CONCISE REPORT

Cerebral venous thrombosis is associated with major vessel disease in Behçet's syndrome

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Objective: To examine the association between the type of central nervous system (CNS) involvement (parenchymal disease and cerebral venous thrombosis (CVT)) and extracranial large vessel events, mainly venous thrombosis, in Behçet's syndrome (BS).

Methods: Conventional venous angiograms, Doppler ultrasonography, computed tomography, and MR angiography were used to study 88 patients with BS, with (n = 88) and without (n = 80) CNS disease for the presence of major vessel disease.

Results: Major vessel involvement among the male patients with and without CNS disease (21/73 (29%) *v* 18/80 (23%), respectively) showed no significant differences (p = 0.374). When patients with CNS disease were stratified according to the type of CNS involvement, 7/11 (64%) patients with CVT had major vessel disease compared with 15/77 (19%) patients with parenchymal disease (p = 0.004). The mean (SD) age of onset of CVT (23.1 (8.8) years) among the male patients was significantly earlier than among the men with parenchymal disease (32.0 (7.5); p = 0.002).

Conclusions: CVT in BS was strongly associated with peripheral major vessel disease and occurred earlier in the disease course than the parenchymal type of CNS disease. As superficial thrombophlebitis also occurs more frequently in patients with major vessel disease in BS, this may suggest a common pathogenic mechanism.

Central nervous system (CNS) disease and major vessel events are the more serious complications of Behçet's syndrome (BS).[1 2] Although CNS disease has been reported in only 5% of patients with BS in a prospective study from Turkey, it may be more prevalent in European and American patients.[3 4] Around 25% of patients have frank vascular disease, mainly in the form of venous thrombosis.[5 6]

An association between deep vein thrombosis and CNS disease in BS has recently been reported.[7] CNS disease in BS occurs mainly in two forms—parenchymal disease and cerebral venous thrombosis (CVT).[8 9] We examine the association between the type of CNS involvement and vascular events, including venous thrombosis. We suggest that peripheral venous events go together with CNS disease in the form of CVT.

PATIENTS AND METHODS

We reviewed the files of 140 patients with BS and CNS disease confirmed by magnetic resonance (MR) angiography at the neuro-Behçet outpatient clinic, part of Behçet's Syndrome Research Centre, Cerrahpasa School of Medicine, Istanbul: 119 (94 male) with isolated parenchymal disease (85%), 19 patients (15 male) with CVT (14%), and two male patients with CVT together with parenchymal disease.

Eighty eight (63%) of the 140 patients with CNS disease confirmed by MR angiography could be contacted and called back to the hospital for re-evaluation. In addition, 80 consecutive male patients with BS attending the same outpatient clinic who did not have CNS disease were evaluated for large vessel events. All patients and controls fulfilled the International Study Group for Behçet's Disease classification criteria.[10]

After a complete history and examination, the files of all patients and controls were reviewed for previous large vessel events. Large vessel disease was diagnosed by conventional venous angiograms, Doppler ultrasonography, computed tomography, and MR angiography.

χ^2, Fisher's exact, and Student's *t* tests were used for comparisons.

RESULTS

The 88 patients with CNS disease (73 male) were older than the 80 controls (mean (SD) 38.9 (8.8) *v* 32.8 (4.1) years; p = 0.007). Furthermore, among the men, the age of the onset of CVT was significantly earlier than the onset of parenchymal disease (23.1 (8.8) *v* 32.0 (7.5) years; p = 0.002). Among the small number of women studied (three) no such trend was observed (data not given).

The frequency of major vessel disease among the male patients with CNS disease (21/73 (29%)) did not differ from that seen among the control patients with no CNS disease (18/80 (23%); p = 0.374)

Table 1 summarises the distribution of major vessel disease among patients with and without CNS disease. As expected, parenchymal disease was more common than CVT both among the men (65/73 (89%)) and the women (12/15 (80%)). All patients with large vessel disease among those with CNS involvement, except for one patient, were men. Localisation of major vessel disease among patients with CNS disease was similar to that of control patients.

Interestingly, when the patients with CNS disease were stratified according to the main two types of CNS disease, 7/11 (64%) patients with CVT (all seven had thrombosis of major veins, one patient with associated pulmonary disease and a second with associated iliac artery disease) had significantly more major vessel involvement than the 15/77 (19%) patients with parenchymal disease (p = 0.004).

DISCUSSION

In this retrospective survey we found that thrombosis in the large veins showed a strong association with CNS disease in the form of CVT and not with parenchymal involvement. A shortcoming of our study was that it was retrospective. We could re-evaluate only 63% of our patients with CNS disease. The possibility cannot be ruled out that those patients with parenchymal CNS disease with concomitant major vessel

Abbreviations: BS, Behçet's syndrome; CNS, central nervous system; CVT, cerebral venous thrombosis; MR, magnetic resonance

Table 1 Types and distribution of major vessel disease among patients with CNS disease and controls

Types and localisation of major vessel involvement	Patients with CNS disease (n = 88; 73M, 15F)		Controls(n = 80; all M)
	Parenchymal disease (n = 77; 65M, 12F)	Cerebral venous thrombosis (n = 11; 8M, 3F)	
Venous thrombosis	11*	5	14
Arterial and venous disease	1	2	2
Arterial disease only	3	0	2

*One female.

disease were underrepresented in our series because they had died or were unavailable for re-evaluation owing to their more severe disease course.[8 9] A prospective study could answer this question. After finishing our study we found that an association similar to that we describe here had been found, again in a retrospective survey, by Wechsler *et al*.[11] They reported that 64% of their patients with BD and CVT had associated major vascular lesions compared with 36% patients without CVT.

In our series there was no significant association between parenchymal CNS disease and major vessel involvement. Thus the proportion of patients with major peripheral vascular disease in our control group without CNS disease was similar to the frequency of major vessel disease in our control group. Our control group of patients without CNS disease were, on average, 6 years younger than our patients with CNS disease. This might be another source of bias. It might be said that the younger patients had not had the time to develop the CNS complication during their disease course. We do not think this was an important bias because the prevalence of peripheral vascular disease (64%) that we report for patients with CVT-type CNS disease is considerably higher than the 19% prevalence found in our patients with parenchymal disease; it is also higher than the prevalence (136/387; 35%) we found in our 20 year survey of a large cohort of patients, recently reported.[12]

It is not quite clear if vasculitis is the main pathology underlying parenchymal CNS disease in BS in all cases.[13] Hadfield *et al* described the postmortem examination of a patient with neurological disease who died after a protracted course. Inflammatory cells had accumulated in the central nervous system, but no evidence of bone fide vasculitis was seen.[14] Our findings support the suggestion that the parenchymal form of CNS disease in BS might not be part of a more generalised vasculitis localised in the CNS system.

A new observation was that CVT usually started nearly a decade earlier than the parenchymal type of CNS disease. It is also well established that CNS disease in the form of CVT has a much better prognosis than parenchymal CNS involvement.[8 9] It might also be proposed that there is a mechanism in some patients with BS that make them more prone to thrombosis in veins of all sizes, including dural sinuses. Support for this also comes from the observation that patients with major vessel disease, in general, have more superficial thrombophlebitis (32%), and most (82%) of the patients with major vessel disease that Koc *et al* described had disease in their major veins, as we found in this study.[6] These three peculiarities of the CVT type of CNS disease support the suggestion that the CVT type of CNS disease in BS may have a different pathogenic mechanism from the parenchymal type of CNS disease.

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