The prevalence of headache in Behçet’s syndrome

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Objectives. Behçet’s syndrome is an uncommon systemic disorder that involves the nervous system in 5% of cases. Headache may arise in conjunction with such complications but also appears to occur independently. We sought to define the prevalence of headache in an unselected group of patients with Behçet’s syndrome, to characterize the headache syndromes and to identify what treatments are being used.

Methods. A questionnaire was sent to an unselected group of patients through their support group newsletter.

Results. The results showed a prevalence of recurrent headache in 82.5% of responders; the majority exhibited symptoms that fulfilled the International Headache Society criteria for migraine, with a higher than normal prevalence of visual or sensory aura of 52%. Using the Migraine Disability Assessment (MIDAS) score for disability in migraine, 62% of responders showed moderate or severe disability. Headache treatment was poor, the majority of sufferers resorting to over-the-counter remedies; preventative treatments had rarely been prescribed.

Conclusions. Recurrent headache is very common in Behçet’s syndrome, is poorly treated and is associated with disablement.

Key words: Behçet’s syndrome, Neurological complications, Headache.
TABLE 1. Details of the second questionnaire sent

<table>
<thead>
<tr>
<th>1. How frequently does your headache occur during an average month?</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Average</th>
<th>Throbbing</th>
<th>Dull</th>
<th>Constant</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. How long does it last?</td>
<td>Behind the eyes</td>
<td>In the forehead</td>
<td>On one side</td>
<td>All over</td>
<td>Worst at the back</td>
<td>In the neck</td>
</tr>
<tr>
<td>3. Is it:</td>
<td>Intolerance of light</td>
<td>Intolerance of noise</td>
<td>Nausea</td>
<td>Vomiting</td>
<td>Worse with movement</td>
<td>Yes/No</td>
</tr>
<tr>
<td>4. Where is it worst?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Are there other symptoms with the headache?</td>
<td>Headache</td>
<td>Migraine prophylaxis</td>
<td>Nil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Is there a visual disturbance before or during the headache?</td>
<td>Always</td>
<td>Sometimes</td>
<td>Rarely</td>
<td>Never</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Is there tingling before or during the headache?</td>
<td>Yes/No</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. What treatment do you take for an average headache?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Is it helpful:</td>
<td>Always</td>
<td>Sometimes</td>
<td>Rarely</td>
<td>Never</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discussion

In this cohort of patients the prevalence of headache was high at 82.5%; clearly there may be bias in the second group in that the questionnaire was focused on headache alone, and it is not, thus, surprising that the prevalence of headache rose in this group. There may be further bias; not all patients with Behçet’s syndrome are members of the Behçet’s Syndrome Society, and it is conceivable that those who are members are more severely affected than those who are not and that those who responded are more severely affected by neurologic symptoms. Others, previously diagnosed who no longer have disease activity, may not have responded, feeling that their headaches were unrelated. The prevalence of Behçet’s syndrome in Hertfordshire was \( 5 \times 10^3 \) in 2002 [7], suggesting that there would be 1500 patients in the UK were the prevalence to be the same throughout the country; hence, the survey cannot claim to represent the experiences of all patients in the UK. However, previous studies of selected groups of patients attending Behçet’s syndrome clinics have also shown high prevalence of headaches [8–10]. The majority of patients in this cohort described headaches that fulfill the International Headache Society criteria for migraine [11]. Only 2% had headache characteristics in keeping with tension-type headache. Of the remainder, a surprisingly high percentage (52.7%) experienced visual aura during most of their headaches. The prevalence of migraine in the general population is 8–17% and the prevalence of aura is only 2–30% [12, 13]; hence, in this population both headache and migraine aura are over-represented. Why might this be? Clearly there are inadequacies in the method used in this study; non-responders were not approached in order to define whether or not the results are skewed in favour of those with more severe and frequent headache symptoms, and the data were not acquired prospectively; rather, the responder was asked to give an impression of headache frequency and severity, which may not therefore be accurate. Nonetheless, it is clear from this and other studies that vascular headache is a common symptom in this disorder.

Migraine is a neurovascular headache in which dysfunction of nociceptive afferent pathways within the brainstem and diencephalic nuclei occurs, leading to excessive discharges from the spinal nucleus of the trigeminal nerve, so causing the appreciation of pain. Dilatation of blood vessels occurs as a secondary phenomenon, leading to further pain. Migraine aura arises as result of cortical hyperaemia immediately followed by oligaemia, which is due to a ‘spreading depression’ of depressed cortical function [14]. Why some patients have aura and others do not is not understood.

In Behçet’s syndrome vasculitis may arise, but perhaps not in the brain [15]; venous thrombosis, including that of the venous sinuses, may arise and, more rarely, aneurysm formation. There is accumulating evidence that factor V Leiden mutations contribute to the vascular complications of uveitis [16] and to venous thrombosis [17]. The prevalence of these abnormalities in headache has not yet been established. Vascular endothelial cell abnormalities also exist, and studies of brachial artery flow-mediated dilatation show impairments in patients with Behçet’s syndrome which were absent in normal controls and which were reversed by the administration of vitamin C, an antioxidant that removes superoxide anion radicals [18]. This study suggested that reduced endothelial cell function in Behçet’s syndrome may be related to increased oxidative stress. Nitric oxide levels are reduced in Behçet’s syndrome, which would be inclined to induce...
vasoconstriction since nitric oxide is a potent vasodilator, and yet vasodilators such as GTN are used to induce migraines in susceptible patients for studies. It is not clear, therefore, how an underlying vascular abnormality in Behçet’s syndrome may contribute to this. Studies of vascular reactivity in migraine show an increased response to exercise, stress and carbon dioxide, which again is the opposite to that seen in Behçet’s syndrome.

Another association to consider would be a linked genetic predisposition; inherited forms of migraine have been linked to the α1 subunit of the P/Q-type voltage-gated calcium channel on chromosome 19 [19]. No genetic association between Behçet’s syndrome and this gene has been found, however, and a recent study in which the genome was screened has shown evidence for linkage on chromosomes 6 and 12 [20].

Vascular headaches are said to be prevalent in systemic lupus erythematosus [21] and Sjögren’s syndrome [22], but again the pathogenesis is not understood. Moreover, a recent meta-analysis of previously published studies of headache in lupus has failed to prove that a true relationship exists between the two disorders [23].

Epidemiological studies of migraine have shown that most patients are undertreated, many having given up on physician advice and resorting to over-the-counter preparations for migraine relief [12]. Such appears also to be the case for this cohort of patients. In the author’s experience, many patients simply presume that frequent headache is part of the difficulty of having Behçet’s syndrome and accept that nothing may be done successfully to alleviate the problem. However, it is also the author’s experience that these patients respond well to standard antimigraine preparations, such as propranolol and pizotifen. No formal trial of the effectiveness of these drugs in the treatment of headache in Behçet’s syndrome has yet been undertaken.

In summary, this study has revealed a very high prevalence of headache in an unselected population of patients with Behçet’s syndrome. The majority of headaches is of neurovascular type and the prevalence of visual or sensory aura is higher than that seen in the general population of migraine sufferers. In general, patients are inadequately treated. Neurovascular headache occurs in patients with and without clinical evidence for inflammatory or vascular neurological complications of the disorder. The reason for the high prevalence of headache in this population is not currently understood and a formal class 1 prospective epidemiological study is currently underway that will investigate this further.

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References