Rare disease

Behçet's disease presenting as new onset of confusion in a male patient of North African origin in the UK

Ross Dolan,^{1,2} Suzanne Watson,² Debbie Bathgate³¹Department of Neurology, University of Dundee, Dundee, UK²Department of Neurology, Ninewells Hospital, Dundee, UK³Department of Neurology, James Cook University Hospital, Middlesbrough, UK

Correspondence to Ross Dolan, rdolan@nhs.net

Summary

A 50-year-old right-handed man presented with headache accompanied by new onset confusion and slurring of speech over a 5-day period. This was initially suspected to be due to a transient ischaemic attack. On examination he had a clear ptosis of his left eye, which had developed just 6 days prior to his most recent admission; however, the rest of his neurological examination was normal. A neuropsychiatric review showed poor verbal recall, below average visual contrast ability and below average verbal learning scores. He had a medical history of recurrent oral ulcerations accompanied by anterior uveitis and recurrent genital ulcerations on the scrotum. Imaging showed increased unilateral signal in the left thalamic area, which when taken together with the clinical history, supports the internationally recognised diagnostic criteria for Behçet's disease. The patient lacked insight into his condition meaning that long-term residential care may be required.

BACKGROUND

Behçet's disease (BD) is a rare autoimmune systemic vasculitis that can affect all major systems in the human body, including the central and peripheral nervous systems. As a result, confusion and neuropsychiatric symptoms can be the initial presenting complaint in many cases. When this is coupled with the increased immigration to the UK from areas where BD is relatively common, such as the Middle East, Asia and North Africa, this otherwise rare condition must be considered as part of the differential diagnosis of any patient between the ages of 40 and 60 years presenting with new onset confusion.

CASE PRESENTATION

A 50-year-old right-handed man presented with headache and new onset confusion and slurring of speech over a 5-day period. Prior to this acute presentation he had begun to exhibit clear personality changes with increased irritability, fatigability and emotional lability.

On examination he had a marked ptosis of his left eye, which had developed 6 days prior to his admission; however, the rest of his neurological examination was normal. A neuropsychiatric review showed poor verbal recall, below average visual contrastive ability and below average verbal learning scores. These findings could have been interpreted as being due to a low premorbid intelligent quotient; however, this was not in keeping with his educational level. Although English was not the patient's first language, these results indicated clear cognitive impairment.

Initially it was suspected that the patient had a vascular event, such as a transient ischaemic attack (TIA), which was supported by his medical history of a recent right branch retinal vein occlusion. As a result, CT and MRI imaging was conducted. Both of these showed a focal haemorrhage located unilaterally in the left thalamic area, which would have supported this diagnosis. However, the

extent of the bleed was not in keeping with such marked cognitive impairment and, as such, other causes needed to be considered. Serum, *venereal disease research laboratory* test, *Treponema pallidum* haemagglutination test and anti-HIV antibody were negative. Thyroid function tests, vitamin B12 and folic acid levels were normal.

The patient had a medical history of recurrent oral ulcerations accompanied by anterior uveitis and recurrent genital ulcerations on the scrotum. When these clinical findings are taken together with the new onset confusion and the isolated area of haemorrhage in the thalamic region, a diagnosis of BD was formulated despite a negative pathergy test result.

INVESTIGATIONS

MRI of the brain found focal haemorrhage in the thalamus and CT of the head confirmed the presence of a thalamic bleed. Repeat MRI findings found further worsening of oedema around the haemorrhagic lesion in the left thalamus with extension into the midbrain and brainstem.

Human leucocyte antigen (HLA)-B27 screen, interleukin 6 (IL-6) *cerebrospinal fluid* (CSF) screen and Behçet's pathergy test were all negative.

DIFFERENTIAL DIAGNOSIS

TIA, cerebral vasculitis, listeria, cerebral tuberculosis, meningeal tuberculosis, toxoplasma and HIV

TREATMENT

Dexamethasone in order to reduce intracranial inflammation, which improved the patient's cognitive state.

OUTCOME AND FOLLOW-UP

The patient showed a clear lack of insight into his condition insisting that there was nothing wrong with him. He

absconded from the ward on several occasions and claimed that he was being held against his will. As a result, at the time of writing this report, a case conference was being organised with the aim of putting together a care package with long-term residential care being the most likely outcome.

DISCUSSION

BD is an autoimmune vasculitis, which can have multi-systemic manifestations; however, its exact pathophysiology is not fully understood.¹ It is very rare in the UK with just 11 cases reported in the literature.^{2–4} There are clear genetic and environmental components to its presentation and pathology and like most autoimmune conditions it is more common in women.⁵ Autoantibodies play a role in the systemic vascular inflammation seen in BD. Specifically, human leucocyte antigens B5 and B51 (HLA-B5 and HLA-B51) are particularly common along the ancient route of the silk road stretching from the Mediterranean to China and the far East.¹ Interestingly, patients in the UK and Northern Europe do not show such a strong association with HLA-B51, with other genetic factors such as HLA-B27 being more common.^{6,7} The preponderance of BD in certain areas suggests that environmental factors, such as endemic infectious agents, could act as triggers in much the same way as gastrointestinal infections can lead to activation of autoantibodies targeted at the host's nervous system in Guillain-Barre syndrome.¹

In this particular case it could be argued that the patient's BD has lead to a firm diagnosis of early onset dementia. This is because dementia is a clinical diagnosis made when acquired cognitive deficits in more than one area of cognition interfere with activities of daily living and represent a decline from a previously higher level of functioning, which certainly is the case with this particular man.⁸ The diagnosis of BD is based on internationally recognised diagnostic criteria that have been in place since the early 1990s and that are outlined in table 1. A positive pathergy test, while strongly suggestive of BD, is not essential for a firm diagnosis to be made. This is due to the difference in the ability of this test to positively identify new cases depending on the target population being investigated. For example, 60% of patients from the Middle East and 44% of Japanese patients have a positive pathergy but it is relatively uncommon in British patients.⁹

Neurological manifestations of BD include new and often debilitating confusion, which has been widely reported in the literature, corticospinal tract abnormalities affecting locomotion and both upper and lower limb power.¹² Brainstem involvement can result in problems with respiratory control and emotional liability, which when

exacerbated by the cognitive impairments and memory dysfunction associated with neurological BD can place strain on interpersonal relationships.¹²

Assessment of memory often shows equal impairment of learning and recall functions in both verbal and visual tasks, while attention deficit and frontal executive dysfunction are also common abnormalities.¹³ Orientation, language, visuospatial functions, abstraction and problem-solving abilities can be relatively well preserved; however, some degree of dysfunction is often seen.¹³ This patient had symptoms suggestive of anterograde amnesia with an apparent difficulty in learning new information. Damage to the hippocampus, fornix, mamillary bodies, anterior and medial thalamic nuclei or basal forebrain can result in anterograde amnesia.¹³ This is in keeping with the patient's MRI images, which show high signal damage and inflammation in the left thalamus. These imaging results are also consistent with the classically unilateral upper brainstem lesion that extends into the thalamus and basal ganglia reported in the literature.¹⁴ However, the thalamic areas are not the only centres of the brain to be affected as BD can also lead to high signal change in the brainstem, thalamus, basal ganglia and white matter of the cerebral hemispheres.¹⁵ BD also has a strong inflammatory component, which can lead to the upregulation of inflammatory cytokines such as IL-6 in the CSF showing active axonal loss and gliosis. This makes investigation of inflammatory markers in spinal fluid essential in any patient with suspected BD.^{16,17}

Currently there is no cure for BD; however, management often focuses on reducing inflammation with systemic steroids and using immunosuppressants to reduce autoantibody activity. It is an important but rare condition to consider in young patients who present with confusing neuropsychiatric symptoms and confusion. This is particularly true of patients of Middle Eastern, North African and Asian descent whose numbers have increased in the UK due to recent immigration patterns. As a result, the assessment of any patient presenting with confusion if they are of non-indigenous descent must include questions about recurrent oral ulceration as well as eye problems, such as anterior uveitis, and skin lesions in order to identify any cases of BD early to allow for prompt treatment.

The extreme difficulty in managing patients with young-onset dementia and BD can be seen by the problems in follow-up care for this particular patient following discharge. A case conference recommended that residential care would have been the preferred option for this man; however, this was not accepted by his wife who decided she could cope with him with significant social work input/supervision. This arrangement proved to be less than ideal

Table 1 International Behçet's Disease Study Group criteria for the diagnosis of Behçet's disease^{10,11}

International Behçet's Disease Study Group criteria for the diagnosis of Behçet's disease^{10,11}

Recurrent oral ulceration must be present: these can take the form of minor or major aphthous ulcers or herpetiform ulceration observed by physician or patient that recur at least three times over a single 12-month period.

Plus two of the following symptoms:

- ▶ Recurrent genital ulceration: aphthous ulcers or scarring observed by physician or patient.
- ▶ Eye lesions: anterior uveitis, posterior uveitis or cells in vitreous on slit lamp examination; or retinal vasculitis observed by an ophthalmologist.
- ▶ Skin lesions: in the form of erythema nodosum observed by physician or patient, pseudofolliculitis, papulopustular lesions; or acneiform nodules observed by physician in post-adolescent patients not on corticosteroids.
- ▶ Positive pathergy test: this is preformed with a sterile 20–22 gauge needle being used for direct skin irritation. A positive result is when an erythematous papule larger than 2 mm develops at the test site after 48 h.

and his apathy caused him to sit most of the time interspersed with impulsive bouts of activity and a tendency to become certainly verbally aggressive when attempts to thwart him in his efforts were made. Indeed, the outpatient management was so difficult that detention under the mental health act was considered; however, before this could be instigated the patient absconded to visit friends and family abroad where he currently still resides. He has instructions to make contact with the health service upon his return to the UK and social workers have been instructed to look out for his return; however, his strongly held belief that there is nothing wrong with him makes management a continued problem.

Learning points

- ▶ BD is a rare vasculitic condition with a strong genetic and environmental component.
- ▶ It is more common in the Mediterranean, North Africa, Middle East and Asia.
- ▶ It should be considered as part of the differential diagnosis of any patient presenting with new onset confusion with recurrent oral ulcerations and skin/eye lesions, particularly if they come directly from or are descended from a population in a BD endemic area.
- ▶ Management is with steroids and immunosuppressants in order to reduce inflammation and immune activity.
- ▶ Cognitive deficits rarely fully resolve and as a result a holistic and multidisciplinary approach to patient care is required with residential care often being the preferred option.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Kontogiannis V**, Powell RJ. Behçet's disease. *Postgrad Med J* 2000;**76**:629–37.
2. **Aldeen A**. Behçet's disease, painful genital ulcerations and steroid pulse therapy. *BMJ Case Reports*. <http://casereports.bmj.com/content/2009/bcr.07.2008.0353.full> (accessed 5 May 2010).
3. **Poon W**, Verity DH, Larkin GL, *et al*. Behçet's disease in patients of west African and Afro-Caribbean origin. *Br J Ophthalmol* 2003;**87**:876–8.
4. **Kermode AG**, Plant GT, MacManus DG, *et al*. Behçet's disease with slowly enlarging midbrain mass on MRI: resolution following steroid therapy. *Neurology* 1989;**39**:1251–2.
5. **Al-Araji A**, Kidd DP. Neuro-Behçet's disease: epidemiology, clinical characteristics, and management. *Lancet Neurol* 2009;**8**:192–204.
6. **Yazici H**, Tüzün Y, Pazarli H, *et al*. Behçet's disease as seen in Turkey. *Haematologica* 1980;**65**:381–3.
7. **Yazici H**, Tuzun Y, Pazarli H, *et al*. The combined use of HLA-B5 and the pathergy test as diagnostic markers of Behçet's disease in Turkey. *J Rheumatol* 1980;**7**:206–10.
8. **Rossor MN**, Fox NC, Mummery CJ, *et al*. The diagnosis of young-onset dementia. *Lancet Neurol* 2010;**9**:793–806.
9. **Davies PG**, Fordham JN, Kirwan JR, *et al*. The pathergy test and Behçet's syndrome in Britain. *Ann Rheum Dis* 1984;**43**:70–3.
10. Criteria for diagnosis of Behçet's disease. International Study Group for Behçet's Disease. *Lancet* 1990;**335**:1078–80.
11. **Lee S**. Diagnostic criteria of Behçet's disease: problems and suggestions. *Yonsei Med J* 1997;**38**:365–9.
12. **Serdaroglu P**. Behçet's disease and the nervous system. *J Neurol* 1998;**245**:197–205.
13. **Park KW**, Seo JH, Yoon GU. Selective anterograde amnesia with thalamus and hippocampal lesions in neuro-Behçet's disease. *Clin Neurol Neurosurg* 2007;**109**:470–3.
14. **Abdallah MA**, Ragab N, Khalil R, *et al*. Circulating immune complexes in various forms of Behçet's disease. *Int J Dermatol* 1995;**34**:841–5.
15. **Buge A**, Vincent D, Rancurel G, *et al*. Behçet's diseases with multiple intracranial arterial aneurysms. *Rev Neurol (Paris)* 1987;**143**:832–5.
16. **Al-Araji A**, Kidd DP. Neuro-Behçet's disease: epidemiology, clinical characteristics, and management. *Lancet Neurol* 2009;**8**:192–204.
17. **Hirohata S**. Central nervous system involvement in Behçet's disease. *Rinsho Shinkeigaku* 2001;**41**:1147–9.

This pdf has been created automatically from the final edited text and images.

Copyright 2010 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Dolan R, Watson S, Bathgate D. Behçet's disease presenting as new onset of confusion in a male patient of North African origin in the UK. *BMJ Case Reports* 2010; 10.1136/bcr.05.2010.2982, date of publication

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow