Behçet’s syndrome and psychiatric involvement: is it a primary or secondary feature of the disease?

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ABSTRACT

Objective. The primary aim of the study was to determine the frequency of psychiatric disorders in Behçet’s syndrome (BS) patients, both with and without neurological involvement. The secondary aims were: to investigate a possible association between disease activity/organ involvement/demographic data and psychiatric profile in BS patients, and to compare the distribution of psychiatric disorders in BS patients compared to patients with other chronic diseases.

Methods. One hundred and sixteen BS patients were studied; in addition, two groups of patients affected by systemic lupus erythematosus and chronic arterial hypertension were included in the study as disease control groups. The end-point was represented by the assessment of disease activity, performed by the evaluation of: the presence/absence of manifestations, BDCAF and clinician’s overall perception of disease activity. Psychiatric comorbidity was evaluated according to the DSM-IV-TR criteria.

Results. The frequency of bipolar disorders resulted significantly higher in BS than in disease controls. The presence of bipolar disorders in BS patients does not seem to be related to the presence of neurological involvement in the history of the disease. Notably, a significant correlation was found between BS disease activity and mood disorders, also in the follow-up.

Conclusion. The study demonstrated a high frequency of psychiatric disorders in BS patients, peculiarly represented by bipolar disorders. The presence of this involvement, independently from the organ involvement, and strictly related to the disease activity, seems to suggest that neuro-psycho-BS may represent an intrinsic aspect of BS.

Introduction

Behçet’s syndrome (BS) is a systemic, chronic-relapsing vasculitis, typically characterised by recurrent oro-genital ulcers, ocular inflammation and skin manifestations; articular, vascular, gastro-enteric and neurological involvement may also occur (1-5).

Since there are no established laboratory findings to define BS, the diagnosis remains mainly dependent on the identification of the typical clinical pictures. In 1990, the International Study Group (ISG) for BS proposed the validated classification criteria; to fulfill these criteria, a conditio sine qua non for the diagnosis had to be the presence of recurrent oral ulcers, together with two or more of the following symptoms: recurrent genital ulcers, eye lesions, skin lesions or a positive pathergy test (6). However, BS is globally characterised by a variable spectrum of disease profile: while prevalent muco-cutaneous lesions and arthritis represent the only clinical features in patients with a benign disease subset, there are other patients who potentially develop sight or life-threatening manifestations, due to ocular, neurological or major vascular involvement (7-9).

Besides the other clinical features, it seems relatively frequent that patients with BS develop a neuro-behavioural syndrome, characterised by euphoria, bipolar disorders and paranoid attitudes, loss of insight/disinhibition, and indifference to their disease, defined as ‘neuro-psycho-BS’ (10-14). To date, the pathogenetic mechanism underlying neuro-psycho-BS has not been determined. In fact, various theories have hypothesised that the pathogenetic mechanism underlying neuro-psycho-BS may be secondary to organic neurological involvement, or it may be related to a poor quality of life and to the

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relapsing course of the disease. Another engaging theory suggests that it could be related to the frequent observation of psychiatric symptoms during relapses or, in some cases, in the phases preceding reactivation of the disease; these elements suggest that psychiatric disorders in BS could represent a crucial element, whether a psychiatric subset or a distinct clinical feature of the disease. Moreover, it has been reported that cognitive impairment in BS can be seen with or without CNS involvement (15). Globally, psychiatric symptoms have been described as multifaceted, ranging from anxiety disorders to depressive–bipolar disorders or to psychotic ones. In addition, some psychological characteristics of BS patients seem to predispose them to maladaptive stress management, which may lead to stress. Therefore, the aim of our study was to explore psychiatric manifestations in patients with BS.

Patients and methods
One hundred and sixteen BS patients with a diagnosis of BS according the ISG criteria were studied; in addition, two groups of patients affected by systemic lupus erythematosus (SLE) and chronic arterial hypertension were included in the study as disease control groups. Demographic profile of the cohort studied is summarised in Table I, while Figure 1 shows the types of organ involvement at time of the evaluation. The primary aim of the study was to determine the frequency of psychiatric disorders in BS patients, both with and without neurological involvement. The secondary aims were: i) to investigate a possible association between disease activity/organ involvement/demographic data and psychiatric profile in BS patients; ii) to compare the distribution of psychiatric disorders of patients with BS with those in patients with other chronic diseases. The subjects studied were consecutive patients evaluated at the Behçet’s Clinic of the Rheumatology Unit of the University of Pisa, which takes place weekly as an outpatient clinic. The Behçet’s Clinic has a multidisciplinary team at disposal, represented by ophthalmologists, neurologists and other specialists, in-
including psychiatrists. During the study period, all consecutive patients seen at the Behçet’s Clinic were evaluated by two psychiatrists (LP, AG), independently from the suspect of psychiatric symptoms. The study design was characterised by 2 phases:

- A cross-sectional phase, which has been conducted on the whole cohort of 116 patients and in which the following aspects were evaluated: prevalence of psychiatric disorders; association between disease activity/organ involvement/demographic data and psychiatric profile; distribution of psychiatric disorders of patients with BS and with other chronic diseases.

- A prospective cohort phase, which has been conducted on 52 consecutive patients who have been evaluated also after a follow-up of at least 6 months and in which any potential association between disease activity and psychiatric profile had been evaluated.

Disease activity was measured using Behçet’s Disease Current Activity Form (BDCAF) score and the patients were divided accordingly into two groups: a higher disease activity group with a score equal to or more than 4 out of 12, and a lower disease activity group with a score less than 4. Moreover, the clinician’s overall perception of the disease activity (from score 1 [best score] to score 7 [worst score]) has been used for clinical evaluation. From the psychiatric point of view, diagnoses were conducted by the same trained psychiatrists according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders fourth edition-Text Revised (DSM-IV-TR) (American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders fourth edition-Text Revised, 2001) (DSM-IV-TR) (16).

Statistical analysis
All the results are expressed in mean ± standard deviation (SD). Chi-square test was used to evaluate the differences among the subgroups. A p value <0.05 was considered statistically significant.

Results
The cohort of BS patients has been subdivided in two subgroups based on the presence of neurological involvement in the course of the disease. The demographic profile of the cohort of BS patients with and without neurological involvement is summarised in Table II. As shown in Figure 2, bipolar disorders (we consider type I and II), major depressive unipolar disorder and insomnia were the psychiatric disorders more frequent in Bipolar Disorders. The frequency of bipolar disorders resulted significantly higher in BS than in disease controls (p<0.001); in addition, regarding unipolar depression and insomnia, no significant differences were noted in the BS, SLE and chronic arterial hypertension groups. Moreover, the presence of bipolar disorders in BS patients (mainly hypomanic episodes) seems to be not related to the presence of neurological involvement in the history of the disease. Moreover, no correlations were found between the presence of psychiatric disorders and a specific organ involvement or demographic data. Notably, a significant correlation was found between BS disease activity and the presence of manic bipolar disorder, also in the follow-up, as shown in Figure 3 and 4.

Discussion
The results of this observational study show a higher frequency of psychiatric disorders in BS patients, compared to other chronic diseases. Specifically, bipolar disorders were the most frequent psychiatric disorder in BS patients, while unipolar depression and...
insomnia did not show a significant prevalence. Within the bipolar disorders cohort of BS patients, hypomanic episodes were more frequent. The literature data, with results from observational studies and anecdotal reports, suggest that some BS patients may have personality structures that predispose them to development of the disease. At present, the mechanism of this potential biological substrate is unknown, while the role in the stress management of these characteristics may be relevant to the genesis of the psychiatric involvement (17-19).

Moreover, anxiety and depression have been found to be common psychiatric disorders in BS patients, in some cases representing a clinical feature preceding the onset of typical symptoms of BS. Finally, bipolar symptoms and acute psychosis also represent a feature reported in BS but may present at a late stage of the disease. At present, few data are available on the therapeutic management of neuro-psycho-BS but, in some reported cases, these symptoms have been resistant to conventional psychiatric therapy. A combination of mood-stabilising drugs, such as sodium valproate, carbamazepine and olanzapine, plus treatment for BS may produce some improvement in the disease (10).

The elevated frequency of bipolar disorders, both in BS patient with and without neurological involvement, suggest that BS patients may be characterised by a specific psychiatric profile: the correlation between disease activity and hypo-manic symptoms could provide the basis for further analysis on larger cohorts, in order to better explore the mechanisms responsible for the occurrence of psychiatric disorders in BS. Indeed, the frequency of the bipolar spectrum disorders was very high in this population compared to several population-based studies which indicate a frequency of 3-6%. The possible explanation may lie under the diagnostic procedure: without using a structured interview technique like the SCID (Structured Clinical Interview for DSM) the frequency of bipolar disorders could have been overestimated. Indeed, this high percent may also be related to treatment options for BS like steroids which, in literature, have been related to mood swings. In future research we should explore if mood disorders in BS should be considered as a specific clinical feature of the disorder and if they could be related to other factors besides the disease severity such as BS treatment options.

Conclusions

The study demonstrated a high frequency of psychiatric disorders in BS patients, peculiarly represented by bipolar disorders. The presence of this involvement, independently from the organ involvement, and strictly related to the disease activity, seems to suggest that neuro-psycho-BS may represent an intrinsic aspect of BS and, for this reason, further studies are needed to better define whether psychiatric symptoms may be considered a clinical feature of BS. Structured Clinical Interview for DSM should be used to evaluate psychiatric comorbidites in BS to assess more precisely the frequency of psychiatric disorders in BS.

Therefore, in order to better manage the psychiatric involvement in BS and to better define the most effective mood-stabilising medication, besides the need of a multidisciplinary approach, specific clinical practice guidelines on BS psychiatric disorder treatment should be developed.

References