BSS 2009 Conference and AGM

The BSS Conference and AGM took place at the Holiday Inn, York, on 17 October 2009. Opening proceedings, BSS Chair Jan Mather said that the meeting would be less formal and more interactive than usual and asked for feedback on the new format. A slide presentation on the highlights of the year included the following:

- Appointment of Lord Evans of Watford as Patron

- Appointment of the Medical Advisory Panel, who have answered on average five questions a month, usually within 24 hours

- Enlistment of Stephanie Negal as Professional Fundraiser – she will be organising events and getting university students involved in raising money

- Achievement of the £25,000 fundraising target – the 2008 Christmas cards sold out and raised £1,700; five people took part in the London 10K run, raising £750; and the abseil event in June raised £2,000

- First full year with Chris Phillips as Director

- Retirement of Kai Li and appointment of Alex Williams as the new Treasurer

- Awareness raising achievements included oral and written evidence provided to Professor Ian Gilmore for the Labour Party review on free prescriptions, trustee representation on National Voices and the Genetic Interest Group, and a presentation on Behçet’s disease to the Conservative Party Conference

- The Helpline volunteers (Linda, Alan, Damian, Guy, Niki and Peter) took 148 calls last year, with the average call lasting 22 minutes

- The website has had more than 32,000 visits in the past 12 months, with 208,000 pages of information viewed; the new forum has over 350 members.
AGM formalities

Richard West introduced the Trustees and presented the minutes of the previous AGM. He announced that the annual subscription would be increased to £20 from September 2010 and that the Grant Aid limit would be £750. Kathryn Proudlock read out a letter from Medical Panel Chair Dr Colin Barnes, who was unable to attend due to prior commitments.

Kai Li then gave his last financial report, saying that the income of £54,415 was lower than the previous year (due to a single £15,000 donation in 2008) but that expenditure had also decreased (to £67,469) as several major projects had finished. The amount raised by fundraising (over £25,000) was the highest ever total. The final balance at 31 August 2009 was £43,623. Jan then thanked Kai for his years of valuable service and presented him with a gift from the Trustees.

In his report, Society Director Chris Phillips concentrated on the partnerships formed with organisations such as National Voices, EURORDIS and Rare Disease UK. Political lobbying has led to greater access to influential people and raised awareness of Behçet’s disease and the BSS. While the fundraising achievements have been outstanding, there is still work to be done to obtain funds from trusts and foundations, which tend to support specific projects, and drug companies. The funding from the British Association of Dermatologists for setting up support groups is very positive. Support groups are a good way of decreasing isolation for people with Behçet’s
The ongoing work to establish National Commissioning Centres of Excellence is very time-consuming (the Medical Panel are involved in this), and Chris and Jan are on the working party for the 2010 International Conference in London.

Jan announced that the next AGM will take place on 10 July 2010 at Queen Mary, University of London. The members present were then asked to visit the various “pods” where they could discuss a variety of topics with individual trustees. Subjects covered included National Commissioning, fundraising, website and youth, and benefits. There was also a non-patient pod for relatives and carers to share information.

The non-patient pod offered a relaxed environment for sharing information.

Medical presentations

Genetics

Dr Graham Wallace, an Immunologist at the University of Birmingham, gave a presentation entitled “Behçet’s disease – travels along the Silk Road”. The genetics of Behçet’s disease may result from the mixing of genes during centuries of travel along the Silk Roads between East and West. Something resembling the condition was first described by Hippocrates in 450 BC. Following a description by Hulushi Behçet based on three patients in 1936, Behçet’s disease was universally accepted in 1947. It is classified as a mixed pattern disease, falling between classic autoimmune and autoinflammatory diseases.
Dr Wallace described the link discovered in 1982 between Behçet’s disease and HLA-B51. (HLA is a molecule on the surface of cells that presents antigens to immune cells.) HLA-B51 has since been shown to be associated with Behçet’s disease in several different patient populations, with frequencies between 50% and 80%. The frequency of HLA-B51 in controls is high in populations around the Silk Road. However, not all Behçet’s disease patients are HLA-B51 positive, so this may just be acting as a marker for another gene in the same region of the human genome.

Tumour necrosis factor (TNF) is a potent regulator of the immune system, which up-regulates vascular adhesion molecules that are involved in vasculitis. TNF production is genetically determined and may predispose individuals to inflammatory disease. High TNF production has been shown to be associated with ocular Behçet’s disease. MICA is another gene in the same region as HLA, expressed mainly in stressed mucosal epithelial cells, and the MICA-009 allele is also associated with Behçet’s disease. Most (88%) people with Behçet’s disease are positive for HLA-B51 and MICA-009, compared with less than half (42%) of controls. HLA-B51 inhibits killing of MICA-positive cells more than HLA-B52 does, and it is possible that this reduced killing leads to persistence of mucosal lesions. In addition, patients with ocular Behçet’s disease tend to have factor V Leiden (a mutation that increases blood clotting), which seems to be associated with Behçet’s disease in the Middle East. While HLA-B51 and MICA-009 may be involved in activating the immune response, TNF and factor V Leiden may be implicated in stimulating blood vessels and thus contribute to the severity of the disease.

Dr Wallace went on to show that the genetic “masterswitches” known to be involved in controlling autoimmunity, such as PTPN22 or CTLA-4, do not appear to be associated with Behçet’s disease, suggesting that it therefore may not be an autoimmune disease. Another possibility is that the condition results from a reaction to infection. Toll-like receptors recognise bacterial or viral products and activate the immune system, but polymorphisms of TLR-2 and TLR-4 do not seem to be associated with Behçet’s disease. However, TIRAP (an adapter molecule associated with toll-like receptors) polymorphism is associated with Behçet’s disease in Europe and is linked to less effective response to pathogen. Rather than an increased response to infections, there may be a failure to effectively clear pathogens. Autoinflammatory
processes involving neutrophils and macrophages (types of white blood cell) also play a role.

Finally, Dr Wallace said that genome-wide studies are ongoing in various countries. A study in Turkey has already identified five new genes. Identifying new genetic markers could help with quicker diagnosis and better treatment. It is hoped that the results of some of these studies will be reported at the 2010 International Conference.

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**Neurology**

Next, Dr Adnan Al-Araji, a Consultant Neurologist in Stoke on Trent, spoke about the neurological effects of Behçet’s disease. The first case of neuro-Behçet’s disease (NBD) was described in 1941, with a series of 38 cases being reported in 1963. NBD is present when there is direct involvement of the brain and spinal cord (central nervous system); the peripheral nervous system is very rarely involved. The most common presenting symptom is headache, but it is important to be aware that most headaches in Behçet’s disease patients are not due to NBD. About half of Behçet’s disease patients have migraine or tension-type headaches, and about 10% have headaches associated with flares of Behçet’s disease. A further 10% have neuro-Behçet’s headaches, and 3% have headaches related to uveitis.

NBD is classified into parenchymal disease and cerebral venous thrombosis. In addition to headaches, the former is characterised by drowsiness, speech difficulty, weakness, unsteadiness and walking difficulties, while the latter presents with vomiting and blurred vision. Diagnosis of NBD is based on the presence of systemic symptoms (flare of Behçet’s disease), inflammatory markers in the blood, a spinal tap or lumbar puncture, or an MRI scan. If these are all negative, then a diagnosis of NBD is very unlikely. Acute attacks of parenchymal disease are treated with high-dose steroids. Maintenance treatment uses immunosuppressive drugs such as azathioprine, methotrexate or cyclophosphamide, or biological agents such as interferon or infliximab. Cerebral venous thrombosis is treated with anti-inflammatory and blood thinning (anticoagulant) drugs.
Dr Al-Araji described the case of a male patient who was diagnosed with Behçet’s disease in 1998 at the age of 24. His clinical course consisted of frequent flares, malaise, fever and oral ulcers. In June 2004, he had a flare and fever, accompanied by severe headache, vomiting, drowsiness, sudden right-sided weakness and speech difficulty. Inflammatory markers, a spinal tap and an MRI scan confirmed parenchymal NBD. The patient was treated with steroids and cyclophosphamide. He had two further neurological relapses and had significant neurodisability. He started infliximab treatment in July 2005 and rapidly felt better than he had in the previous 7 years. He was able to gradually reduce his steroid dose to zero, has had no significant flares of Behçet’s disease and has returned to work.

As regards prognosis, Dr Al-Araji said that parenchymal NBD can be very disabling if not successfully treated, while cerebral venous thrombosis usually has a good prognosis but can result in loss of vision if not treated early enough. Prognosis has improved in recent years. Future prospects should include earlier diagnosis, more rapid referral, improved treatment options and more research into NBD. The Neuro-Behçet’s Study Group of the ISBD is producing a consensus statement on the diagnosis and treatment of NBD.

In response to a question from the audience, Dr Al-Araji said that the funding of drugs such as infliximab can be difficult but is hopefully improving. He responded to a question on recurrence of NBD episodes by saying that in one study a third of patients had further episodes, a third had progressive symptoms and a third had no further episodes.

*Rheumatology*

Finally, Professor Ann Morgan, who runs the Regional Behçet’s Service at St James’s University Hospital in Leeds, presented a rheumatologist’s perspective of Behçet’s disease. She said that rheumatologists deal with diseases of the bones, joints and muscles, as well as the immune system. There are more than 200 types of arthritis.

Professor Morgan began by giving some background on Behçet’s disease. In addition to the characteristic oral and genital ulcers, patients may have inflammation of the
skin, joints, eyes, blood vessels, bowels and nervous system. About 98% of patients have mouth ulcers, and many also have genital ulcers. Eye disease occurs in 25–75% of people with Behçet’s disease and may lead to blindness. Skin lesions occur in more than 75% of patients, while the nervous system is affected in less than 20%. Small-vessel vasculitis accounts for many of the features of Behçet’s disease, and large vessels are involved in around a third of cases.

About a third of people with Behçet’s disease experience morning stiffness and about half have aching in the joints (arthralgia), which is usually of short duration and is worse during flares. This most commonly affects the medium and large joints, including the knees, ankles and wrists. Arthritis (inflammation and swelling in the joints) is uncommon and usually short-lived in Behçet’s disease and does not usually lead to long-term damage, unlike other forms of arthritis. Methods for looking at joints include X-rays and CT scans, which show the bones, and ultrasound, which gives good images of soft tissues such as tendons. MRI scans can show the cartilage and tendon attachments, while PET scanning gives a very accurate picture of inflammatory activity but is not in routine use. More research into joint involvement in Behçet’s disease is needed, using the newer imaging techniques, but the short-lived nature of the arthritis makes this difficult.

Treatment choices depend on the individual symptoms. Ulcers and skin rashes tend to be treated with local steroid therapy and colchicine, while other organ manifestations typically require treatment with steroids and other immunosuppressive agents. Avoiding excessive weight gain can help to reduce joint problems, as can taking rest during flares and exercising the joints as long as they are not inflamed. It should be remembered that any joint problems experienced may not be due to Behçet’s disease. Bone and joint diseases are very common in the population, especially in people aged over 55, and are increasing. Bone is built up during childhood and adolescence and slowly lost during adult life. Measures to reduce bone loss include taking weight-bearing exercise, ensuring adequate intake of calcium and vitamin D, and stopping smoking and reducing alcohol intake.

In response to a question from the audience, Professor Morgan said that the amount of exercise needs to be judged on an individual basis. Some exercise is good for the joints and can help to maintain cartilage, but too much can damage the joints. Local
leisure centres have trained staff who can develop guided exercise programmes using low impact equipment.

Medical Panel

The day finished with the three medical speakers answering questions from the audience. The panel were asked for advice on factors that would help with benefits claims. They said that it is essential to list all the relevant features of Behçet’s disease, including fatigue. How far a person can walk is an important factor. People with neuro-Behçet’s and those with visual loss usually qualify for benefits.

The medical panel consisted of Dr Graham Wallace, Professor Ann Morgan and Dr Adnan Al-Araji

In response to a question about the incidence of Behçet’s disease in China, the panel said that it used to be thought to be uncommon but more data are becoming available suggesting that there are more cases than previously believed. Ocular Behçet’s disease seems to be becoming less common in Japan, and disease severity is decreasing, and it is thought that this may be linked to an increase in allergy. However, the same has not been seen in other countries where allergy is also increasing.

Another question related to whether there may be a connection between Behçet’s disease and restless legs syndrome (RLS). The panel did not think that RLS was linked to any specific condition. One research paper described a small group of
patients with Behçet’s disease and RLS. However, the two conditions generally affect different age groups, with RLS being most common in people in their 40s and 50s.

Asked about how Behçet’s disease may be treated in 10 years’ time, the panel pointed out how much treatment had changed in the previous 10 years. There is much to be learnt from other conditions, and genetic studies will lead to new inflammatory pathways being considered. Targeted drugs developed to treat other diseases may be used to treat Behçet’s disease, and treatment will probably become increasingly individualised. The anti-TNF agents such as infliximab block the symptoms of Behçet’s disease, but in future it may be possible to block the cause of disease.

Clare Griffith, BSS Editor