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Churg-Strauss Syndrome: Clinical and Immunological Features

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1. Introduction

The vasculitides include a broad spectrum of disorders that span a clinical spectrum from benign, self-limited disease to fulminant conditions that are fatal in the absence of therapy. Whereas the large-vessel vasculitides consist of 2 principal disorders, giant cell arteritis and Takayasu arteritis, the medium- and small-vessel vasculitides are much more diverse, including multiple diseases that can affect nearly every organ system (Seo & Stone, 2007). This article is the second of a 2-part series that focuses on the challenges faced by clinicians who care for patients with vasculitis. The first article in this series discussed the large-vessel vasculitides. The problem of systemic autoimmune diseases such as systemic vasculitis with vascular lesions of medium and small vessels, including: Wegener granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis, nodose poliarteritis, attracts every year more attention of doctors, due to the worldwide relentless increase of patients with these diseases (Lhote & Guillevin, 2009; Tsukadaira, 2009). Recently, several reports have suggested that vasculitis is becoming more common.

Systemic vasculitis is a group of heterogeneous diseases (syndromes), characterized by inflammation and damage to blood vessels and which compromises or destroys the vessel wall leading to haemorrhagic and/or ischaemic events, giving impetus to the development of a wide spectrum of symptoms and signs. The forms of vasculitis may be varied: primary [idiopathic, e.g. cutaneous leukocytoclastic angiitis, Wegener’s granulomatosis, Churg-Strauss syndrome and microscopic polyangiitis] and secondary [a manifestation of connective tissue disease, infection, adverse drug eruption, or a paraneoplastic phenomenon], local and generalized, transient, recurrent and chronic; included group of diseases in which vasculitis is a primary characteristic. They are general in nature, though sometimes a local clinic can manifest symptoms. General damage of blood vessels may occasionally appear and disappear, but in most cases there are long-term. Each new escalation leads to the increase of clinical symptoms. Clinical implications of SV course depend on a number of factors, including etiology, location, size and number of blood vessels, the extent and severity of disease, its activity and nature of treatment.

Systemic vasculitis as the existing disease was first described by A. Cussmaul and I. Maier, when they reported a case of necrotizing arteritis and called it nodose periarteritis. There are over twenty different forms of Systemic vasculitis. One of the first classification was their classification by P. Zeek’s, which included five categories of Systemic vasculitis: nodose
periarteritis, hypersensitivity angiitis, allergic granulomatous angiitis, rheumatic angiitis, temporal arteritis. It was based on pathological data and damage and on their sizes. On the basis of etiologic and pathogenetic, clinical and pathomorphological criteria has been done many classifications of SV. But they are all flawed, because there are several factors that may affect the objectivity of classification opinions. They include: location and technology collection of fabrics, including various vascular pools, the possibility of angiography, variability in cellular composition depending on the morphogram stage, previous treatment options etc.

Primary systemic vasculitis has an incidence of more than 100 new cases per million. Currently, the most widely adopted vasculitis classification system is that of Chapel Hill Consensus Conference (CHCC), which is based on pathological criteria. The other widely used system is that of the American College of Rheumatology (ACR), which is based predominately on clinical findings.

The etiology of the systemic vasculitis is largely unknown, although they are widely believed to be autoimmune in origin, triggered by different environmental events. Epidemiologic studies have indicated factors, including silica exposure, infection, seasonal variation in occurrence, drugs, ultraviolet radiation and vitamin D, latitudinal gradient and etc.

Pathogenic mechanisms remain uncertain. In the modern literature widely discusses the pathogenic role in the development of systemic vasculitis of neutrophils, eosinophils, antineutrophil cytoplasmic antibodies, circulating immune complexes, lymphocytes, cytokines, total IgE and etc.

In general, systemic symptoms accompany all cutaneous vasculitic syndromes, and these symptoms include fever, malaise, weight loss, arthritis and/or arthralgias. In the majority of patients, vasculitic lesions will affect the lower extremities, mostly at dependent sites or underlying tight-fitting clothes. Upper extremity, trunk and head and neck involvement are infrequent and often signal the presence of more severe disease or coexisting systemic vasculitis. The subtlety and diversity of symptoms in the initial phase of vasculitis can be a real diagnostic problem, and thus early recognition of a vasculitic condition relies on the experience of a team of dedicated professionals from several different subspecialties, including laboratory medicine. The initial assessment will be to make a diagnosis, categorize disease severity and formulate a management plan. A structured approach, based on careful disease staging and evaluation, is the cornerstone of good disease management. Initial evaluation includes a comprehensive clinical assessment, serological tests, radiology and histology. The first step in the patients management is clinical history and examination, the second one of the initial investigations include full blood count, inflammatory markers [C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)], renal function such as epidermal growth factor receptor (eGFR) and serology to include antiglomerular basement membrane antibodies. Inflammatory markers provide a non-specific tool for assessing inflammatory activity and monitoring treatment. Urinalysis detects proteinuria and haematuria.

Specific diagnostic is based on detection of specific markers: characteristic autoantibodies are formed towards enzymes and bactericidal proteins within the cytoplasmic granules of neutrophils and monocytes in a substantial proportion of patients with systemic vasculitis manifesting as Wegener’s granulomatosis, microscopic polyangiitis and Churg-Strauss syndrome, as well as in patients with limited forms of these conditions. Histological examination of biopsy material is useful in confirming a diagnosis in the context of clinical findings and laboratory data. Also, skin biopsy is the gold standard for the diagnosis of
vasculitis type. For subsequent evaluations, it is effective and practical to measure clinical disease status for most patients with small and medium vessel vasculitis. Therapy is based on the pattern of vasculitis and on careful evaluation of the extent and activity of disease. The treatment of vasculitis comprises induction of remission followed by maintenance. Remission should be induced rapidly, balancing potential target organ damage against drug toxicity. Maintenance with immunosuppression should limit the amount of corticosteroid use and prevent relapse. Concomitant medication is used to treat or prevent adverse events from immunosuppressive treatment.

2. Connection between systemic vasculitis, bronchial asthma, eosinophilic syndrome and churg-strauss syndrome

The unreleased question of eosinophilic background in patients with systemic vasculitis and its influence on the disease activity, is very actual today. The most important eosinophilic-associated systemic vasculitis between all vascular processes is Churg-Strauss syndrome, that occur with eosinophilia as diagnostic criterion due to ACR,1990. Since its first description as allergic granulomatous angiitis in 1951 (Churg and Strauss, 1951), and subsequently its affiliation with the small-sized vessel systemic necrotizing vasculitides and, more specifically, the so-called subgroup of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides in the early 1990s, knowledge about the pathophysiological mechanisms of Churg-Strauss syndrome has greatly improved. Its natural clinical history and progression are better understood, but the syndrome’s potential subsets are not yet totally elucidated. Major advances have also been made in the therapeutic management of affected patients, but much remains to be done because sustained off-treatment remissions are quite rare and patients often require a long-term low-dose corticosteroid therapy (Cohen et al., 2007; Ribi et al., 2008). International studies and workshops on vasculitis classification, immunology, genetics, and treatments are ongoing or planned. Here, we review the current known aspects of Churg-Strauss syndrome (Pagnoux, 2010). Churg-Strauss syndrome is a rare disease, with an annual incidence ranging between 0.5 and 6.8 per million inhabitants and a prevalence of 10.7-14 per million inhabitants (Pagnoux et al., 2007; Watts et al., 2005), with a mean age at onset around 50 years and no sex preponderance. No strong evidence of a differential geographical distribution pattern has been reported so far, nor a blatant change in its frequency over the past decades. However, some studies reported a slightly higher prevalence in northern, as opposed to southern, Europe, and in urban, as compared to rural, regions.

Several exogenous triggering factors for disease onset or flares have been identified or, more cautiously, suspected in some European or North American studies. They include vaccinations, desensitizations, and drugs, such as macrolides, carbamazepine, quinine, and also anti-asthma agents, like leukotriene-receptor antagonists and, more recently, omalizumab, a recombinant monoclonal anti-immunoglobulin E (IgE) antibody (Bibby et al., 2010; Pagnoux et al., 2007). These latter two often provide the opportunity for substantial tapering or withdrawal of corticosteroids in asthmatic patients, thereby unmasking an underlying ‘forme fruste’ of Churg-Strauss syndrome, which had so far been controlled by corticosteroids, but a direct triggering role of these agents cannot be excluded (Bibby et al., 2010). Whether or not “common” asthma represents a risk factor for Churg-Strauss syndrome per se has not been clearly determined, because both conditions share some underlying mechanisms. The earliest studies reported a higher annual incidence of Churg-
Strauss syndrome in asthmatic patients treated with non-leukotriene-modifying asthma drugs (64.4 per million asthmatics) or a leukotriene-receptor antagonist (about 60 per million asthmatics). A more recent study reported a somewhat lower Churg-Strauss syndrome incidence of 34.6 per million asthmatics per year (Harrold et al., 2005), which remains higher than in the general population; but other reported incidences varied from 0 to 67 according to disease definition. Whereas asthma often clusters in families, familial cases of Churg-Strauss syndrome are exceptional, diminishing the gene and environmental factor impact on the latter. However, results of several genetic studies suggested some predisposing hereditary factors, like the HLA-DRB1*04 and HLA-DRB1*07 alleles and the HLA-DRB4 gene, which are more frequent in Churg-Strauss syndrome patients than healthy controls, the interleukin IL10.2 haplotype, which is associated with enhanced IL-10 expression, and possibly the CD226 Gly307Ser polymorphism (Wieczorek et al., 2010).

Its most typical presentation consists of the appearance, in a patient with late-onset asthma, of vasculitic manifestations, like fever, cutaneous purpura and mononeuritis multiplex. In such a setting, the combination of blood eosinophilia and inflammatory syndrome is highly suggestive of the diagnosis, which can be further supported by the detection of antineutrophil cytoplasmic antibodies (ANCA), especially P-ANCA (perinuclear-ANCA) with anti-myeloperoxidase specificity and the presence of eosinophilic granulomas and/or necrotizing vasculitis in an affected-tissue biopsy. Asthma is the most common sign of Churg-Strauss syndrome, but Churg-Strauss syndrome can cause a variety of problems, ranging from hay fever, rash and gastrointestinal bleeding, to severe pain and numbness in your hands and feet. The wide range of symptoms — and their similarity to symptoms of other disorders — make Churg-Strauss syndrome challenging to diagnose. Biological phenotypes of interest for assessing severity of Churg-Strauss syndrome may be IgE level, ANCA, cytokines (IL-2, 4, 5, 10) and eosinophilia. Phenotypes other than usual Churg-Strauss syndrome need to be considered. Phenotypic heterogeneity may help to disentangle etiologic heterogeneity. Churg-Strauss syndrome, its verification and activity could be mediated by different pathogenetic mechanisms and realized mediators, such as ANCA, eosinophils, cytokines, total IgE etc. Severity of eosinophilia in patients with Churg-Strauss syndrome represent a clinical subphenotype of interest, and studying severe eosinophilia (extreme phenotype) may increase the power to detect linkage. It would be useful to define Churg-Strauss syndrome phenotypes unencumbered by the activity of disease, which may depend heavily on nongenetic factors, and free of gene-trigger interactions. Besides the activity, environmental factors and inadequate treatment can modify the severity of the Churg-Strauss syndrome phenotype. Consideration of treatment as a marker of severity implies that the relevant phenotype for etiological research is masked by the treatment.

Intermediate Phenotypes

Intermediate phenotypes are important with respect to pleiotropy and etiological heterogeneity. Bronchial hyperresponsiveness, total IgE, eosinophilia, ANCA-presentation and vascular involvement are usually considered intermediate phenotypes for Churg-Strauss syndrome.

Refinement of Phenotypes

Considering environmental factors and potential interactions with genetic factors may increase our ability to detect genetic factors in multifactorial diseases such as Churg-Strauss syndrome.
NS- not significant

There were found some peculiarities of immunological parameters in patients with Churg-Strauss syndrome, such as significantly lower proportional level of CD3+lymphocytes (p<0.05), higher proportional and absolute level of CD19+-lymphocytes (p<0.05), intensively expressed proportional (p<0.01) and absolute (p<0.001) early count of lymphocyte activation marker (CD25+) and significantly intensively proportional (p<0.05) and absolute (p<0.01) expression of CD95+ in patients with Churg-Strauss syndrome compared with patients with bronchial asthma and eosinophilia. Compared with patients with systemic vasculitis with eosinophilia, patients with Churg-Strauss syndrome had a significantly higher proportional (p<0.05) and absolute (p<0.05) mean of CD4+lymphocytes, intensively expressed proportional (p<0.05) and absolute (p<0.01) count of early lymphocyte activation marker (CD25+) and significantly intensively proportional and absolute expression of CD95+ (p<0.05).

There were found some immunological signs in patients with Churg-Strauss syndrome depending on eosinophilia severity too, that is presented in the Table 6.

<table>
<thead>
<tr>
<th>Indexes</th>
<th>Patients with CSS and mild eosinophilia (AEC 600-1500 cells/μL) (n=12)</th>
<th>Patients with CSS and moderate eosinophilia (AEC 1500-5000 cells/μL) (n = 13)</th>
<th>Patients with CSS and severe eosinophilia (AEC &gt;5000 cells/μL) (n = 5)</th>
<th>P 1-2</th>
<th>P 1-3</th>
<th>P 2-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eosinophils</td>
<td>cells/μL</td>
<td>0.59±0.05</td>
<td>3.58±0.82</td>
<td>5.81±0.92</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>cells/μL</td>
<td>1.61±0.15</td>
<td>2.24±0.47</td>
<td>3.01±0.15</td>
<td>NS</td>
<td>0.05</td>
</tr>
<tr>
<td>CD3+</td>
<td>%</td>
<td>56.7±1.66</td>
<td>48.5±2.26</td>
<td>46.50±1.18</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>CD4+</td>
<td>%</td>
<td>36.5±2.16</td>
<td>41.20±3.97</td>
<td>50.30±4.21</td>
<td>NS</td>
<td>0.05</td>
</tr>
<tr>
<td>CD8+</td>
<td>%</td>
<td>19.65±1.72</td>
<td>18.50±2.68</td>
<td>16.67±2.33</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>CD16+/56+</td>
<td>%</td>
<td>20.05±1.86</td>
<td>22.03±2.61</td>
<td>25.0±2.12</td>
<td>NS</td>
<td>0.05</td>
</tr>
<tr>
<td>CD19+</td>
<td>%</td>
<td>49±0.05</td>
<td>49±0.05</td>
<td>49±0.05</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>CD25+</td>
<td>%</td>
<td>28.33±2.73</td>
<td>29.82±1.89</td>
<td>30.4±1.58</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>HLA DR+</td>
<td>%</td>
<td>20.05±1.68</td>
<td>26.50±1.46</td>
<td>31.9±2.48</td>
<td>NS</td>
<td>0.05</td>
</tr>
<tr>
<td>CD95+</td>
<td>%</td>
<td>20.73±1.27</td>
<td>23.50±2.67</td>
<td>29.9±7.06</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 6. Trends of lymphograme indexes and lymphocytes activity markers in patients with Churg-Strauss syndrome depending on eosinophilia severity (M±m).

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There were found some peculiarities of immunological markers in patients with Churg-Strauss syndrome and different eosinophilia severity, such as the highest eosinophils level in patients with Churg-Strauss syndrome and severe eosinophilia in comparison to the patients with mild eosinophilia (p < 0.001) and moderate eosinophilia (p < 0.05), significantly lower absolute level of lymphocytes in patients with Churg-Strauss and severe eosinophilia p < 0.05) in comparison to patients with mild eosinophilia; significantly lower proportional and absolute level of CD3^+ lymphocytes (p < 0.05), CD4^+ lymphocytes (p < 0.05), CD19^+ lymphocytes (p < 0.05), significantly intensively expressed early lymphocyte activation markers such as (CD25^+) (p < 0.01), late lymphocyte activation markers such as (HLA DR^+) (p < 0.001) and significantly intensively expression of CD95^+ (p < 0.001) in patients with Churg-Struss syndrome and severe eosinophilia compared with patients with Churg-Strauss syndrome and mild eosinophilia. There were found some significantly lower proportional and absolute level of CD4^+ lymphocytes (p < 0.05), absolute level of CD19^+ lymphocytes (p < 0.001), significantly intensively expressed early lymphocyte activation markers such as (CD25^+) (p < 0.05), late lymphocyte activation markers such as (HLA DR^+) (p < 0.05) and significantly intensively expression of CD95^+ (p < 0.05) in patients with Churg-Struss syndrome and severe eosinophilia compared with patients with Churg-Strauss syndrome and moderate eosinophilia.

No significant peculiarities were found in patients with Churg-Strauss syndrome and mild or moderate eosinophilia.

We have also analyzed the features of serum interleukins (IL-2, IL-4, IL-5, IL-10) in patients with Churg-Strauss syndrome and other examined groups, that is showed in the Table 7.

<table>
<thead>
<tr>
<th>Interleukins</th>
<th>Patients with BA and eosinophilia (n = 30)</th>
<th>Patients with SV and eosinophilia (n = 19)</th>
<th>Patients with CSS (n = 30)</th>
<th>P_{1-2}</th>
<th>P_{1-3}</th>
<th>P_{2-3}</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-2 pg/ml</td>
<td>3.79±0.98</td>
<td>6.31±0.75</td>
<td>8.78±0.26</td>
<td>0.05</td>
<td>0.05</td>
<td>0.01</td>
</tr>
<tr>
<td>IL-4 pg/ml</td>
<td>8.17±0.17</td>
<td>5.38±0.55</td>
<td>6.64±0.16</td>
<td>0.01</td>
<td>0.05</td>
<td>NS</td>
</tr>
<tr>
<td>IL-5 pg/ml</td>
<td>6.60±1.26</td>
<td>12.4±2.28</td>
<td>97.9±17.5</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-10 pg/ml</td>
<td>2.88±0.19</td>
<td>3.27±0.29</td>
<td>2.12±0.14</td>
<td>NS</td>
<td>0.05</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Table 7. Trends of pro-inflammatory (IL-2) and anti-inflammatory (IL-4, IL-5, IL-10) cytokines in patients with bronchial asthma, systemic vasculitis with eosinophilia and with Churg-Strauss syndrome (M±m)

NS - not significant

Comparing realizing possibility of pro- and anti-inflammatory mechanisms of cytokines such as IL-2, IL-4, IL-5 and IL-10 in patients with bronchial asthma with eosinophilia, systemic vasculitis with eosinophilia and Churg-Strauss syndrome it was found significant increase of IL-4 (p < 0.01) and IL-5 (p < 0.001) level in patients with bronchial asthma and eosinophilia, increase of IL-2 (p < 0.05), IL-4 (p < 0.05) and IL-5 (p < 0.05) in patients with systemic vasculitis with eosinophilia, increase of IL-2 (p < 0.05) and IL-5 (p < 0.001) level and decrease of IL-10 (p < 0.05) level in patients with Churg-Strauss syndrome.
There were found some cytokines production peculiarities in patients with Churg-Strauss syndrome depending on eosinophilia severity, that is presented in the Table 8.

<table>
<thead>
<tr>
<th>Interleukins</th>
<th>Patients with CSS and mild eosinophilia (AEC 600-1500 cells/μL) (n=12)</th>
<th>Patients with CSS and moderate eosinophilia (AEC 1500-5000 cells/μL) (n = 13)</th>
<th>Patients with CSS and severe eosinophilia (AEC &gt;5000 cells/μL) (n = 5)</th>
<th>P₁,₂</th>
<th>P₁,₃</th>
<th>P₂,₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-2 pg/ml</td>
<td>8,44±0,11</td>
<td>8,74±0,16</td>
<td>9,18±0,08</td>
<td>NS</td>
<td>0,05</td>
<td>NS</td>
</tr>
<tr>
<td>IL-4 pg/ml</td>
<td>5,7±0,13</td>
<td>6,8±0,11</td>
<td>7,42±0,09</td>
<td>NS</td>
<td>0,05</td>
<td>NS</td>
</tr>
<tr>
<td>IL-5 pg/ml</td>
<td>32,7±7,5</td>
<td>49,4±9,6</td>
<td>211,6±29,5</td>
<td>NS</td>
<td>0,001</td>
<td>0,001</td>
</tr>
<tr>
<td>IL-10 pg/ml</td>
<td>2,34±0,08</td>
<td>2,04±0,09</td>
<td>1,98±0,05</td>
<td>NS</td>
<td>0,05</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 8. Trends of pro-inflammatory (IL-2) and anti-inflammatory (IL-4, IL-5, IL-10) cytokines in patients with Churg-Strauss syndrome depending on eosinophilia severity (M±m)

**NS - not significant**

Analyzing realizing possibility of pro- and anti-inflammatory cytokines such as IL-2, IL-4, IL-5 and IL-10 in patients with Churg-Strauss syndrome and different eosinophilia severity, it was fixed significant increase of IL-2 (9,18±0,08 pg/ml, p<0,05), IL-4 (7,42±0,09 pg/ml, p<0,05), and IL-5 (211,6±29,5 pg/ml, p<0,001) and decrease of IL-10 (1,98±0,05 pg/ml, p<0,05) level in patients with Churg-Strauss syndrome with severe eosinopilia compared with patients with Churg-Strauss syndrome and mild eosinophilia. Also, it was fixed significant higher IL-5 level in patients with Churg-Strauss syndrome and severe eosinophilia compared with patients with moderate eosinophilia (p<0,001) too.

The patients with systemic vasculitis and eosinophilia and with Churg-Strauss syndrome were divided in some subgroups depended on ANCA –presence.

In our series of patients, we found that ANCA positivity was correlated with renal involvement, especially with the histologic picture of necrotizing crescentic glomerulonephritis, and, to a lesser extent, with constitutional symptoms. Moreover, ANCA-positive patients had a significantly higher frequency of certain organ system clinical manifestations, such as pulmonary hemorrhage, purpura, and mononeuritis multiplex. In contrast, ANCA-negative patients had a higher frequency of heart and (less severe) lung disease.

Limited data have been reported on the correlation between ANCA positivity and the clinical features in CSS, even though it should be noted that most (if not all) reported cases of necrotizing crescentic glomerulonephritis in CSS involved ANCA-positive (usually MPO pANCA) patients, as in our cohort. Moreover, the results of studies of small series of patients have suggested that MPO ANCAs may be associated with the onset of glomerular disorder in CSS.

There were fixed some morphological peculiarities in patients with Churg-Strauss syndrome depending on eosinophilia severity, that is presented in pictures 1,2 and 3.
We have selected the three most informative results of skin-muscular samples biopsies patients with Churg-Strauss syndrome with different eosinophilia severity, that reflected in three figures.

Fig. 1. Churg-Strauss syndrome: Tissue eosinophilia is a frequent finding in cutaneous lesions of Churg–Strauss syndrome. Hematoxylin, eosin × 300; clinical: light/mild eosinophilia

Fig. 2. Churg-Strauss syndrome: Skin biopsy which was indicative of small vessel vasculitis, showing the presence of an inflammatory infiltrate predominantly constituted by eosinophils and plasmocytes around blood vessels. Hematoxylin, eosin × 400; clinical: medium eosinophilia

The analysis of the founded morphological features, that were identified in patients with Churg-Strauss syndrome with different eosinophilia severity, shoved eosinophilic infiltration of the dermis in patients with Churg-Strauss syndrome and mild eosinophilia
(Fig.1); necrotizing changes in the center of granulomas, extensive infiltration of neutrophils, eosinophils of vessel wall until the formation of circular eosinophil infiltrates in the vessels of patients with Churg-Strauss syndrome and severe eosinophilia (Fig.3)

Fig. 3. Churg-Strauss syndrome: Skin-muscular biopsy which showing eosinophilic circular infiltration of the intermuscular arteriole. Hematoxylin, eosin × 400; clinical: severe eosinophilia

4. Conclusion

Substantial advances have been made in the understanding of immune mechanisms (especially eosinophils, circulating immune complexes, total IgE, antineutrophicytoplasmic antibodies, cytokines) implicated in Churg-Strauss syndrome and its management. While it definitively remains a systemic necrotizing small-sized vessel vasculitis, its membership in the ANCA-associated vasculitis group has become more controversial. More complex and numerous mechanisms are involved in Churg-Strauss syndrome (Hoffman and Langford, 2005; Pagnoux and Guillevin, 2010). Similarly, one of its earlier denominations, allergic granulomatous angitis (Churg and Strauss, 1951), has become dated because not all patients have (eosinophilic) granulomas. Moreover, several disease subgroups have been identified, essentially based on clinical or biological findings (Walsh & August, 2010). There are a large number of works devoted to studying of the problem of rare disease – Churg-Strauss syndrome – especially its clinical and laboratory features, but it was firstly by us described clinical, immunological and morphological features of Churg-Strauss syndrome with different severity of eosinophilia in these patients.

It was fixed special clinical signs in patients with Churg-Strauss syndrome and severe eosinophilia such as: underproductive, complicated nasal breathing cough, erythematous rash, erythema multiforme, palpable spot haemorrhagic rush and haemorrhagic rash with confluence ability, hyperpyrexia, arthritis, lymphadenopathy, diarrhea and polyneuropathy. There were found some peculiarities of immunological markers in patients with Churg-Strauss syndrome and different eosinophilia severity, such as the highest eosinophils level in patients with Churg-Strauss syndrome and severe eosinophilia in comparison to the patients with mild eosinophilia (p<0,001) and moderate eosinophilia (p<0,05), significantly lower absolute lymphocytes level in patients with Churg-Strauss and severe eosinophilia.
(p<0.05) in comparison to patients with mild eosinophilia; significantly lower proportional and absolute level of CD3+ lymphocytes (p<0.05), CD4+ lymphocytes (p<0.05), CD19+ lymphocytes (p<0.05), significantly intensively expressed early lymphocyte activation markers such as (CD25+) (p<0.01), late lymphocyte activation markers such as (HLA DR+) (p<0.001) and significantly intensively expression of CD95+ (p<0.001) in patients with Churg-Strauss syndrome and severe eosinophilia compared with patients with Churg-Strauss syndrome and mild eosinophilia. Other subgroups may be brought forth in the future, relying on more subtle molecular and genetic characteristics (IL-4, IL-5, IL-5RA gene polymorphism).

Therapeutic strategies also require further improvement. Treatment should be adapted as closely as possible to each patient’s characteristics. New treatments (monoclonal antibodies) are needed to lower the rate of frequent, low-dose but long-term, corticosteroid-dependence that represents a major issue and the lingering disappointment in current therapeutic strategies for Churg-Strauss syndrome.

5. References


This book represents the culmination of the efforts of a group of outstanding experts in vasculitis from all over the world, who have endeavored to devote their work to this book by keeping both the text and the accompanying figures and tables lucid and memorable. Here, you will find an amalgam between evidence-based medicine to one based on eminence, through an exciting combination of original contributions, structured reviews, overviews, state-of-the-art articles, and even the proposal of novel pathogenetic models of disease. The book contains contributions on the etiology and pathology of vasculitis, the potential role of endothelial cells and cytokines in vascular damage and repair as well as summaries of the latest information on several primary and secondary vasculitis syndromes. It also covers selected topics such as organ-specific vasculitic involvement and quality of life issues in vasculitis. The editor and each of the authors invite you to share this journey through one of the most exciting fields of the medicine, the world of Vasculitis.

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