The Churg Strauss Syndrome

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During the first half of this century, several authors reported a variant of a small vessel vasculitis that appeared similar to the then recognized polyarteritis nodosa. The condition was distinguished by a significant atopic component, in the form of allergic rhinitis, bronchial asthma, and hypereosinophilia (1). Such patients frequently had a poor prognosis, with many patients dying as a result of cardiac complications, often within months of diagnosis. Although it has previously been called by several names including allergic angiitis and granulomatosis, it is now most commonly referred to as the Churg Strauss syndrome (CSS). Renal involvement in this condition is frequent although usually mild; however, an increasing number of case reports attest to the potential for severe renal disease to occasionally develop.

Several lines of evidence suggest that CSS is not simply the coincidental development of vasculitis in patients with asthma. The asthma seen in CSS is notable for being of late onset; it is frequently severe and is associated with a greater degree of eosinophilia than is typically seen in bronchial asthma. There is often no personal or family history of atopic disease (2). In addition, cases are well described in which the asthma develops shortly before or simultaneously with vasculitis (3,4). The recognition of CSS as a separate disease entity is important, because its distinctive natural history (2,5), its frequent rapid response to treatment, and its good overall prognosis (4) suggest pathogenic mechanisms that differ either in nature or in degree compared with other forms of necrotizing vasculitis.

Diagnosis

The accurate diagnosis of CSS remains problematic. None of the disease features, either clinical or histologic, is on an individual level pathognomonic of the condition. The syndrome is frequently phasic in nature, with the pathologic findings varying not only with the anatomical site examined but also with the phase of the illness (2). CSS classically develops as new onset asthma and/or allergic rhinitis, which progresses to hypereosinophilia, often with an associated tissue infiltration, before culminating in frank vasculitis. This sequential development of findings is not seen in all cases, and even when present the time course over which progression occurs can be highly variable. Therefore, rather than being dependent on any single symptom or pathologic finding at one time point, the accurate diagnosis of Churg Strauss syndrome requires the presence of a constellation of findings that may have presented and evolved over a period of years.

Churg and Strauss in their original 1956 article outlined three pathologic features associated with the disease: an eosinophilic tissue infiltration, granuloma formation, and a necrotizing vasculitis involving small and medium-sized vessels (5). Eleven of the 13 patients they described had been studied by post mortem examination, and all had advanced disease without the benefit of effective treatment. Even so, only 10 of their 13 patients demonstrated all three pathologic features. Thus, it is not surprising that this triad of pathologic findings should yield a low sensitivity for the diagnosis of CSS, especially with the development of rapidly effective treatment and with histologic studies frequently limited to small volume biopsy specimens.

To help overcome these limitations, Lanham et al. proposed a combined clinical and pathologic diagnostic scheme (Table 1) (2), and although the validity and accuracy of this scheme has never been assessed objectively, it has nonetheless been widely used. More recently, the American Rheumatology Association has proposed alternative diagnostic criteria for CSS (6). The presence of at least four of six findings (Table 1) was diagnostic of Churg Strauss, with a sensitivity of 85% and a specificity of 99.7% within the source population. However, these results have not as yet been validated in an independent sample of patients. The 1994 Chapel Hill consensus conference further defined CSS as an “eosinophil-rich and granulomatous inflammation involving the respiratory tract, and necrotizing vasculitis affecting small to medium sized vessels, and associated with asthma and eosinophilia” (7).

All of these classification systems and definitions have obvious limitations, especially in patients with mild or limited disease or in those who have already been started on therapy (8), especially as the peripheral hypereosinophilia of CSS responds rapidly to treatment with corticosteroids. Cases have also been reported that overall are suggestive of CSS but lack a typical feature of the syndrome such as asthma, even in the absence of prior treatment (9). These diagnostic difficulties highlight our need to better understand the underlying pathogenesis of the vasculitides to avoid being dependent on superficial overlapping clinical features for the purpose of diagnosis.
Clinical Features

Prodromal Phase

Allergic rhinitis is often the first evidence of disease (12) and occurs in up to 70% of cases. It is frequently severe and may be associated with nasal polyposis, obstruction, and recurrent sinusitis, but unlike Wegener’s granulomatosis, the presence of nasal pain or frank hemorrhage is uncommon. Histologic examination usually reveals diffuse eosinophilia; upper airway granulomata are only rarely found. Asthma usually precedes the development of vasculitis by a period of weeks to years (3,4); it is often progressively severe and eventually requires oral steroids for adequate control. Eosinophilic tissue infiltration most commonly presents within the lungs as Loffler’s pneumonia or less commonly in a more chronic relapsing form as chronic eosinophilic pneumonia. Gastrointestinal tract infiltration may present as eosinophilic gastroenteritis. Although these conditions are disease entities in their own right, they all form part of the spectrum of eosinophil-mediated disease, which may progress to a more generalized multisystem disease process in the form of CSS (12).

Vasculitic Phase

Systemic disease features during the vasculitic phase include weight loss, anemia, and fever. Rash occurs in up to 70% of cases and may include an erythematous maculopapular eruption, vasculitic ulcers, and/or subcutaneous nodules (3). Myalgia and a migratory nonerosive polyarthritis are common but are usually not severe.

Pulmonary involvement represents a vasculitic process with a varying degree of eosinophilic infiltration. It may be associated with progressive dyspnea, alveolar hemorrhage (4), pleurisy, and the development of eosinophil-rich pleural transudates. Radiographic findings are generally nonspecific and, unlike Wegener’s granulomatosis, cavitation rarely develops (3). Transbronchial biopsy revealed evidence of the disease in four of six cases studied by Schnabel et al., even in the absence of focal radiologic abnormality (13). Bronchial alveolar lavage usually reveals a normal total cell count, but with a dramatic increase in the percentage of eosinophils (mean 31%; range, 6 to 66%).

Cardiac involvement is a common, although often late, manifestation of the disease. It was the primary cause of CSS-related death in the pre-corticosteroid era (2), and it still results in occasional fatalities despite modern treatment (3,4,9). Acute pericarditis may occur in up to one-third of cases and may be associated with pericardial effusion. Cardiac tamponade may develop and should be considered before initiating aggressive fluid removal with dialysis. Myocarditis may lead to postinflammatory fibrosis and congestive cardiac failure, while coronary vasculitis may result in ischemic heart disease.

Gastrointestinal involvement is common and often severe, resulting in abdominal pain, ascites, diarrhea, and/or hema-tochezia (2,3,14). It resulted in 8% of the deaths reviewed by Lanham in his literature review (2).

Involvement of vasa nervorum results in a mononeuritis multiplex and was found in 72% of cases in Guillevin’s series and most commonly involved the common peroneal (84%) and the ulnar (55%) nerves (4). Cerebral vasculitis may predispose to hemorrhagic cerebrovascular events, especially in association with uncontrolled hypertension.

Renal Disease

Traditionally, renal involvement in CSS has been reported as being mild. In the pre-corticosteroid literature, early deaths due to cardiac disease may have limited the potential for widespread renal involvement, while the absence up until recently of widely accepted diagnostic criteria may also have resulted in many cases of CSS with a significant azotemic component being labeled as having an alternative diagnosis.

As shown in Table 2, several series have reported a considerable degree of renal involvement. In Churg and Strauss’ original report, they comment that mild hematuria and albuminuria were commonly present (5). Three of their 11 patients had azotemia and one died from uremia. Chumbley reported that the incidence of renal involvement was 20% (3). Six of his 30 patients had microscopic hematuria, three had slight elevations of serum urea and creatinine, and one died from renal failure. The incidence of proteinuria is not reported and no renal biopsies were performed. Lanham et al., in his literature review, found 49% of cases to have mild or moderate renal involvement and renal failure in 9% (2). Renal failure was second only to cardiac disease as a cause of death (occurring in

Table 1. Diagnostic criteria for the Churg Strauss syndrome

<table>
<thead>
<tr>
<th>Lanham’s criteria (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>asthma</td>
</tr>
<tr>
<td>peak peripheral blood eosinophil count ( &gt;1.5 \times 10^{6}/cc )</td>
</tr>
<tr>
<td>systemic vasculitis involving two or more extrapulmonary organs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ARA criteria (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>eosinophilia ( &gt;10% )</td>
</tr>
<tr>
<td>neuropathy</td>
</tr>
<tr>
<td>nonfixed pulmonary infiltrates</td>
</tr>
<tr>
<td>paranasal sinus abnormality</td>
</tr>
<tr>
<td>extravascular eosinophils</td>
</tr>
</tbody>
</table>

*ARA, American Rheumatology Association.

Epidemiology

CSS is global in its distribution and has no significant gender predilection. It occurs in all age groups, although it has been most commonly reported in the third through fifth decades of life. The mean (95% confidence interval) annual incidence of CSS in northern England between 1988 and 1994 was 2.4 (0.9 to 5.3) per million population. This incidence was 30% of that estimated for Wegener’s granulomatosis and was similar to the incidence of microscopic polyangiitis (10). In a retrospective study from Norway, the estimated prevalence of CSS was 1.3 per 100,000 population, compared with 3.3 per 100,000 for microscopic polyangiitis (10). In the study from Norway, the estimated prevalence of CSS was 1.3 per 100,000 population, compared with 3.3 per 100,000 for microscopic polyangiitis (10).

Histologic examination usually reveals diffuse eosinophilia; upper airway granulomata are only rarely found. Asthma usually precedes the development of vasculitis by a period of weeks to years (3,4); it is often progressively severe and eventually requires oral steroids for adequate control. Eosinophilic tissue infiltration most commonly presents within the lungs as Loffler’s pneumonia or less commonly in a more chronic relapsing form as chronic eosinophilic pneumonia. Gastrointestinal tract infiltration may present as eosinophilic gastroenteritis. Although these conditions are disease entities in their own right, they all form part of the spectrum of eosinophil-mediated disease, which may progress to a more generalized multisystem disease process in the form of CSS (12).
18% of recorded fatalities). In the most recent and largest individual case series by Guillevin et al., 25 of 96 patients (26%) had proteinuria with levels in excess of 1 g/d. Five patients are reported as having renal insufficiency, although the degree of azotemia is not provided, and eight patients were diagnosed as having glomerulonephritis (4).

Clutterbuck et al., reviewing the results at Hammersmith Hospital, reported that renal disease was present in 16 of 19 patients with CSS and was frequently severe (15). This high incidence of severe renal involvement may partly reflect referral bias; however, only five of the 16 patients were referred from other hospitals. Microscopic hematuria was present in 13 patients, granular casts in nine, and red cell casts in three. Twelve patients had proteinuria, with three patients having an established nephrotic syndrome. Four cases presented with a serum creatinine >500 μmol/L (5.6 mg/dl), two being dialysis-dependent from the time of presentation. A similar potential for severe renal involvement is also shown by numerous recent case reports (16–22). The presence or absence of azotemia therefore does not reliably distinguish CSS from other forms of renal necrotizing vasculitis.

Renal histology may on occasion reveal frank vasculitis (Figure 1). Vasculitis involving arteries of varying sizes was found in seven of the 13 cases in the Churg autopsy series (5) and in two of the 19 subjects in Clutterbuck’s biopsy series (15). These resembled the changes found in other necrotizing vasculitides but are distinguished, at least before treatment, by a widespread infiltration of activated eosinophils. As in any necrotizing vasculitis, there may be destruction of the internal elastic membrane and aneurysm formation, as demonstrated in one of eight angiograms in Clutterbuck’s report (15) and in nine of 30 in that of Guillevin (4). The more typical histologic finding by percutaneous renal biopsy is a focal segmental (Figure 2) or a diffuse necrotizing (Figure 3) glomerulonephritis. This frequently occurs in the setting of an intense eosinophil-rich interstitial infiltrate (Figure 2). Churg described these glomerular changes as usually being mild and affecting only a minority of glomeruli (5). However, in the Hammersmith series of 13 renal biopsy specimens, 11 showed focal glomerulonephritis, with necrotizing features present in eight and crescents in nine (15).

<table>
<thead>
<tr>
<th>Author</th>
<th>Total</th>
<th>Renal Involvement</th>
<th>Mild/Moderate</th>
<th>Advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Churg and Strauss</td>
<td>13</td>
<td>8 (62%)</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Chumbley et al.</td>
<td>30</td>
<td>6 (20%)</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Lanham et al.</td>
<td>16</td>
<td>14 (88%)</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Shimamoto et al.</td>
<td>64</td>
<td>52 (81%)</td>
<td>52</td>
<td>0</td>
</tr>
<tr>
<td>Clutterbuck et al.</td>
<td>19</td>
<td>14 (74%)</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Reid et al.</td>
<td>23</td>
<td>13 (57%)</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Guillevin et al.</td>
<td>96</td>
<td>25 (26%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>261</td>
<td>132/261 (51%)</td>
<td>100/107 (94%)^b</td>
<td>7/107 (6%)^b</td>
</tr>
</tbody>
</table>

^a NA, not available.
^b Expressed as percentage of those with renal involvement of known severity.

Interstitial changes usually consist of edema and a diffuse eosinophilic infiltrate with associated lymphocytes, neutrophils, and plasma cells, and on occasion may be associated with only minimal glomerular pathology (15,23). Interstitial granulomata, usually with a core of degenerating eosinophils and situated adjacent to a venule, as described in Churg and Strauss’ original autopsy series (5), have since only rarely been described in renal biopsy specimens (2). Tubular changes are...
usually mild and nonspecific. Immunofluorescence microscopy has revealed only nonspecific staining in areas of segmental necrosis, while electron microscopy typically reveals the absence of dense deposits.

In addition to intrinsic renal disease, renal dysfunction may also result from an obstructive uropathy due to vasculitic involvement of the ureters and the lower genito-urinary tract. Chumbley et al. described granulomatoid involvement of the prostate in three patients (3), with one of the three patients presenting with obstructive uropathy. In Churg and Strauss’ original series, one patient had thickened nodular dilated ureters (5), and several case reports have confirmed the potential for ureteric vasculitis with an associated stenosis and obstruction (4,24–26).

**Laboratory Findings**

Typical laboratory findings in CSS include a normochromic normocytic anemia, leukocytosis, and an acute-phase response with elevated erythrocyte sedimentation rate and C-reactive protein levels. In the study by Lanham et al., the peak eosinophil count varied from 1,500 to 29,000 × 10⁶/L. In the same study, six of eight patients in whom levels were measured had elevated Ig E levels (2). Low levels of circulating IgE immune complexes, rheumatoid factor (2,3), and antinuclear antibodies (4) have also occasionally been described, but in most cases appear to be nonspecific. Measurements of complement, cryoglobulin, and infectious hepatitis serology are usually unremarkable.

**Anti-Cytoplasmic Neutrophil Antibodies**

An analysis of the association between CSS and anti-cytoplasmic neutrophil antibodies (ANCA) is difficult, because various studies have used different diagnostic criteria for CSS, as well as varied methods in the performance and interpretation of ANCA assays. Approximately one-half to two-thirds of reported patients with CSS are ANCA-positive. Individual studies have found ANCA in seven of 17 (41%) (27), 20 of 42 (47%) (4), 10 of 17 (58%) (9), six of nine (60%) (28), six of nine (60%) (29), nine of 14 (64%) (30), and 11 of 13 patients (85%) (31).

A relatively small number of research groups have published widely on various aspects of ANCA testing both in CSS and in other vasculitides. Due to the relative rarity of CSS, many different reports that refer to CSS in different contexts, from each individual center, are based on the same small number of patients. As a result, therefore, there is a considerable degree of
overlap in the published literature. To help overcome this bias, we have summarized the single most informative report from each group that refers to ANCA type in three or more patients with CSS (Tables 3 and 4). Most reviews of CSS refer to a predominance of perinuclear staining by direct immunofluorescence; however, as shown in Table 3, the presence of a cytoplasmic staining pattern is not uncommon. Whether this variation in the ratio of perinuclear to cytoplasmic staining in different studies reflects random variation, differences in diagnostic criteria, or other potential factors such as genetic or geographical variability is not established. Studies examining antigen specificity by enzyme-linked immunosorbent assay have shown a strong predominance of anti-myeloperoxidase antibodies in subjects with CSS. Several patients have been described who showed a cytoplasmic staining pattern by indirect immunofluorescence, but who failed to demonstrate the usually associated anti-proteinase 3 (PR3) antibody with the enzyme-linked immunosorbent assay (30). Whether these patients have an alternative ANCA target other than the PR3 antigen, or whether these discrepant results reflect the difficulties in standardizing anti-PR3 assays (29) is unknown.

**Etiology**

The etiology of CSS is difficult to investigate because evidence of the initiating event may no longer be present by the time the disease reaches clinical attention. Several authors have implicated inhaled allergens in both this condition and in Wegener’s granulomatosis. Support for this theory comes from case reports of CSS developing and recurring following exposure to inhaled antigens (4), as well as a proposed seasonal predominance of cases of CSS. Guillevin et al. reported 14 patients as having undergone desensitization with a variety of agents and four as having been vaccinated in the immediate period before CSS being diagnosed (4). CSS has also been described in association with macrolide antibiotics and the leukotriene receptor antagonist Zafirlukast (32). However, whether the above associations are causative or the result of confounding by indication, with early disease-related symptoms leading patients to receive the treatment, is unclear. Zafirlukast blocks the leukotriene LT-B4 and LT-D4 receptors, thereby inhibiting smooth muscle contraction and interstitial edema formation, but it does not show the wider spectrum of anti-eosinophilic effects of corticosteroids. If treatment with steroids had been commenced for asthma, associated with early, undiagnosed CSS, then the subsequent replacement of steroids by Zafirlukast might well be expected to be temporally associated with an increase in the underlying disease activity and with it, the diagnosis of clinically evident CSS.

The pathogenic role, if any, of ANCA antibodies in the development of CSS is unknown. Their absence in approximately one-third of patients suggests that at least in their currently described form, they are not a necessary requirement for the presence of the syndrome. In addition, neither the presence nor type of ANCA has been shown to be associated with a particular disease feature or outcome in CSS.

**Pathophysiology**

The central feature of CSS is an eosinophil-associated small vessel vasculopathy. The degree of eosinophil infiltration is greatly in excess of that seen in ordinary inflammatory states. Using monoclonal antibodies, Tai et al. were able to demonstrate that activated eosinophils and eosinophil degranulation products were present within both vessel walls and granulomata (33). Several authors have been able to show a correlation between the eosinophil level (and eosinophil degranulation products) and CSS disease activity.

The pathophysiology of eosinophil-mediated disease has recently been reviewed elsewhere (34). From the viewpoint of CSS, it is noteworthy that activated eosinophils are able to induce vascular endothelial cell activation (35). As in other inflammatory states, this depends on the interaction of a complex network of chemical mediators. The novel, relatively eosinophil-specific chemokine eotaxin (35) may play an important role in this process. Eotaxin upregulates the expression of the adhesion molecules ICAM-1 and VCAM-1 and selectively increases eosinophil binding to activated endothelial cells. Moreover, its actions may be specific for certain vascular beds (36). Recently, Wada et al. isolated eotaxin in the urine of a patient with a severe renal eosinophilic interstitial infiltrate but not from patients with the hypereosinophilia syndrome but no renal disease (37). The eotaxin level in addition correlated with the original patient’s disease activity.

The eosinophil may also be directly responsible for some of the classical disease features of CSS, by virtue of the release of its stored cationic proteins, such as eosinophilic cationic protein, which is implicated in the cardiotoxicity that is seen in both CSS and in the hypereosinophilia syndrome, and eosino-

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**Table 3. Direct immunofluorescence anti-neutrophil cytoplasmic antibody assay results in the Churg Strauss syndrome**

<table>
<thead>
<tr>
<th>Center/Research Group</th>
<th>Total</th>
<th>p-ANCA</th>
<th>c-ANCA</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hammersmith Hospital, London (30)</td>
<td>14</td>
<td>3</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>University of Lubeck, Bad Bramstedt, Germany (27)</td>
<td>17</td>
<td>2</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Project for ANCA Assay Standardization (29)</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>French Vasculitis Study Group (4)</td>
<td>42&lt;sup&gt;b&lt;/sup&gt;</td>
<td>15</td>
<td>1</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>82 (100%)</td>
<td>23 (30%)</td>
<td>12 (15%)</td>
<td>43 (52%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> ANCA, anti-neutrophil cytoplasmic antibodies; p, perinuclear; c, cytoplasmic.

<sup>b</sup> Pattern not specified in four subjects.
phils–derived neurotoxin, which may contribute to the development of peripheral neuropathy.

**Treatment**

CSS frequently responds rapidly to corticosteroids (4). Corticosteroids suppress gene transcription of various cytokines, and inhibit the prolongation of eosinophil survival in extravascular tissues (38). In the Hammersmith experience, several patients with azotemia but with serum creatinine levels <200 µmol/L (2.3 mg/dl) on presentation were treated with prednisolone alone. The creatinine level returned to normal in all patients, despite four having crescentic disease associated with necrotizing features on biopsy (39).

Some authors recommend the routine use of cyclophosphamide either by the oral or intravenous route in all patients with CSS, using a protocol devised for other necrotizing vasculitides (12). One justification for this approach is the concern that by the time it is evident that steroids are inadequately controlling the disease, significant irreversible tissue damage may already have occurred (12), although the frequency with which this occurs is unclear. Eosinophilia in some patients is known to be relatively resistant to steroid suppression, possibly due to alterations in steroid receptor density or to variations in transcription factors (40). This variability may partly explain the inadequate response of some patients to steroids alone and suggests that it is this subgroup that might benefit most from adjuvant immunosuppressive therapy.

Although the routine use of cyclophosphamide has proven beneficial in other forms of necrotizing vasculitides, these benefits may not be identical in patients with CSS. In particular, in steroid-sensitive patients, the potential long-term complications of cyclophosphamide may negate any additional benefits of its use. Interferon-α is also a potent inhibitor of eosinophil effector functions (41). It has recently been reported to achieve control in four patients with aggressive disease, two of whom had achieved an incomplete remission after treatment with steroids and cyclophosphamide (42). Azathioprine (3,9), cyclosporin (43), and immunoglobulin infusions (44,45) have also been used in an adjuvant setting in CSS, although their role in disease treatment remains uncertain. A future potential avenue of treatment is the development of monoclonal antibodies against targets such as interleukin-5. The eotaxin receptor offers a potentially potent target for such an intervention, as a result of its relative selectivity for eosinophils (34).

The only prospective randomized clinical trial of treatment of CSS has been conducted by the French “Polyarteritis Nodosa Study Group;” however, interpretation of their findings is limited because their studies include patients with CSS, classical polyarteritis nodosa, and microscopic polyangiitis. Their results are not stratified by the underlying diagnosis. They found that for this heterogeneous group, the use of cyclophosphamide in addition to steroids did not improve 10-yr survival rates, but did appear to result in fewer episodes of disease relapse and better quality of life (46). The addition of plasmapheresis with either steroids alone or combined treatment with steroids and cyclophosphamide did not appear to offer any additional benefit.

**Prognosis**

Overall, the prognosis for treated CSS appears to be good (3,4,47). Guillevin et al. reported a 6.5-yr actuarial survival rate of 72%, with an initial clinical remission being achieved in 91% of patients (4). With follow-up, 22 of 96 patients suffered from a total of 28 relapses, which were preceded in most cases by an elevation in serum eosinophil levels. Only three patients suffered from multiple relapses. Seventeen of the 22 patients who relapsed responded to an increase in immunosuppression. However, four patients failed to respond and died (4). In the Hammersmith experience, six of 16 patients relapsed, four of these episodes were preceded by a decrease in steroid dose, and only one patient suffered from multiple relapse (2). The renal prognosis is also favorable. In the Hammersmith series, three of four patients who presented with advanced azotemia regained independent function; the exception had evidence of chronic scarring on biopsy and failed to respond to therapy (39). In the Guillevin series, no patient was recorded as suffering from a renal relapse after remission (4). Multivariate analysis of the presenting features of the 96 patients reported by Guillevin showed that cardiac and gastrointestinal, but not renal, involvement were significantly associated with a poor outcome.

Long-term morbidity after the remission of active disease usually relates either to the sequelae of damage sustained during the vasculitic phase or to complications of the immu-

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**Table 4. Antigen-specific anti-neutrophil cytoplasmic antibody in the Churg Strauss syndrome**

<table>
<thead>
<tr>
<th>Center/Research Group</th>
<th>Total</th>
<th>Anti-MPO</th>
<th>Anti-PR3</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>University Hospital, Gröningen, The Netherlands (31)</td>
<td>13</td>
<td>10</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Hammersmith Hospital, London (30)</td>
<td>14</td>
<td>9</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>University of Lubeck, Bad Bramstedt, Germany (27)</td>
<td>17</td>
<td>2</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Project for ANCA Assay Standardization (29)</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>French Vasculitis Study Group (4)</td>
<td>11b</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>61 (100%)</td>
<td>34 (56%)</td>
<td>8 (13%)</td>
<td>13 (21%)</td>
</tr>
</tbody>
</table>

*a MPO, myeloperoxidase; PR3, proteinase 3; NA, not available.

*b ANCA pattern reported as nonspecific in one case.*
nosuppressive therapy. Asthma may persist and require ongoing steroid therapy, while slowly progressive congested heart failure may also occur. Peripheral neuropathy is often a frequent and troublesome long-term complication.

Summary

The Churg Strauss Syndrome is an eosinophil-associated small vessel vasculitis. Although its pathogenesis may be distinctive and the association with severe late-onset asthma typical, the clinical features during the vasculitic phase widely overlap with those of the other forms of necrotizing vasculitis, and no single clinical or histologic feature is pathognomic of the condition. Renal involvement is common, although usually mild, and even when severe it tends to respond well to treatment. The prognosis for both patient and renal survival with adequate treatment is in general good. The optimal treatment strategy, however, is uncertain, and may differ from that for the other vasculitides. In particular, in contrast to Wegener’s granulomatosis, the need for routine cyclophosphamide treatment is unconfirmed and requires further study.

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References


