High prevalence of Behçet's disease in southern Italy

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ABSTRACT

Objectives. *This paper aims to estimate the prevalence of Behçet's disease (BD) in the city of Potenza, the regional capital of Basilicata (or Lucania) Region, in southern Italy.*

Methods. *Patients with BD living in Potenza for at least 12 months prior to diagnosis were identified through the following sources: general practitioners, community-based specialists, San Carlo Hospital specialists, the Basilicata centralised index and the Basilicata database for rare diseases. All identified patients were contacted by phone and were recalled to our outpatient clinic for re-evaluation. Patients were classified as having complete BD if they met the International Study Group (ISG) criteria for BD.*

Results. *By surveying a population of 69.060 subjects, 13 patients with a diagnosis of BD were identified. All were white and Italian by descendent. Eleven out of these satisfied the ISG criteria and allowed us to obtain a prevalence rate of 15.9 per 100.000 (95%CI 8.9–28.5), which is the highest ever found value in Europe.*

Conclusion. *This cross-sectional population-based study suggests that BD is more frequent in the southern part than in the northern part of Italy and confirms that the prevalence of the disease increases in a north-to-south manner within the European continent.*

Introduction

Behçet's disease (BD) is a multisystem vasculitis with a distinct worldwide prevalence distribution (1). It is more common in populations along the Old Silk Road, stretching between the Mediterranean basin, the Middle East and Far East, than in northern Europe, sub-Saharan Africa, the Americas and Oceania (1-15).

Although HLA-B51 accounts for a percentage ranging from 19% to 52% of the genetic susceptibility to BD (11, 16), an association exists between this allele and the disease (1). As a consequence, the prevalence of BD is usually higher in populations with the highest frequency of HLA-B51. The frequency of this allele in the Italian population is more than 10%, which is one the highest value in Europe (8). In the only Italian population-based epidemiologic study on BD carried out in a northern area, the Reggio Emilia district, the prevalence of the disease was 3.8 per 100.000 (8). Previously, a frequency of approximately 19% of the HLA-B51 allele had been found in the general population living in that area (12).

The aim of the present work was to evaluate in a cross-sectional population-based study the prevalence of BD in the population of Potenza, the largest city of Basilicata (or Lucania) Region, in southern Italy. A recent study has estimated a frequency around 17% of HLA-B51 in the population of Basilicata (13).

Patients and methods

Study setting

The study was performed in Potenza (Fig. 1), the regional capital of Basilicata (or Lucania), in January 2010. The adult population of the city was 69.060 and was predominantly constituted by white Caucasians with only 0.9% of immigrants. In the city, there are 61 general practitioners (GP) taking care of all inhabitants aged over 16 years. In Italy, it is compulsory to be followed by a GP, each of whom cannot have under surveillance more than 1500 citizens. In Potenza, there is only one hospital, San Carlo Hospital, to which every GP and community-based specialist refer patients. There are no private hospitals or rheumatologists in private practice. In 1998, San Carlo Hospital was provided with a specific outpatient clinic for BD, belonging to the Rheumatology Department of Lucania, to which patients with BD have been referred also by the other specialists working in the hospital.

Identification of patients

Patients with BD living in Potenza for at least 12 months prior to diagnosis

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Fig. 1. City of Potenza in Basilicata (or Lucania) Region.

were identified through the GP database. Other confirming sources were community-based specialists, San Carlo Hospital specialists, the Basilicata centralised index and the Basilicata database for rare diseases.

Each GP working in the city of Potenza was visited or contacted by phone to know if there was any subject suffering from BD among his patients. The same was done with hospital- and community-based specialists covering dermatology, neurology, ophthalmology, gastroenterology, angiology and urology. The Basilicata centralised index includes all diagnosis of hospitalised patients made by community- and hospital-based specialists working in the region and in other parts of Italy. Therefore, this index also allows the identification of patients living in Basilicata who are followed for their disease outside the region. On the contrary, the Basilicata database for rare diseases was generated with the aim to exempt patients with rare diseases, including BD, from payment of disease-related medical costs.

The lists of patients obtained from these different sources were compared to be certain of the identification of every patient with BD living in Potenza. No new cases were discovered using either the Basilicata centralised index or the database for rare diseases.

All identified patients were contacted by phone and were recalled to the outpatient clinic for re-evaluation. Information on clinical manifestations, laboratory findings, disease course and treatment was obtained by interviewing the patients and reviewing their medical records. HLA B51 typing was performed by PCR-SSP. Patients were classified as having complete BD if they met the International Study Group (ISG) criteria for BD (14).

Statistical analysis

Prevalence was established in January 2010. The point prevalence rate was obtained by dividing the number of patients who had the disease by the number of individuals in the Potenza population. We also calculated 95% confidence intervals (95%CI).

Results

Thirteen patients with a diagnosis of BD were identified. All were white Caucasians and Italians by descendent. Their ancestors had been living in Italy for several generations. Two out of the 13 were excluded, since they did not meet the ISG criteria. The first was an HLA-B51-positive woman with anterior uveitis and arthritis, the second an HLA-B51-negative woman with recurrent oral aphthosis and erythema nodosum. The remaining 11 satisfied the ISG criteria and allowed us to obtain a prevalence rate of 15.9 per 100.000 (95%CI 8.9–28.5).

The clinical characteristics of the 11 patients (6 men and 5 women) are reported in Table I. The median age at evaluation in January 2010 and the median duration of disease, evaluated by the day of appearance of the first symptoms of BD, were 49 years (range 24–60 yrs) and 22 years (range 5–39 yrs), respectively. The majority had the disease onset in the third decade of life, 2 before the age of 16, 1 at 33 and 1 at 45 years. As far as the mucocutaneous findings are concerned (17), oral aphthosis was experienced by all patients, but in 2 (18%) it was preceded by genital ulcers and uveitis, respectively. Skin lesions were developed by all patients, but the pathergy test was positive in only 1. Erythema nodosum was developed by 2 males and 1 woman. Ocular involvement was developed by 7 (64%) patients (5 men and 2 women), of whom only 1 (male) had isolated anterior uveitis. One patient experienced reduced muscle strength in his limbs during the disease course, suggesting nervous system involvement, but he showed no neurological symptoms and a normal cerebral MRI at the last examination. Regarding vascular involvement, no patient had venous manifestations, but 2 developed thrombosis of left temporal artery and coronary arteries, respectively. The first had thrombosis that was not possible to ascribe to another cause when he was only 26

Table I. Clinical characteristics of 11 patients with Behçet's disease.

Age (median)	49 yrs (24–60)
Men/women	6/5
Race	11 white Caucasians
Age onset first manifestation (median, range)	21 yrs (2–45)
Disease duration (median, range)	22 yrs (5–39)
Oral ulcers	11 (100 %)
Genital ulcers	8 (73 %)
Skin lesions	11 (100%)
Papulopustular	11 (100%)
Follicular	1 (9%)
Erythema nodosum	3 (27%)
Positive pathergy test	1 (9%)
Ocular lesions	7 (64%)
Anterior uveitis	3 (27%)
Posterior uveitis and retinal vasculitis	6 (55%)
Neurological involvement	1 (9%)
Vascular	2 (18%)
Superficial thrombophlebitis	0
Deep venous thrombosis	0
Arterial thrombosis	1 (9%)
Acute myocardial infarction	1 (9%)
Intestinal involvement	2 (18%)
Arthritis	2 (18%)
Systemic symptoms	5 (45%)
Fever	4 (36%)
Fatigue	3 (27%)
HLA-B51 positivity	9 (82%)

Values are the number (percentage) or otherwise indicated.

years old. The second had acute myocardial infarction at the age of 38 years, when BD was active in the absence of risk factors for cardiac ischaemic disease. Interestingly, 2 patients showed biopsy-proved intestinal involvement of BD. Two patients developed arthritis and 5 systemic symptoms, including fever and fatigue. Nine patients (82%) were HLA-B51-positive. Six and 5 patients were successfully treated with traditional and anti-TNF drugs, respectively (18, 19).

Discussion

The results of our cross-sectional population-based study greatly contributes to the knowledge of the epidemiology of BD in native European populations. In a recent population based study carried out in a multiethnic population living in France, Mahr *et al*. (9) found a higher prevalence of BD in immigrants of North African or Asian ancestry than in the European-origin population. Interestingly, the prevalence rates in immigrants were comparable with those reported from North Africa and Asia and not related to age at immigration, thus suggesting that the risk to BD is influenced by ethnicity rather than the geographic environment. Our study was performed in a population with a low rate of immigration and with a favourable organisation for epidemiological studies. All individuals of the city of Potenza are followed by GPs who greatly collaborated in this study. In addition, we examined other sources (community- and hospital-based specialists, the Basilicata centralised index and the Basilicata database for rare diseases) to be sure that no patient with BD escaped. Of course, we can have missed patients with milder disease showing only some manifestations of BD not requiring medical evaluation. Nevertheless, our estimate of prevalence rate of 15.9 per 100.000 adults constitutes the highest prevalence rate ever found in residents of European ancestry and confirms the hypothesis that the frequency of BD increases in a north-to-south manner within the European continent. Reported prevalence rates in Europe are as follows: Sweden 1.18 (5), England 0.64 (2), Scotland 0.27 (4), Germany 0.55 (7), France 2.4 (9), and Reggio Emilia area in northern Italy 3.8 (8). It should be stressed that the prevalence in Potenza was four times higher than in Reggio Emilia in spite of similar frequency of HLA-B51 in the general population (19% in Reggio Emilia district and 17% in the Basilicata region). These findings confirm that this allele accounts only partially for the genetic predisposition to BD (11, 16). As far as the comparison of clinical characteristics of our patients with those of the Reggio Emilia study is concerned, no speculations can be done due to the small number of cases.

Conclusion

In conclusion, our epidemiologic study suggests that BD is more frequent in the southern part than in the northern part of our country. This is not a completely unexpected finding since the south of Italy is closer to the countries with a higher frequency of BD surrounding the Mediterranean Sea. It is desirable that other population-based epidemiological studies are performed in other parts of southern Italy.

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