Postgraduate Educational Afternoon

Imperial Vasculitis Centre, Hammersmith Hospital, Imperial College, London

Wednesday 5th June 2013

(Attended by Richard Eastoe)

In June Richard Eastoe attended the first Vasculitis education session at the newly formed Imperial Vasculitis Centre at Hammersmith Hospital in London. The event was organised by Professor Justin Mason who is a Vascular Rheumatologist at Hammersmith.

The event was very well attended with around 100 Professors, consultants and post-graduates present. Professor Mason told me later (when they ran out of coffee) that they had only planned for about 50 !

Professor Charles Pusey opened the event by welcoming everyone and outlining the purpose of the newly formed Imperial Vasculitis Centre of Excellence. He very kindly acknowledged my presence and their need for patient involvement. He went on to highlight the work we do at Vasculitis UK with particular praise for the Route Map.

The first presentation was entitled “Behçet’s Syndrome – The benefit of experience” by Professor Dorian Haskard, a Vascular Rheumatologist at Hammersmith.

Professor Haskard outlined the diagnostic criteria for Behçet’s to show why the disease required a multidisciplinary approach to treatment.

He listed the drugs that have been used to treat Behçet’s. Interestingly he noted that historical treatments such as Colchicine are not very effective and many drugs such as Thalidomide, Chlorambucil, Ciclosporin and Cyclophosphamide are all outdated now and superseded by the new biologic, anti-TNF (Tumour Necrosis Factor) agents. He mentioned that trials were currently on-going with anti IL1B (Interleukin 1 Beta) drugs and also Interferon.

Discussing mortality and morbidity he noted that men with Behçet’s generally have a much more severe form of the disease than women and have a correspondingly higher mortality rate.

Referring to a case study he reported that Cyclophosphamide had virtually no effect on the disease whereas Infliximab (an anti-TNF agent) had brought on a good remission.

He summed up by highlighting the point that patients should not undergo any corrective surgery (for aneurysms etc) until the inflammation was under control. He also remarked that patients shouldn’t be put on anti-coagulants (such as Aspirin) although many may already be taking them which poses the question whether to stop. Also warning against dentistry (potentially causing ulcers), arterial catheters (causing aneurysms) and the general risk from surgery.

During the break, Professor Haskard told me that unfortunately, due to the recent opening of the Behçet's centres of excellence, he was no longer having new Behçet's patients referred to him and would probably have to close down his research into the disease.

The next presentation was by Professor Justin Mason entitled "Takayasu Arteritis – Is the outlook improving ?".

Professor Mason described the pathology of Takayasu's; the symptoms used for diagnosis and some of the common problems. Stenotic lesions (the narrowing of a blood vessel) being present in 90% of cases with Aneurysms (a bulge in a blood vessel) occurring in about 25%.

He said that his aim was to prevent the disease from progressing to stenosis.

He described the tools available to help with diagnosis; FDG-PET scans (a radioactive dye is injected into the patient to allow the scanner to map tissues and the blood flow through the heart), CT Angiography (an iodine based dye is injected into the patient to map the blood vessels), MR Angiography (a form of MRI - Magnetic Resonance Imaging) and Ultrasound.

MRA in particular can show oedema (swellings in the blood vessels) before stenosis sets in. Imaging in this way over say five years can show the remodelling of arteries if the disease is treated early (before stenosis).

Professor Mason told us that he is looking at quantitative scoring for diagnosis (basically giving a numerical value to the likelihood of having the disease).

The recommended treatment for Takayasu's is currently Prednisolone combined with Methotrexate or Azathioprine or Mycophenolate. Interestingly he noted that with the advent of the Biologics, pulsed Cyclophosphamide is becoming less used nowadays.

As was mentioned for Behçet's, Professor Mason advised that it was best to supress disease activity before any corrective surgery was undertaken.

In the future, Professor Mason suggested that Pentraxin 3 (PTX3 – a protein that can be produced by cells in response to primary inflammatory signals) might be used as a biomarker for disease activity. He also alluded to improved MRA imaging allowing the cross sectional display of arteries.

His conclusion was that there was an improved outlook for patients with Takayasu's; diagnostic time is being reduced, diagnostic imaging is getting better and immunosuppressive treatment is improving all the time. He summed up saying that 80% of patients have only a short term disease (about 2 years) with the remaining 20% relapsing.

The final talk was by Dr Alan Salama, a Nephrologist at the Royal Free Hospital in London. His talk was called “Predicting Relapse and Tolerance in ANCA Associated Vasculitis (AAV)”.

Dr Salama made some interesting statements about the different approaches to induction and maintenance of remission :-

For inducing remission :

Cyclophosphamide is better than Methotrexate

Cyclophosphamide is equal to Rituximab

Rituximab is better than Cyclophosphamide for relapses

Cyclophosphamide is equal to Mycophenolate plus Steroids

For maintaining remission :

Azathioprine is equal to Methotrexate

Azathioprine is better than Mycophenolate

Rituximab is still an unknown

Dr Salama said that relapses were more common in ANCA-PR3 then ANCA-MPO Vasculitis. This has led to a study to make Granulomas in the test tube as they are more common in ANCA-PR3 Vasculitis.

ANCA is not a good predictor of relapse but biomarkers may be the way forwards. New research shows that monitoring the CD8 T cell signature can predict relapse in many autoimmune diseases including AAV, Lupus and Inflammatory Bowel Disease.

He said that there were also on-going studies to see if Calprotectin is also a predictor of relapse. He also noted that there is on-going research into the connection between the Thyroid and AAV.

Finally he talked about current evidence for the role of regulatory B cells in retaining remission in Lupus. This is also relevant for AAV and even across all the Vasculitides and may lead to cellular therapy in the future. The Immune Tolerant Network is currently funding a trial to monitor regulatory B cells in AAV patients.

Dr Salama pointed out that many side effects may be due to steroids and not Cyclophosphamide. He said that the thought is that with drugs such as Rituximab specifically targeting B cells, they may not need to immunosuppress patients long term and thus reduce the risks from side effects.

Following a break came three case studies entitled “The Vasculitides – A Clinical Challenge”.

The first was an interesting case of Henoch Schönlein Purpura (HSP) in an elderly patient, presented by Dr P Patel.

Dr Patel reminded us that HSP is most common in children and tends to present with skin, Kidney and Gastro Intestinal involvement. GI involvement includes oedema (fluid retention causing swelling) and haemorrhage (bleeding) in the small bowel wall. This leads to abdominal pain.

The case study patient also had inflammation of the pancreas (rare) and pulmonary (lung) involvement (very rare). A CT scan of his lungs showed “ground glass” changes indicating diffuse alveolar haemorrhage. Dr Patel warned that a skin biopsy often gives a false negative for HSP and a kidney biopsy is actually the only way to confirm diagnosis.

Dr Patel told us that treatment can be controversial. This is because the disease most often affects children, steroids don’t help with the long term kidney problems and there has been shown to be no benefit from using Cyclophosphamide. However from their experience with this patient, Rituximab has shown promise when combined with steroids.

The second study was a case of double positivity in an elderly patient, presented by Dr A Tanna.

Dr Tanna told us that the patient presented with ANCA-MPO Vasculitis plus Anti GBM disease. He had Pulmonary and kidney involvement and was treated with Cyclophosphamide and Plasmapheresis. This was followed by Mycophenolate and steroids for maintenance and led to a good recovery.

Dr Tanna warned that there is a greater risk in immunosuppressing the elderly with comorbidities (two or more diseases). Dr Tanna said that kidney function improves with treatment in the elderly but morbidities (sicknesses) remain the same due to the side effects of the drugs.

The last case study was about Microparticles, Behçet's and Malignancy (Cancer) by Dr E Khan.

Dr Khan told us that there was a 20% chance of Behçet's patients developing Thromboses (blockages in veins). But this was 9 times more likely in male patients. He told us that standard blood clotting tests were of no use and that better biomarkers are required.

Dr Khan said there is a hypothesis that thrombosis relates to Tissue Factor (TF) Microparticles. TF Microparticles are small cell elements circulating in the blood. Studies have found "platelet dust" that might explain the tendency for clotting. The thought is that Microparticles might be used as biomarkers indicating the risk of thrombosis.

Dr Khan said that a case study had shown that breast cancer promotes Microparticles and consequently an increased risk of thrombosis. He also thought there was an opportunity for research into the role of TF Microparticles where present in Vasculitides other than Behçet's, for example in predicting Deep Vein Thrombosis etc.

The meeting ended here with my head reeling from the amount of information that had been provided. But as ever with these clinical seminars, I was impressed with the enthusiasm and interest that doctors, consultants and professors have for learning about Vasculitis and treating the disease. Sometimes these presentations can sound cold and clinical but I came away feeling that all the speakers had a real empathy for their patients and often struggled with the choices they regularly had to make in treating them.