HOW TO ADDRESS THE CHALLENGES AND MAXIMISE PATIENT OUTCOMES IN THE ASSESSMENT AND MANAGEMENT OF AUTOIMMUNE DISEASE?

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INTRODUCTION AND PATIENT EXPERIENCE

Autoimmune disease is a huge umbrella term that encompasses a vast number of diseases, with some being better known than others. More commonly known examples include rheumatoid arthritis and systemic lupus erythematosus (SLE) and while these have their issues with assessment and management there is an even greater impact in the rarer conditions. Public and professional knowledge of the rarer conditions can be limited and this can form barriers to a rapid diagnosis and block the pathway to treatment.

There are many challenges that patients with autoimmune disease face. Some examples of these difficulties faced include lack of awareness by both public and professionals, slow progression of the diseases, a broad spectrum of presentation with large variation between cases, complex treatment and the limitations of available treatment to fix the symptoms rather than the underlying pathology. Each of these points will be discussed in more detail throughout the essay.

During my studies, I have come across patients with autoimmune disease, but one, in particular, has stood out for me. I had just started my third year of medical school and it was my very first unsupervised patient clerking of my medical training. When speaking to this 34 year old female, I listened to her story and she told me about all of the various symptoms that she has had since her early 20s, all of the tests that were involved and the length of time it took to receive her final diagnosis. The sense of difficulty and struggle she had been through over the last decade really hit home and it made me aware of the impact of having a rare autoimmune condition. Her complex list of symptoms included: severe asthma, nasal polyps, loss of sensation in her fingers, severe pain in her fingers and toes, and a sudden loss of vision in both eyes. With my very limited knowledge of autoimmune disease at the time, I had no idea as to what she might have. She informed me she had Churg-Strauss syndrome, also known as eosinophilic granulomatosis with polyangiitis. I had never heard of this condition, let alone know the manifesting presentations and appropriate treatment. This unawareness seemed to be a common occurrence for the patient and she was an expert in her own condition. She was extremely kind and patient and explained what she had and what exactly this means for her, with 4 hospitalisations in the last 6 years, it was having a phenomenally large impact. I spent a lot of time with this patient on the ward, following her through her treatment changes, to the point where she thankfully regained her vision and she was allowed home.

I will be focusing this essay on the challenges faced for those with autoimmune vasculitis, in particular, those with Churg-Strauss syndrome.

CHURG-STRAUSS SYNDROME

Churg-Strauss syndrome, also known as eosinophilic granulomatosis with polyangiitis is a rare autoimmune condition. It is a systemic necrotising vasculitis affecting the small and medium-sized blood vessels within the body. It is associated with severe asthma, eosinophilia and antineutrophil cytoplasmic antibody (ANCA). Incidence is 1 per 100,000 per year, with a slight male predominance. The presenting symptoms are varied and can affect multiple organ systems. The disease is characterised by asthma, pulmonary infiltrates, eosinophilia and systemic vasculitis.

ASSESSMENT CHALLENGES

There are many challenges faced in the diagnosis and assessment of a patient with vasculitis. These will be discussed further here.

VARYING PRESENTATION

There is a diverse collection of symptoms that can fit into autoimmune disease, and Churg-Strauss syndrome is no exception. There are no clinical diagnostic criteria for the syndrome (Eustace, Nadasdy, & Choi, 1999), however, criteria have been defined for research purposes (figure 1).

One study recorded the presenting features of a group of 32 patients and the sheer number of presenting symptoms is staggering and can be found in figure 2 (Solans, 2001). This information is reiterated throughout with more recent and substantial studies most notably by the French Vasculitis Study Group (Comarmond, et al., 2013).

The presence of four or more of these six clinical criteria in the setting of vasculitis suggests Churg-Strauss Syndrome with a sensitivity of 84%

- Asthma
- Peak peripheral eosinophilia of >10% of the total WBC count
- Peripheral neuropathy attributable to a systemic vasculitis
- Transient pulmonary infiltrates on chest radiographic imaging
- Paranasal sinus abnormality
- Blood vessel biopsy demonstrating extravascular eosinophils

Figure 1 – the American college of rheumatology – diagnostic criteria for Churg-Strauss syndrome (Masi, et al., 1990)

Symptom	Number of patients at presentation (out of 32)	Symptom	Number of patients at presentation (out of 32)
Asthma	32	Sensorimotor neuropathy	7
Fever, weight loss	22	Stroke	1
Pulmonary infiltrates - Patchy - Nodular - Nodular cavitated	17 - 15 - 1 - 1	GI Involvement - Abdominal pain - Small intestine perforation - Diarrhoea	12 - 7 - 3 - 2
Bilateral pleural effusion	6	Horner's syndrome	1
Alveolar haemorrhage	1	Hypertension	5
Skin involvement - Palpable purpura - Maculopapular rash - Digital ischaemic ulcers - Erythematous nodules	22 - 13 - 9 - 3 - 2	Cardiac Involvement - Myocarditis - Pericardial effusion - Myopericarditis - Ischaemic myocardiopathy	9 - 1 - 1 - 3 - 4
Renal Involvement - Glomerulonephritis - Renal Insufficiency - Haematuria	4 - 1 - 1 - 2	Ophthalmic involvement - Orbital pseudotumour - Sudden blindness	2 - 1 - 1
Mononeuritis multiplex	14	Raynaud's phenomenon	1
Arthralgia, myalgia	12		

Figure 2 - symptoms at presentation of those diagnosed with Churg-Strauss syndrome (Solans et al., 2001)

The number of symptoms seen in Churg-Strauss patients highlights the difficulties that are faced when diagnosing a patient. Some presenting features are nonspecific, causing a large number of differential diagnoses to be considered and ruled out before reaching the correct diagnosis. Symptoms and signs vary on a case-by-case basis with a wide variety of potential presentations. The patient I spoke to had some "popular symptoms" from this list including asthma and myalgia, however, she was also presenting with rarer symptoms, sudden blindness, and sensorimotor neuropathy. It is clear from the literature that patients often present with an unusual collection of

symptoms with a number of unusual presentations documented in case reports (Parent, Larue, & Ellezam, 2014) (Choi, et al., 2016). While there is not a typical presentation of Churg-Strauss syndrome, some symptoms are more indicative of the diagnosis, an example being severe asthma.

The difficulty with recognising such a diverse collection of symptoms lies with the rarity. While a particular symptom may have presented previously in another patient, a practicing clinician from another hospital or even another part of the world may be completely unaware. One solution to this is to stress the importance of case reports for unusual presentations as it is important that those working in the specialty are fully aware of the potential and rarer presentations. Recently there has been a published large case series which may assist with this in the future (Mahr, et al., 2014).

LATE DIAGNOSIS

In addition to the varying symptoms, Churg-Strauss syndrome there is usually a long period of time before a patient received the diagnosis and this is due to various confounding factors. This includes the symptoms themselves. While there is big variation, many of the presenting symptoms are very non-specific, for example, myalgia, fever, and weight loss, with no real indication of an autoimmune cause. Furthermore, symptoms can often occur in isolation with no additional features indicative of vasculitis. This creates a large problem with getting an accurate and timely diagnosis.

Churg-Strauss syndrome has several phases and these include (Lanham, Elkon, Pusey, & Hughes, 1984) (Pagnoux & Guillevin, 2010):

- Prodromal phase: occurs in the 20s and 30s - atopic disease, allergic rhinitis, and asthma
- Eosinophilic phase: eosinophilia and eosinophilic infiltration of organs particularly lungs and gastrointestinal tract
- Vasculitic phase: occurs in 30s and 40s - life-threatening systemic vasculitis

The presence of disease phases often means that some manifestations like asthma can be present for many years before any further indicators of vasculitis become clinically apparent, further lengthening the time to diagnosis.

There are many complications regarding a late diagnosis and one of these is patient management. Without a diagnosis, treatment is purely symptomatic. In addition, patients can often struggle with significant symptoms with no diagnosis. The presence of persistent symptoms with no diagnosis can have a huge psychological impact on the sufferer. The patient can often

view that there is no cause for their symptoms up until the point of the diagnosis and may feel like medical professionals think they are making it up if there is no concrete evidence behind the cause. This can be very emotionally difficult to manage. Non-specific symptoms can result in multiple hospital visits and tests with no improvement and over time this is physically tiring. This is particularly pertinent with Churg-Strauss syndrome as there is no definitive test for a diagnosis that might give the patient the answer they need. The diagnosis is based on a collection of symptoms and investigation findings. This is why it is important that throughout the process, the patient is treated holistically and offered support.

While there are a number of factors leading to delayed diagnosis – some of these cannot be altered. In this case, the best way forward is to support the patient and manage the patient's symptoms until a time in which a diagnosis is made.

RAISING AWARENESS – PATIENTS

One way in addressing the long diagnostic process for a patient with vasculitis is to raise awareness.

While it would be ideal for all patients to present in a manner that can be easily described and detected, this is not the case for autoimmune conditions, Churg-Strauss syndrome included. While nothing can be done about the way in which patients present, there is potential for improvement. Increasing the awareness of autoimmune disease to both medical professionals and the public may aid with this. Many autoimmune conditions are rare and so raising the profile of each individual condition in the public domain would be a huge task and the message may be lost in the process. When it comes to public information regarding autoimmune disease there may be minimal benefit in promoting disease specifics, but there is potential to raise the typical symptoms that may otherwise be dismissed by a person. This could help to bring people to the GP earlier, attempting to speed up the already lengthy process of acquiring the autoimmune diagnosis.

Public health adverts raising awareness of worrying symptoms are being more common. The main focus of these campaigns to date has been cancer, with the most recent being the lung cancer campaign urging anyone with a cough for over 3 weeks or increasing breathlessness to see their GP. Evidence has shown that more members of the population had greater knowledge of breathlessness being a sign of lung disease and heart disease since the start of the campaign. In addition, there was an increase in GP attendances with patients with a cough (Watson, 2016). While cancer campaigns have been successful, this does not mean that the same could be said regarding autoimmune disease. The reasons behind these campaigns are to get patients with red flag symptoms to medical help as soon as possible in order to get earlier treatment, and ultimately

a better prognosis. Earlier treatment in autoimmune disease, particularly Churg-Strauss Syndrome can improve prognosis and alleviate or improve symptoms, however, it is not curable. In addition, it is also worth considering the prevalence of autoimmune disease is significantly less than that of cancer and as a result, any national campaign may not be as effective as the target group is significantly smaller.

Although not on a national level, there are groups like the Churg-Strauss Association who aim to educate and promote public awareness using seminars and workshops and there are various groups applicable to the relevant autoimmune diseases.

RAISING AWARENESS IN THE MEDICAL PROFESSION

Perhaps one way forward in increasing awareness for autoimmune disease is to develop a greater understanding within the medical profession responsible for diagnosis. The teaching of autoimmune disease within the medical curriculum could be increased, so that every doctor has the basic knowledge to at least raise the suspicion of autoimmune disease and prompt a referral to the relevant autoimmune specialist. It appears that the experience described by the patient I spoke to was not unusual and commonly patients are passed from speciality to specialty before a final diagnosis is made with referrals depending on the main presenting symptom at the time. Increasing professional suspicion of vasculitis and other autoimmune diseases may lead to a quicker rheumatology referral and a more prompt diagnosis.

MANAGEMENT CHALLENGES

MULTIDISCIPLINARY TEAMS

There are many challenges that clinicians face when managing a patient with Churg-Strauss Syndrome. One large component of this is the many presenting symptoms and organ systems affected. There is a focus now within medical care surrounding multi-disciplinary teams (MDTs) and rheumatology is no exception. NICE and The British Society for Rheumatology produced a set of guidelines and components for managing long term conditions and the main focus was the MDT including – consultants, specialist nurses, patient education, physiotherapist, rapid cross referral to linked specialities and specialist rheumatology serves are just a snap-shot (BSR & BHPR, 2015). This can and should be applied to vasculitis and other autoimmune conditions. Working as part of an MDT often provides a quicker diagnosis and better treatment for those with a worsening condition. Joint planning and patient support can lead to not only better treatment of the patient's symptoms but overall improved patient care and satisfaction.

MEDICATION

Management of Churg-Strauss is mainly using corticosteroids with many patients entering remission with corticosteroids alone (Ribi, et al., 2008). If a patient scores any five-factors score (FFS) points, this can alter the management (figure 3) (Guillevin, Lhote, & Gayraud, 1996). However, patients often relapse with 79% requiring long-term corticosteroid therapy with or without the addition of an immunosuppressant to keep on top of the disease. The most commonly used immunosuppressant is cyclophosphamide and this is an essential part of management in those with any FFS points (Cohen, et al., 2007). Those that are treated with corticosteroids and cyclophosphamide had an 85% remission rate, but when stopping the treatment there was a 73.8% relapse rate. In addition, at follow up 82% still required long-term low dose corticosteroids (Cohen, et al., 2007).

Five Factors Score

- Cardiac involvement
- GI disease (bleeding, perforation, infarction or pancreatitis
- Renal insufficiency
- Proteinuria
- CNS involvement

One point per factor present.

Figure 3 - FFS Scoring (Guillevin, Lhote, & Gayraud, 1996)

NICE guidance is not available for the management of Churg-Strauss syndrome and it is often treated as Wegener's granulomatosis due to its similarities. More data and evidence are required to recommend the best dosage and delivery of cyclophosphamide. Making these recommendations is difficult, particularly as it is problematic to acquire enough data as the patient pool is very small. However, continuing research in this area will only improve treatment in the future.Newer therapies are being trialled to attempt to get better control of Churg-Strauss syndrome including rituximab with mixed responses (Pepper, et al., 2008) (Bouldouyre, Cohen, & Guillevin, 2009), interferon alpha, omalizumab and imatinib (Pagnoux C. , 2010).

The issues with current treatment are the high relapse rate and the requirement for many patients to be on continuous low-dose steroids. Corticosteroids are associated with many complications including immunosuppression, osteoporosis, cataracts and adrenal insufficiency. In addition to the complications of the treatment available, it is not always successful causing relapses and a high mortality rate. The 5-year mortality rates from Churg-Strauss syndrome are 12% with no FFS present, 26% with one factor and 46% if 4 or more factors (Guillevin, Lhote, & Gayraud, 1996). Further research into treatments is required in order to further improve the mortality and morbidity rates associated with vasculitis.

SUPPORT

It is important that a patient is supported throughout this process. This can be done in both primary and secondary care. Once a diagnosis is made, there is an additional avenue for support which is often overlooked – support from the community. There are several groups who work to raise awareness in addition to offering support. In the UK there is the Churg-Strauss Association and this gives people the platform to talk about their experiences. This also offers those reading about others some confidence that they are not in this alone. Support groups and online message boards can be incredibly useful, especially immediately post-diagnosis to help people better understand their disease and what they can expect.

CONCLUSION

Churg-Strauss syndrome as with most autoimmune disease is complex and its pathology is not well understood. Patients face many challenges, even before acquiring the diagnosis. Symptoms are complex, often non-specific and life altering. The length of time to diagnosis is impacted by multiple factors including slow disease progression, late presentation to medical help and a general lack of awareness. The use of MDTs and increasing disease awareness may aid to speed the process to ensure the patient receives adequate treatment. This process of unawareness of what is happening to the patient is often difficult and support and symptomatic help should be offered.

The diagnosis is not the end when considering vasculitis. The available treatments are not curative and come with many side effects with some patients requiring long-term corticosteroids. Future research into the area is vital to ensure an improvement in the quality of life of those affected and to ultimately improve the outcome from those suffering with Churg-Strauss syndrome.

Word Count 2934 excluding references

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STATEMENT OF ORIGINALITY

I can confirm that this submission is my own original work. References used are indicated above.

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28/09/2016