

## Behcet's disease seen in China: analysis of 334 cases

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**Abstract** For the purpose of investigating Behcet's disease in China, all the patients diagnosed as Behcet's disease in our hospital during the past 2 years were recruited into the study. The clinical and laboratory data of the patients were recorded and further analyzed; 334 patients were included with 195 males and 139 females. The mean age at onset was  $35.8 \pm 11.1$  years. The most frequent initial manifestations were oral aphthae and genital ulceration. The common manifestations observed throughout the disease course were oral aphthae, genital ulceration and various cutaneous lesions. Besides these, many organs/systems including joint, eye, vessel, gastrointestinal, nervous system, cardiovascular system, and pulmonary system were also involved in 28.4, 26.1, 17.4, 16.8, 9.6, 8.1, and 4.8 % of our patients, respectively. Involvement of ocular and vascular was more common in males than in females. Behcet' disease most frequently affects the Chinese patients aged 30–39 and displays a wide clinical spectrum with varieties of severe internal organ involvement. The disease is more common and severe in males than in females in Chinese populations.

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### Introduction

Behcet's disease (BD) is a systemic disorder, characterized by mucous ulceration and different variety of manifestations suggesting vasculitis and multiorgan involvement. Involvement of important internal organs, for instance, large vessel, heart, gastrointestinal, nervous system, may lead to a worse prognosis. BD has important geographic particularities. BD is not rare in Chinese population. Here, we make a report as a component of world atlas of BD.

### Methods

All the registered and referred patients who were diagnosed as BD during the period from January 2007 to December 2009 were recruited in this study. The clinical manifestations and laboratory data of these patients were recorded into a template form specifically designed for this study and then analyzed. The odd ratio was calculated when the difference was statistically significant tested by Mantel–Haenszel method ( $\chi^2_{MH}$ ). SPSS 14.0 software was used for the data analysis, and 0.05 was set as the margin of statistical significance.

### Results

#### Epidemiology

A total of 334 patients with BD were included in this study. On average, 4 patients were diagnosed as BD in every 100

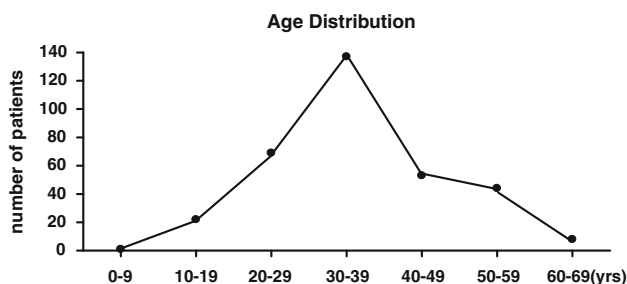
patients seen in our clinic. The prevalence of BD estimated on the number of patients seen in general population is approximately 14/100,000 [1].

#### Age and gender distribution

BD was found to affect Chinese population aged from 1st decade to 6th decade, and it most frequently happens to the patient aged between 30 and 39 years (Fig. 1). The mean age of these patients was  $35.8 \pm 11.1$  years (mean  $\pm$  standard deviation). A clear male predominance was displayed among our serial BD patients, in which 195 were male and 139 were females with a male-to-female ratio of 1.4:1.

#### Initial manifestations

The initial manifestations of BD in our patients, in decreasing order of frequency along with 95 % confidence interval (CI), were shown in Table 1. Importantly, although the most frequent initial manifestations were oral aphthae and genital ulceration, some other complains, especially some clinically severe events such as uveitis, thrombosis, and gastrointestinal perforation could also be the presenting manifestations of BD.



**Fig. 1** The age distribution of 344 patients with BD

**Table 1** Initial manifestations

Initial clinical manifestations	Frequency		95 % CI
	Number	Percentage	
Oral aphthous ulcers	277	82.9	4.0
Genital ulcers	49	14.2	3.8
Fever	22	6.6	2.7
Inflammatory ocular diseases	16	4.8	2.3
Erythema nodosum	14	4.2	2.2
Gastrointestine involvement	11	3.3	1.9
Arthralgia/arthritis	7	2.1	1.5
Deep vein thrombosis	6	1.8	1.4

#### Clinical manifestations

Oral ulceration, genital ulceration, and cutaneous lesions were the commonest manifestations, which occurred to more than half of the patients. Almost all the important systems can be involved in our BD patients. The frequency and 95 % CI of each system involvement and relevant manifestations were illustrated in Table 2.

Our data revealed that involvement of joint, eye, vessel, gastrointestine, nerve, heart and lung was, respectively, 28.4, 26.1, 17.4, 16.8, 9.6, 8.1, and 4.8 %. Peripheral joint involvement, mainly arthralgia with different types of arthritis is common in our patients, but no sacroiliitis was observed; 9.6 % of our patients presented neurological manifestations, of which more central nervous system was involved than peripheral nervous system (22 vs. 6 patients).

In general, veins were more commonly involved in BD than arteries (36 vs. 26 patients). Thrombosis is the most leading manifestation of venous involvement, while for artery involvement, both dilation (including aneurysm) and narrowing were found (14 and 9 patients, respectively).

Many types of cardiac manifestations were found. Valve involvement and pulmonary hypertension seemed to be the most common and prominent problems, especially insufficiency and regurgitation of cardiac valves, including aortic, tricuspid, and mitral valves. Pulmonary hypertension was detected in 10 patients by echocardiography based on systolic pressure higher than 40 mmHg. The average pulmonary pressure of the 10 patients measured by echocardiography was 50.3 mmHg (41–115 mmHg). Pulmonary hypertension was confirmed by right heart catheterization in 1 patient.

The involvement of each important system between males and females was compared (Table 3), and significant differences were observed in ocular and vascular lesions.

Twenty BD patients (5.99 %) overlapped with other diseases. Tuberculosis was seen in 6 patients (1.80 %), and myelodysplastic syndrome was confirmed in 5 patients (1.50 %). Other overlapped diseases were hepatitis B (3 patients), hemolytic anemia (1 patient), adenocarcinoma of intestine (1 patient), and adenocarcinoma of stomach (1 patient). Familial history of BD was recorded in 5 patients. One patient had familial history of oral aphthosis without definite BD.

#### Laboratory and other auxiliary tests

Elevated erythrocyte sedimentation rate was ever found in 225 (67.4 %) patients throughout the disease course, and 19 patients (17.3 %) showed positive HLA-B51 typing among 110 patients who accepted the testing. Urinalysis revealed proteinuria in 6 patients (1.8 %) and microscopic hematuria in 1 patient (0.3 %). No cast was noticed in urine

**Table 2** Major clinical manifestations of BD

Clinical manifestations	Frequency		95 % CI
	Number	Percentage	
Oral aphthous ulcers	326	97.6	1.6
Genital ulcers	251	75.2	4.6
Skin manifestations	213	63.2	4.4
Pseudofolliculitis	86	25.7	
Erythema nodosum	135	40.4	
Skin aphthosis	25	7.5	
Others	9	2.7	
Ocular manifestations	87	26.1	4.7
Anterior uveitis	57	17.1	
Posterior uveitis	45	13.5	
Retinal vasculitis	32	9.6	
Cataract	3	0.9	
Conjunctival aphthosis	3	0.9	
Neurologic manifestations	32	9.6	3.2
Central manifestations	22	6.6	
Peripheral manifestations	9	2.7	
Isolated headache	3	0.9	
Joint manifestations	95	28.4	4.8
Arthralgia	79	23.7	
Monoarthritis	18	5.4	
Oligo arthritis (subacute)	16	4.8	
Chronic arthritis	13	3.9	
Ankylosing spondylitis	0	0	
Gastrointestinal manifestations	56	16.8	4.0
Esophagus or gastroduodenal ulcer	28	8.4	
Acute abdomen	37	6.8	
Chronic diarrhea	11	3.3	
Proctorrhagia	16	4.8	
Vascular lesions	58	17.4	4.1
Arterial thrombosis	9	2.7	
Aneurysm	14	4.2	
Superficial phlebitis	7	2.1	
Phlebitis of limbs or thrombosis	18	5.4	
Large vein thrombosis	13	3.9	
Arterial narrowing or occlusion	9	2.7	
Epididymitis	8	2.4	1.6
Hepatosplenomegaly	7	2.1	1.5
Cardiac manifestations	27	8.1	2.9
Pericarditis	13	3.9	
Valve disorders	10	3.0	
Aortic valve regurgitation	8	2.4	
Tricuspid valve regurgitation	3	0.9	
Mitral valve regurgitation	1	0.3	
Pulmonary hypertension	10	3.0	
Angina pectoris	4	1.2	
Myocardial infarction	2	0.6	

**Table 2** continued

Clinical manifestations	Frequency		95 % CI
	Number	Percentage	
Heart failure	3	0.9	
Arrhythmia	2	0.6	
Pulmonary manifestations	16	4.8	2.3
Pleuritis	7	2.1	
Embolism	5	1.5	
Vasculitis	5	1.5	
Infection	4	1.2	
Nodule	4	1.2	
Fibrosis	1	0.3	

in our patients. Kidney biopsy was carried out in 2 of these patients, and the pathological changes were slight mesangial proliferation and minor changes. Positive anti-phospholipid antibody was found in 3 patients (0.9 %) and lupus anticoagulant in 1 patient (0.3 %). Skin pathergy test was ever seen in 124 patients (37.13 %).

## Discussion

Behcet' disease in Chinese population is multifaced, which could involve almost all of the systems. Besides high occurrence of oral and genital mucous and skin involvement, significant injuries in eye, vessel, gastrointestinal, nervous system, heart, lung and hematology present in our patients at 26.1, 17.4, 16.8, 9.6, 8.1, 4.8, and 1.5 %. Many of these complications led the patients to poor prognosis, such as permanent visual impairment, heart failure, and further increased morbidity and mortality.

The characteristics of BD in Chinese population were ever reported in some Chinese and English literatures, but relatively small number of patients was included in most of the studies except one in which 1996 cases with BD were analyzed [2–4]. Compared to the largest study previously reported, the involvement of vessel, gastrointestinal, nervous system, heart, and lung seemed to be more in this study. We think the differences were probably attributed to the patients recruited in each study. Based on the fact that our hospital is a medical center designated for diagnosis and treatment of complicated and difficult diseases, most of the patients referred from other hospitals or registered in our department were relatively more complicated and severe. We see relatively few BD patients without severe complications. Therefore, the features of 334 patients in this study may be not representative enough for our nationwide BD patients.

**Table 3** The gender distribution of systemic involvements in BD

Clinical manifestations	Males ( <i>n</i> = 195)		Females ( <i>n</i> = 139)		<i>P</i> values	Odds ratio
	No.	%	No.	%		
Inflammatory ocular diseases	67	34.4	20	14.4	>0.001	2.389*
Nervous system involvement	16	8.2	16	11.5	>0.05	
Gastrointestinal involvement	30	15.4	26	18.7	>0.05	
Large vessel involvement	44	22.6	14	10.1	>0.005	2.238*
Heart involvement	17	8.7	10	7.2	>0.05	
Pulmonary involvement	11	5.6	5	3.6	>0.05	
Hematological involvement	2	1.0	3	2.2	>0.05	

\*  $\chi^2_{MH} > \chi^2_{MH0.05}$ , the difference was significant

Gender difference was observed in our BD patients. Our data illustrated that BD occurred more frequently to males than to females and furthermore, male BD patients presented more severe diseases than female patients did. Inflammatory eye involvement and vessel involvement, the most common complications among all the major systemic manifestations in Chinese BD patients, both happened to more males and females (34.4 vs. 14.4 %,  $P < 0.001$  and 22.6 vs. 10.1 %,  $P < 0.005$ ). The conclusion on male-to-female distribution is very consistent with all of the previous reports in Chinese BD patients [2–5]. This suggests that male sex is associated with more severe disease and additional immunosuppressive therapies may be needed in Chinese male BD patients.

BD is seen everywhere in China, a big country with 56 nationalities. There are many reports from case series studies on the clinical manifestations of BD from different parts of China. Although clinical manifestations varied in these reports, the general pattern of the disease seemed to be the same in all of them. We have not seen significant variations of the clinical picture due to ethnical variation.

## Conclusions

BD is a common vasculitis in China. It starts frequently at the age of third decade. The disease is more common and severe in males than in females. BD in Chinese populations is characterized by a wide variety of clinical manifestations, with multiple system involvements. BD in some of our patients does not run a benign course.

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