BSS 2016 Conference and AGM

The 2016 BSS Conference and Annual General Meeting took place at The Plough and Harrow, Birmingham, on 15 October. It was attended by 73 people.

AGM business

Rachael Humphreys opened proceedings by welcoming everybody and running through the programme for the day. Alan Booth introduced the Trustees, as well as Administrator Julie Collier and Newsletter Editor Clare Griffith.

Treasurer's report

Alan Lane reported that membership of the Society is still increasing. As of 1 September 2016, there were 1050 members. These included 945 full members, eight junior members and 50 associate members (mostly medical professionals). The number of possibly lapsed members is down to 10. There is a preponderance of female members (752 versus 283 males), and most members (855) are patients. The average age is 51 years, with a majority between 30 and 70 years. Most (860) members live in England, with 80 in Wales, 53 in Scotland, 26 in Northern Ireland, seven in the Channel Islands and 14 overseas.

Almost half (47%) of the Society's income is from donations, with 21% coming from subscriptions and 14% from fundraising. Gift Aid is an important source of income, contributing 7%, with another 7% coming from the Behçet's Patient Centres (BPC). The Society receives no government grants and depends on its members for funds. In the last year, about 20% of the money spent went on producing the newsletter, 16% on fundraising and another 16% on the AGM. A further 13% was spent on charitable support and 10% on the website.

The Society's income in 2015/16 was £45,700 (compared with £63,400 in 2014/5), and expenditure was £39,200 (compared with £43,300 in 2014/15). The Society now has an operating surplus of £81,400, which is very healthy. The Society will be looking for ways to provide more services for members, as the aim is not to keep a large amount of money in the bank. The research fund, which contained £6,500 at the

end of 2014/15, now has £12,400. The Society will be looking for a suitable project to spend this on.

Society news and Helpline update

Judi Scott confirmed that the annual subscription will stay at £20 for 2015/16 and the Grant Aid limit will remain £750. She encouraged members to send contributions to the newsletter, especially good news stories and photographs. Julie Collier then gave an update on the Helpline, on behalf of Tony Wright (who was unable to be present). The Helpline volunteers are Tony, Alan Booth and Fionnuala McKinley, who take 1 week each in turns. Since July, they have received 30 calls and a similar number of emails. Most calls are from people who have been recently diagnosed or are seeking a diagnosis, and the initial call usually lasts about an hour. Judi sends out information packs to new patients, and the volunteers signpost them to the BPC or a local consultant with experience of Behçet's disease (BD). There is a handbook for new Helpline volunteers, and they would not need to commit to doing a whole week. Tony reported that he had gained a lot of knowledge about BD and how it affects people by working on the Helpline, and that he enjoys talking to the different people who call.

Rachael then informed everyone that next year's Annual Conference will be in Manchester. She showed a video montage of many of the fundraising events that took place in the past year, as well as a video she made for Rare Disease Day to raise awareness of BD.

Medical presentations

Overview of Behçet's disease and therapies

Dr Deva Situnayake, Clinical Lead at the Birmingham Centre, began by saying that recognising BD is not easy. The estimated prevalence of 2 cases of BD per 100,000 people in northern Europe suggests a total of 1060 cases in England; the three centres have 1221 patients under active follow-up. Of the 53 million people in England, about 10 million have mouth ulcers at some time and more than a million have genital ulcers (mostly caused by herpes simplex virus). There are many possible causes of mouth ulcers, and lots of different possible diagnoses for people with mouth ulcers

and systemic symptoms such as those seen in BD. With no blood test for BD, diagnosis relies on applying the criteria once other more likely diagnoses have been ruled out. Multidisciplinary assessment is needed to make the diagnosis, and patients must be followed up to be certain the diagnosis is correct.

Several subsets of BD are recognised, with different patterns of manifestations, and each of the subsets resembles other conditions. For example, neuro-BD can be similar to multiple sclerosis and gastro-BD often looks a lot like Crohn's disease. Symptoms of BD also overlap with those of psoriasis, psoriatic arthritis, ankylosing spondylitis and ulcerative colitis. These conditions also have common genetic markers, and it is thought that a particular combination of genes and environmental factors leads to development of disease. Patients with one of these conditions quite often have a family history of another.

About three-quarters of BD patients have genital ulcers, and a similar number have skin involvement such as erythema nodosum or an acneform rash. Topical steroids are the first-line therapy for these mucocutaneous manifestations, followed by colchicine and then immunosuppressive agents such as azathioprine. A new biologic drug, apremilast, also seems to be very effective. About half of patients have arthritis, which is almost always non-erosive and is treated initially with colchicine and then with intra-articular steroids and immunosuppressive agents including TNF inhibitors and interferon.

Ocular disease often presents early in BD; it is the first manifestation in 10–15% of patients and rarely appears for the first time in people over 50. It is more common in male than female patients. Ocular BD can sometimes be recognised in the absence of any other symptoms. As the prognosis can be poor, there is a trend towards using more aggressive treatments (including steroids, azathioprine, TNF inhibitors and interferon) earlier than for other manifestations. Gastrointestinal manifestations of BD include abdominal pain and diarrhoea. Perforations are more common in BD than in Crohn's disease, while strictures are less common, but there is considerable overlap. The diagnosis can be confirmed with endoscopy and imaging, and it is important to rule out other causes. Perforation, obstruction or major bleeding requires urgent surgery, while steroids are used for acute exacerbations and immunosuppressants are used if necessary.

Vascular manifestations occur in up to 18% of patients, with deep venous thrombosis being the most common. Again, men are more likely to be affected than women. Serious complications are rarer, but include arterial aneurisms (dilated blood vessels). Arterial puncture and surgery can trigger a further aneurism, so immunosuppression should be used before surgery. The blood clots seen in BD patients do not respond well to anticoagulants; they are due to inflammation in the vessel lining, so thinning the blood is not helpful. In addition, anticoagulants may cause an aneurism to burst. It is important to reduce the inflammation to decrease the risk of future clots. Steroids and immunosuppressants such as azathioprine, cyclophosphamide and cyclosporine are recommended, with TNF inhibitors in refractory cases.

Finally, neuro-BD can be either parenchymal (affecting the brain, brainstem and top of the spinal cord) or non-parenchymal (affecting the blood vessels). Potential symptoms include encephalopathy and raised intracranial pressure. High-dose steroids are recommended for acute presentations, followed by tapering of the steroid dose and introduction of an immunosuppressant such as azathioprine. TNF inhibitors can be considered first line or in refractory cases.

Dr Situnayake concluded by describing the BioBehçet's study which has just started recruiting patients to compare infliximab (a TNF inhibitor) and interferon as the first biologic agent. Both are effective in BD, but they have never been compared head to head. The study will also be looking for markers that might predict which patients will respond best to which drug. This is a step towards personalised medicine, and Dr Situnayake expressed the hope that achievement and maintenance of remission will be the aim of BD therapy in the future.

Current research in Behçet's disease

Dr Graham Wallace, Senior Lecturer in Immunity and Infection at the University of Birmingham, explained that HLA-B51 (a member of the MHC class I proteins present on all cells in the body) has been recognised as being associated with BD for a long time, but its exact role is still unclear. HLA-B molecules pick up peptides formed from the breakdown of proteins and allow cells that have become tumour cells or have been infected with a virus to be recognised and killed. Recent work has shown that different combinations of HLA-B51 and other HLA alleles may determine the risk of

BD, with some alleles such as HLA-A3 being protective. Another molecule called ERAP1 has also been found to be associated with BD; ERAPs cleave peptides to provide the best fit into MHC class I molecules. An ongoing project in London is sequencing genes in 250 BD patients and putting together combinations to see what associations exist. There are geographical differences in gene polymorphisms, with different associations seen in different areas of the world. Genetic studies are looking at known polymorphisms in the UK, the Middle East and China. The next step will be to look at the pathways that the various genes are involved in; the different genes associated with BD in different areas may be involved in common pathways.

Many different genes and proteins are involved in the pathogenesis of BD, and machine learning algorithms are now used to apply big data techniques in BD research to look at individual cells types involved in pathways. For example, the Supercell method is being used to identify markers on CD8 T-cells that can differentiate ocular from non-ocular BD. Neutrophils, a type of white blood cell, are known to be highly active in BD and may be involved in the vascular manifestations. New ways of analysing neutrophils have identified neutrophil extracellular trap (NET) structures, which are extruded from the neutrophils to bind and kill bacteria, fungi and parasites.

Dr Wallace finished by discussing the recent Northern Ireland mapping project, which was partly funded by the BSS. Of 360 GP practices sent questionnaires, 125 (35%) responded and reported 80 people with BD. This is an incidence of around 4 per 100,000 population for these practices, corresponding to 12.7 per 100,000 overall, which is higher than the overall UK incidence and approaching that of Turkey. The patients were distributed around the counties of Northern Ireland and were more often female than male. Doctors with BD patients may have been more likely to respond to the letter, but this alone would not account for the high incidence compared with the rest of the UK. Dr Wallace speculated that the cluster may have arisen from an immigrant group arriving 100–200 years ago. He hopes that further work will be done to identify the genetic and/or environmental factors involved.

Next, Liying Low, a researcher working with Dr Wallace at the University of Birmingham, presented her PhD Clinical Fellowship proposal on characterising host–microbiome interactions in BD. Gut microbes are important in the development and

maintenance of a healthy immune system, and alterations can lead to inflammation. Recent research in mice has shown that gut microbes can activate T-cells that target the retina and cause inflammation in the eye. It is possible that the interaction between gut microbes and the immune response in genetically predisposed people drives the inflammatory process in BD. Liying proposes to compare the gut microbes of BD patients and healthy volunteers, as well as the immune responses of patients with and without the HLA-B51 gene, and to look at changes in gut microbes after interferon treatment. For the first part, she will need faecal samples from BD patients, which will be collected by mail. The second part will involve taking blood samples, and the third part will be a clinical study. Anyone willing to volunteer to help with this project can contact Liying at lowliying@gmail.com or l.low@bham.ac.uk.

Psychological factors in living with Behçet's disease

Dr Steve Higgins, Clinical Psychologist at the London Centre, started by saying that mental and physical health are closely linked. His role mainly involves assessment, brief interventions (often in the form of self-help) and follow-up. For patients who cannot come to the centre, he can connect them with local services and hopefully liaise with these. Support groups have a crucial role in helping people with the social aspects of living with BD. A biopsychosocial approach is taken, as pure psychological problems are rare. Narrative and constructionalist therapy can help by witnessing and validating people's experience and helping them to normalise it. Cognitive-behavioural therapy (CBT) helps people to understand their thoughts and feelings and how to cope with them.

Dr Higgins used several examples of hypothetical patients to illustrate his work. The first one was a man with low self-esteem who had been suffering with recurrent episodes of depression since childhood. He was successful and driven by a fear of failure and a need to prove himself. It became apparent that his periods of depression actually coincided with flares of BD. This patient needed to work on his self-esteem, come to terms with his diagnosis and re-evaluate his past 'boom and bust' experiences. The second case was a successful career woman who tended to deny her symptoms and her frequent relapses, leading to low mood, stress and exhaustion. Compassion-

focused therapy looked at the origins of her self-critical thinking and helped her to develop a different relationship with herself, using mindfulness and pacing techniques.

The next case was a man who was unable to work and support his family due to frequent relapses of BD and chronic depression. He had feelings of shame and helplessness. Acceptance and commitment therapy helped him to focus on what is meaningful and rebuild his values. Another hypothetical patient who presented with anxiety and panic attacks, as well as stress and BD relapses, had been repeatedly physically abused in childhood. In this case, long-tern treatment was needed, including specific CBT for the panic attacks and post-traumatic stress disorder, as well as compassion-focused therapy and mindfulness techniques. Dr Higgins noted that PTSD can influence the immune system. His final case was a woman who avoided intimate relationships due to low desire, altered appearance, pain and fear of triggering ulcers. This patient needed specific sex therapy and CBT relating to her body image.

Dr Higgins summed up by saying that psychologists can help with a wide variety of problems in people living with chronic diseases. The relapsing-remitting nature of BD means that patients experience a lack of control and find themselves letting people down, which can lead to withdrawal from society. Patients need to maintain flexibility in their lives. Pain and fatigue and are important issues for people with BD. Pain has emotional as well as physical components, while fatigue can be primary (caused by the inflammatory process) or secondary as a result of lack of fitness due to BD. Many self-help books are available, which can serve as a foundation as patients learn how to apply the techniques to BD and how it affects them.

Behçet's disease in children

Professor Tauny Southwood, Consultant Paediatrician at Birmingham Children's Hospital, works with the Birmingham Centre to run 3-monthly paediatric BD clinics. He said that earlier recognition of BD in children may make earlier treatment possible, which might improve the prognosis and help to prevent future complications. Studying BD in children may also provide information about the genetics of the disease. BD may be a manifestation of a very active immune system that protects

against infection. The immune system continues to develop up to reproductive age, so studying BD in adults may be too late to see what is really happening.

Professor Southwood pointed out that oral ulcers are very common in children, but BD is extremely rare. It would be useful to be able to distinguish an ulcer due to BD, but this is not yet possible. The criteria for paediatric BD comprise age under 16 years, recurrent oral ulcers and other systemic symptoms. However, there are various other childhood diseases that could present the same clinical picture. French data shows that 52% of paediatric patients have skin manifestations, 45% have a positive pathergy test and 34% have eye involvement. Almost all children with BD have headaches, but these can have a variety of causes and are often not due to neuro-BD.

Up to a quarter of BD patients may have had disease onset before the age of 16. The prevalence of paediatric BD in France is 1 in 600,000. Of 200 cases identified, half fulfilled the criteria for BD. The average age of onset of the first symptom was 8 years, and the average diagnostic delay was 3.7 years. Of the 476 BD patients attending the Birmingham Centre, about 12% fulfilled the criteria before the age of 16, although double that number reported having oral ulcers during childhood. Some genetic testing has been done in Turkey, but so far no differences have been seen between children and adults with BD. There may be combinations of genes that affect the developing immune system.

Professor Southwood suggested that an approach of trying lots of different treatments in short bursts as part of the diagnostic process might be a good idea. However, doctors are always wary about over-treating patients, especially children. There is very little data on the long-term implications of starting BD treatment in childhood. Data in 1500 patients with juvenile arthritis who have been treated with similar drugs for 15 years suggest that they are safe, although the patients still have many decades of life left.

BPC update

John Mather, Operations Manager of Behçet's Patients Support, presented some findings from the health-related quality of life (HRQoL) survey conducted in 2014/15. The questionnaire was sent to 959 BD patients (BSS members and BPC patients), of

whom 317 (33%) responded. Of these, 116 had attended a Centre of Excellence. Three-quarters of the respondents were female, and 94% were white British. Three-quarters had had to make career changes, and almost half had had to stop working; 61% had claimed benefits. HRQoL was better among those who had continued working. Smoking had a negative effect on HRQoL, while oral hygiene had a positive effect. Diet seems to be an important factor in BD. Consumption of fruit and vegetables was low, possibly due to effects on oral ulcers.

Among the respondents who had attended a Centre of Excellence, 62% were very satisfied, 21% were somewhat satisfied, 7% were neutral, 9% were somewhat dissatisfied and 4% were very dissatisfied. The next survey will look in more detail at the impact of the centres on quality of life.

Role of the Support Co-ordinator

Rebecca Hyder (Birmingham) and Jackie Pooler (Liverpool) gave the final presentation of the day, speaking about the role of the support co-ordinators. Rebecca and Jackie, as well as Jean in London, provide emotional and practical support to patients attending the centres. They attend the adult and paediatric clinics and follow up patients' non-clinical support needs, working autonomously but in collaboration with the BSS, NHS and other agencies. As well as meeting patients at the centres, the support co-ordinators are in contact with patients via phone, letter, email and text message; they also do occasional home visits. They write to employers to remind them about their obligations under the Equality Act (e.g. to make 'reasonable adjustments'), and to schools to explain Behçet's disease.

Patients with long-term conditions have needs beyond medical care, and the support co-ordinators offer a different type of care that can enhance their quality of life. They are part of the multidisciplinary team caring for patients and are bound by the same duty of confidentiality as NHS health professionals. Patients may mention things to their support co-ordinator that they have not told their doctor. This charity-funded support model in the NHS is relatively rare but could be replicated in other chronic diseases. A formal evaluation of what this role brings to patient care is needed, as most of the evidence so far is anecdotal.

Feedback

Feedback sheets were completed by 25 attendees. All of them found the conference relevant and informative and said that it met their needs. Several suggestions were made for the content and organisation of future conferences.

Clare Griffith, Editor