but less likely persistent. Genital aphthosis in men and external genital aphthosis in women can be replaced by scar after improvement. Ocular inflammation is including anterior uveitis, intermediate/posterior uveitis and retinal vasculitis. Skin lesions are including pseudofolliculitis, erythema nodosum, acneiform lesions, pustular lesions, pyoderma gangrenosum, dermal aphthosis, superficial thrombophlebitis and so on. Vascular involvements are including vasculitis of small, medium and large sized vessels, arterial and venous type. Hemorrhage, stenosis and especially aneurysm formation and thrombosis are all of the vascular features of this disorder. Initial presentations of BD are commonly Oral aphthosis, Genital aphthosis and eye lesions and sometimes skin lesions and articular involvement. There are 16 sets of classification criteria for this disease including International Study Group (ISG, 1990) criteria, International Criteria for Behcet’s Disease (ICBD, 2006), ICBD revised (ITR-ICBD, 2013) and etc., but we don’t have any criteria for early diagnosis of it. In this letter the corresponding author wants to deliver Persian Gulf criteria for early diagnosis of BD.

Keywords
Behcet's Disease, ISG Criteria, ICBD Criteria, ICBD Revised Criteria, Persian Gulf Criteria

1. Introduction
Behcet’s disease (BD) is a chronic inflammatory multisystem disorder belongs to the vasculitides characterized by oral aphthosis, genital aphthosis, ocular inflammation, skin lesions and vascular involvement. It is more common along the ancient Silk Road especially Turkey, Iran, Iraq, Saudi Arabia, Chorea, China and Japan. It is rare in North American and Northern European countries. Behcet’s disease typically affects young adults 20 to 40 years of age with no significant difference in gender (1-5). Oral aphthosis is classically recurrent and it can be multiple or major but less likely persistent. Genital aphthosis in men and external genital aphthosis in women can be relapsed by scar after improvement. Epididymo-orchitis, salpingitis and varicoceles may also occur (6, 7). Ocular inflammation is including anterior uveitis, intermediate/posterior uveitis and retinal vasculitis. When all of above ocular features are seen together, called panuveitis. Conjunctivitis, episcleritis and xerophthalmia are uncommon (8). Skin lesions are including pseudofolliculitis, erythema nodosum, acneiform lesions, pustular lesions, pyoderma gangrenosum, dermal aphthosis, superficial thrombophlebitis and so on (9-11). Vascular involvements are including vasculitis of small, medium and large sized vessels, arterial and venous type. Hemorrhage, stenosis and especially aneurysm formation and thrombosis are all of the vascular features of this disorder (12-14). Articular, gastrointestinal and neurologic manifestations can occur but they are not characteristic for BD. Articular involvement is more similar to SpondyloArthritis (15-16). Gastrointestinal involvement of BD or enterobehcet is similar to Inflammatory Bowel Disease (IBD) (17). Neurologic manifestations that are compatible to BD called neurobehcet. They are including parenchymal and non-parenchymal
lesions. Sometime neurobehcet is mistaken with Multiple Sclerosis. The neurologists can detect the neurobehcet only after the confirmation of the diagnosis of BD by Rheumatologists (18, 19). Renal, cardiac and pulmonary involvements are uncommon.

Initial manifestations of BD are including (1):
- Oral aphthosis: > 80%
- Genital aphthosis: about 10%
- Ocular disease: < 10%
- Joint involvement: < 5%
- Other manifestations (mainly skin): about 7.5%

In Middle East (e.g. Iran) the Pathergy test is positive in about 50% of the patients with BD (1, 20). The rate of Pathergy test positivity in Eastern Asia (e.g. Japan) is the highest and it is lowest in Western countries. The HLA-B5 especially B51 is positive in about 50% of the patients (1). Neither Pathergy test nor HLA-B5 are pathognomonic for BD.

2. Main Body

As same as other Rheumatic diseases, the diagnosis of BD can be made by clinical/laboratory judgment of an expert Rheumatologist. There are 16 sets of classification criteria for this disease the most of which have been designed to classify BD for research purposes (21). Here we review three classification criteria among them including:
- International Study Group (ISG, 1990) criteria
- International Criteria for Behcet’s Disease (ICBD, 2006)
- ICBD revised (ITR-ICBD, 2013)

The ISG criteria for BD require the presence of recurrent oral aphthosis along with at least two of the following items when any other disorders cannot be suggested (22):
- Recurrent genital aphthosis
- Ocular lesions: anterior and/or posterior Uveitis and/or retinal vasculitis
- Skin lesions: erythema nodosum and/or papulopustular rash and/or pseudofolliculitis
- Pathergy test positivity

The ICBD criteria is including the following items:
- Recurrent genital aphthosis 2 points
- Ocular lesions (as same as ISG) 2 points
- Recurrent oral aphthosis 1 point
- Skin lesions: pseudofolliculitis or erythema nodosum 1 point
- Vascular lesions: thrombosis and/or aneurysm 1 point
- Pathergy test positivity 1 point

The presence of at least 3 points out of above total 8 points delivers the diagnosis of BD (23).

After two changes including delivery of 2 points for oral aphthosis and the addition of neurobehcet item with one point, the ICBD revised has been developed. In this criteria with at least four points out of 10, the diagnosis of BD can be established (24).

3. Conclusion

In this letter, corresponding author doesn’t want to evaluate anyone of the classification criteria for BD. I don’t want to compare their sensitivity/specificity and accuracy. I would like to remind all of the Rheumatologists in the world that we have a lot of classification criteria for BD but we don’t have any criteria for early diagnosis of it. We know that, delay in diagnosis of BD is common, especially in nonendemic areas and this delay increases morbidity and mortality. Here please let me show you some cases of BD that I have seen in practice while by using the classification criteria, their diagnosis have been delayed.

Case 1: A 25 year old man with the first episode of 5 distinct oral aphthosis along with panuveitis.

Case 2: A 22 year old woman with the first episode of one major aphthosis in mouth and one skin aphthosis in right axillary region. The Pathergy test with pustular reaction and HLA-B5 both were positive in this patient.

Case 3: A 26 year old man with panuveitis, one skin ulcer of aphthosis like and positive HLA-B5 test.

Case 4: A 30 year old woman with recurrent oral aphthosis, positive Pathergy test with pustular reaction and HLA-B5 positivity.

Case 5: A 20 year old woman with first episode of multiple oral aphthosis (one of them was major), along with some erythema nodosum in the skin of leg and Pathergy test positivity.

Case 6: A 40 year old man with anterior and posterior uveitis along with retinal vasculitis and HLA-B5 positivity.

Case 7: A 28 year old woman with recurrent oral aphthosis, multiple erythema nodosum and pustular lesions in skin.

Case 8: A 24 year old man with the first episode of multiple oral and scrotal aphthosis along with positive Pathergy test with pustular reaction.

Case 9: A 35 year old man with the first episode of multiple oral aphthosis (including 2 major aphthae), multiple pustular dermal lesions, arthritis of both ankles and positive Pathergy test.

Case 10: A 19 year old woman with anterior/posterior uveitis of both eyes and the first episode of a major aphthae in mouth and HLA-B5 positivity.

Anyone of the above cases could not be classified as BD according to the ISG, ICBD and ICBD revised criteria in initial presentation of them. Finally all of them after several weeks to several months were classified by at least one of those criteria.

The corresponding author of this letter has been trained for BD in one of the major center of Behcet’s disease (Iran) in the world. I have seen several hundreds of cases of BD whose diagnosis have been confirmed by Behcet’s man of Iran. So, after many years of practice regarding Behcet’s disease, I want to deliver Persian Gulf criteria for early diagnosis of BD that is presented in table A. Finally, the corresponding author of this letter would like to ask all of the Behcet’s men in the world to evaluate this new diagnostic criteria for Behcet’s disease along with all of above classification criteria in the initial presentation of their cases with BD diagnosed by clinical judgment.
For definite diagnosis of Behcet's disease we need at least 4 points out of the presence of the criteria.

References


Table A. 2015 Persian Gulf criteria for early diagnosis of Behcet's Disease**.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral aphthosis</td>
<td>Up to 2 points</td>
</tr>
<tr>
<td>• Multiple</td>
<td>1 point</td>
</tr>
<tr>
<td>• Major</td>
<td>1 point</td>
</tr>
<tr>
<td>• Recurrent</td>
<td>2 points</td>
</tr>
<tr>
<td>Genital aphthosis</td>
<td>Up to 2 points</td>
</tr>
<tr>
<td>• History of aphthosis</td>
<td>1 point</td>
</tr>
<tr>
<td>• The scar of aphthosis</td>
<td>1 point</td>
</tr>
<tr>
<td>• Observation of aphthosis</td>
<td>2 points</td>
</tr>
<tr>
<td>Ocular lesions</td>
<td>Up to 3 points</td>
</tr>
<tr>
<td>• Anterior uveitis</td>
<td>2 points</td>
</tr>
<tr>
<td>• Intermediate/posterior uveitis</td>
<td>2 points</td>
</tr>
<tr>
<td>• Retinal vasculitis</td>
<td>2 points</td>
</tr>
<tr>
<td>Dermal lesions</td>
<td>Up to 2 points</td>
</tr>
<tr>
<td>• Erythema nodosum</td>
<td>1 point</td>
</tr>
<tr>
<td>• Pustular lesions and/or pseudofolliculitis</td>
<td>1 point</td>
</tr>
<tr>
<td>• Skin aphthos</td>
<td>2 points</td>
</tr>
<tr>
<td>Vascular lesions</td>
<td>Up to 1 point</td>
</tr>
<tr>
<td>• Thrombosis and/or aneurysm</td>
<td>1 point</td>
</tr>
<tr>
<td>Pathergy test</td>
<td>Up to 2 points</td>
</tr>
<tr>
<td>• Papular reaction with peripheral erythema</td>
<td>1 point</td>
</tr>
<tr>
<td>• Pustular reaction</td>
<td>2 points</td>
</tr>
<tr>
<td>HLA-B5 positivity</td>
<td>1 point</td>
</tr>
</tbody>
</table>

a: Upon history and physical examination: no other diagnosis can better explain the presence of the criteria.

b: For definite diagnosis of Behcet's disease we need at least 4 points out of 13.

c: The number of aphthosis≥3

d: The diameter of aphthosis≥1 cm

e: At least 3 episodes of aphthos per year.

f: If repeated in dermal lesions, just the highest score is acceptable.

g: It can be used when the Pathergy test is negative.