# DECREASED FIBRINOLYTIC ACTIVITY IN BEHÇET'S SYNDROME

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## SUMMARY

Fibrinolytic activity was studied in eight patients with Behçet's syndrome (BS) and some of their relatives. It was observed that all patients had decreased plasma fibrinolytic activity (DPFA) independently of disorders involving coagulation troubles, like thrombophlebitis. It was also observed that relatives who had in their past, history of recurrent oral ulcers, althought not exhibiting a typical clinical picture of BS, presented a DPFA. Based on the afore mentioned facts we can admit that DPFA may probably be a determinant or codeterminant factor in the pathogenesis of the vasculitis lesions, instead of its consequence. Besides, we can not exclude the possible role of genetic factors, but further studies are needed to establish this.

## RESUMO

**Redução da actividade fibrinolitica no sindrome de Behçet**

Foi estudada a actividade fibrinolítica do plasma em 8 doentes com sindrome de Behçet e em alguns dos seus familiares. Verificou-se que havia em todos os doentes déficit da actividade fibrinolítica independentemente da ocorrência de tromboflebites. Nos familiares sofrendo de aftose recidivante, embora sem sindrome de Behçet, verificou-se idêntica alteração. Estes resultados levam-nos a admitir que o déficit da actividade fibrinolítica do plasma é provavelmente mais um factor determinante ou codeterminante das lesões de vasculite que a sua consequência não se podendo excluir o seu eventual carácter genético.

## INTRODUCTION

Vascular alterations in patients with Behçet's syndrome (BS) have been described by several authors.[1-6] They include either small vasculitic lesions or even thrombosis of vena cava. Lesions of vasculitis, whether generated or not by the deposition of antigen-antibody complexes[7, 8] activate the coagulation cascade system and subsequently fibrinolysis. The most striking observation concerning coagulation studies among BS patients, is a high concentration of fibrinogen.[5, 9] Alterations of fibrinolysis have been described both in cases of cutaneous vasculitis and BS.[1, 5, 9, 10]

In the present report we suggest that alterations of fibrinolysis are a common finding in BS patients whether they suffer from thrombophlebitis or not; those alterations can also affect some of their relatives exhibiting an apparently low grade clinical manifestation of BS.

TABLE 1 **Behçet's syndrome: Clinical manifestations in patients**

| Patients | | Age/Years | Oral ulcers | Genital ulcers | Ocular lesions | Arthropathy | Thrombophlebitis | Enteropathy | Nodose lesions | Pyoderma | CNS lesions |
|---|---|---|---|---|---|---|---|---|---|---|---|
| AI | ♀ | 25 | + | + | — | + | — | + | + | + | — |
| GNR | ♀ | 40 | + | + | + | + | — | + | + | + | + |
| AC | ♀ | 16 | + | + | — | + | — | — | — | + | — |
| BC | ♀ | 29 | + | + | — | — | — | — | + | + | — |
| ML | ♀ | 31 | + | + | + | — | — | — | + | — | — |
| AP | ♂ | 28 | + | + | + | + | — | — | + | (b) | — |
| MA | ♀ (a) | 25 | + | + | + | + | — | — | + | — | — |
| VL | ♂ | 26 | + | + | — | + | + | — | + | — | — |

(a) Eight months pregnancy.

(b) Not investigated.

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## MATERIAL AND METHODS

### Patients

Eight BS patients, of both sexes (6 females and 2 males), with ages ranging from 16 to 40 years, were studied. Oral and genital ulcers were presented in all of them. Four patients had eye lesions, six suffered from arthritis, seven exhibited subcutaneous inflammatory nodules, four had cutaneous pustules, two patients had enteritis and only one suffered from thrombophlebitis at the time of our studies. In some cases, not all these symptoms were presented at the same time, but occurred at least once in their past clinical histories (Table 1).

### Relatives

It was possible to examine one patient's sister, two daughters of another one, a sister and the parents of a third patient and the mother of a fourth one. All the sisters and the two daughters had suffered in the past from oral ulcers (Table 2).

TABLE 2 **Clinical manifestations in family members. Patients initials in parenthesis**

| Relatives | Age/Years | Recurrent oral ulcers | Other symptoms |
|---|---|---|---|
| Sister (AI) | 31 | + | — |
| Daughter (GNR) | 9 | + | — |
| Daughter (GNR) | 14 | + | — |
| Sister (AC) | 25 | + | — |
| Mother (AC) | 52 | — | — |
| Father (AC) | 56 | — | — |
| Mother (AP) | 64 | — | — |

### Controls

Eight healthy and normal individuals (4 males and 4 females) aged between 28 and 45 years were studied as controls for the fibrinolysis tests.

### Study of the plasma fibrinolytic activity

Blood from patients, relatives and controls was obtained in the morning between 11 and 12 o'clock, and studies on fibrinolysis were carried out in the plasma according to the Ratnoff's method.[11]

In the patients, three fibrinolytic studies were performed during three months and only the minimum value was considered. For the relatives and controls only one study was performed.

## RESULTS

A marked depression on the plasma fibrinolytic activity was noticed in all patients when compared with normal controls (Table 3). In fact, in controls, fibrinolysis was observed as early as 72 hours. However, among patients it never started before 168 hours (2 patients only), being detected in most of them only after 200 hours.

Decreased plasma fibrinolytic activity (DPFA) was also observed in some relatives of BS patients. Interestingly, these members did not show, at the time of our observation any symptoms of BS, but all had suffered in the past from recurrent oral ulcers. The fibrinolysis pattern of patients, relatives and controls was not related with sex and age.

TABLE 3 **Time of onset of plasma fibrinolytic activity among BS patients, relatives and controls and its relationship with sex and age**

| BS Patients | | Age/Years | Onset of fibrinolysis | Mean ± 1 SD |
|---|---|---|---|---|
| AI | ♀ | 25 | 360 hours | |
| GNR | ♀ | 40 | 598 » | |
| AC | ♀ | 16 | 216 » | |
| BC | ♀ | 29 | 288 » | *279* ± 135 (a) |
| BA | ♀ | 31 | 240 » | |
| AP | ♂ | 28 | 168 » | |
| MA | ♀ | 25 | 168 » | |
| VL | ♂ | 26 | 192 » | |
| **Relatives** | | | | |
| Sister (AI) + | | 31 | 672 » | |
| Daughter (GNR) + | | 9 | 264 » | *474* ± 210 (a) |
| Daughter (GNR) + | | 14 | 696 » | |
| Sister (AC) + | | 25 | 264 » | |
| Mother (AC) | | 52 | 120 » | |
| Father (AC) | | 56 | 120 » | 120 ± 0 |
| Mother (AP) | | 64 | 120 » | |
| **Controls** | | | | |
| GS | ♂ | 45 | 96 » | |
| JP | ♂ | 30 | 120 » | |
| CC | ♂ | 39 | 120 » | |
| AV | ♂ | 34 | 72 » | |
| MM | ♀ | 29 | 96 » | 111 ± 21 |
| MF | ♀ | 40 | 120 » | |
| OB | ♀ | 28 | 144 » | |
| GL | ♀ | 29 | 120 » | |

(a) Significantly different from controls $p < 0.001$. Student test.

\+ BS patients relatives with oral ulcers in their past clinical histories.

## DISCUSSION

DPFA has been described in BS complicated or not by thrombophlebitis although DPFA has not been considered a general occurrence among those patients.[9]

The present report indicates, however, that DPFA is probably a much commoner phenomenon in BS patients than previously stated. It may even be an usual complication in those patients.

In fact, all the eight patients we studied had a clear DPFA when compared to control values.

One possible explanation for these different results may involve the methods employed. Others [1, 9] studied fibrinolysis by the euglobulin lysis time which does not detect plasma fibrinolytic inhibitors [12] which might be the main responsible factor for the DPFA observed among BS patients and relatives. The method we used allows for such detection.

Immune complexes are probably involved in the physiophatologic processes of BS.[13, 14] If this is the case, they can be the initiating factor of the coagulation activity and subsequent fibrinolysis as a consequence of its deposition on the walls of small vessels.[15] The absence of the fibrinolytic reparative process can be theoretically explained either by the increased consumption of fibrinolytic activators, or by a gene-

tically conditioned decrease of their production. Alternatively, the DPFA can be interpreted as a consequence of a genetically determined high production of inhibitory factors.

The incidence of familial BS has been described in rare instances [5, 6, 16] but it is possible that incomplete forms could be discovered in many more cases through a careful family history. In our study we included four relatives who have recurrent oral ulcers but not other symptoms necessary to fulfill the minimal criteria of the BS, and we think that they have possibly a monosymptomatic form of the syndrome.

The plasma fibrinolytic activity observed among the patients and the above mentioned relatives showed abnormalities in contrast with the values observed among the normal controls and BS relatives without lesions.

DPFA has been reported in several types of vasculitis and it has been suggested that it could be the effect, rather than the cause of the lesions.[17] However, we think this is difficult to accept as we could find no correlation between DPFA and the presence and/or the severity of the symptoms.

So, it looks more likely for DPFA to be a determinant or codeterminant factor and its occurrence among some relatives may suggest a familial predisposition under genetic control or not.

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