

## Churg-Strauss Syndrome.

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### CASE:

A 44 year old female nurse with a 20-year history of severe, steroid-dependent asthma, hypertension, hematuria, pleuritis, and sinusitis was referred from her ophthalmologist in January 2000, with the question of possible bilateral scleritis. The patient was treated with topical steroid (prednisolone acetate 6 times daily) for anterior uveitis, systemic prednisone (50mg per os) and steroid inhalers for her asthma, and oral hypertensive medication.

On presentation to us the patient complained of ocular pain, lacrimation, photophobia, blurred vision and bilateral ocular redness. Her visual acuity at presentation was 20/25 for both eyes. Bilateral episcleral injection was noted. Slit lamp examination revealed deep and quiet anterior chambers and bilateral areas of thinning of the superior sclera. We thought that she had had scleritis and uveitis. The patient was treated with non-steroidal anti-inflammatory drops (diclofenac sodium 6 times daily) with a tapering of the steroid drops. The patients visual acuity had returned to 20/20 by the time of her next appointment with us 7 days later. The following laboratory studies were normal: hemogram, erythrocyte sedimentation rate, Lyme titer, fluorescent treponemal antibody absorption (FTA-ABS), complement levels, angiotensin converting enzyme (ACE), C-reactive protein, antinuclear antibody (ANA), antineutrophil cytoplasmic antibodies (ANCA), anticardiolipin antibodies and HLAB27. Urine analysis showed microscopic hematuria. A chest x-ray was normal.

The patient was referred for rheumatologic evaluation. The rheumatologist, after taking into account the patients medical history and the ocular manifestations, proposed the diagnosis of CSS syndrome and suggested biopsy (lung and sinus) for histopathologic support of the clinical diagnosis; the patient refused biopsy.

Six months after her first visit, in an effort to achieve a steroid sparing effect, we introduced systemic methotrexate orally at a dose of 10mg every week, with tapering doses of prednisone (initially 50mg/day). The patient developed cramping abdominal pain and petechial rash on her lower extremities; these resolved two months later without sequelae. Further relevant laboratory investigations were negative and these symptoms were considered as part of the systemic vascular involvement.

Over the next three months, while systemic steroid taper proceeded, the patient developed a severe asthma and sinusitis flare, pleural and pericardial effusion, polyneuropathy and multiple episodes of transient ischemic attacks (TIA) associated with vision loss, vomiting and sweating. Ophthalmologic evaluation disclosed low-grade anterior segment ocular inflammation. Prednisone was increased to 60 mg/day, methotrexate was discontinued, and cyclophosphamide, 150 mg per os daily, was begun. Three years after her first visit to us, the patient is still on the same treatment, except that prednisone had been reduced to 17.5mg/day, without recurrence of signs or symptoms of ocular or extravascular inflammation.

The patient described feeling the best that she has felt in many years, with improved asthmatic symptoms, at the time of our last evaluation of her in October, 2002.

### DISCUSSION

Churg and Strauss reported 13 cases of patients with severe bronchial asthma and disseminated necrotizing vasculitis in 1951.<sup>1</sup> Fever, peripheral eosinophilia and multi-systemic involvement were associated with a histologic pattern of necrotizing arteritis, tissue eosinophilia and extravascular granulomas were features of the syndrome in these patients. Churg and Strauss distinguished these findings from those of polyarteritis nodosa, which was previously used to describe all inflammatory vascular diseases, and named this entity allergic granulomatosis and angiitis, later to be called eponemously Churg-Strauss syndrome (CSS). CSS is now considered to be a well-defined vasculitis, clearly distinct from other small or medium sized vessel vasculitides. According to the American College of Rheumatology<sup>2</sup>, in order to establish a clinical diagnosis of CSS, four of six criteria must be met (asthma, hypereosinophilia >10%, mononeuropathy or polyneuropathy, non-fixed pulmonary infiltrates, paranasal sinus abnormality and extravascular eosinophils). CSS is considered a very rare syndrome, affecting as estimated, 1.8 per million people worldwide<sup>3</sup>. There have been few reports in the literature regarding CSS, and despite the multisystemic involvement ocular manifestations have been very rarely noted<sup>4-12</sup>.

Asthma is the cardinal clinical feature of CSS, and it usually presents eight to ten years before the first symptoms of vasculitis<sup>3</sup>. It is typically severe and steroid-dependent; CSS patients often need hospitalization for asthma attacks or respiratory failure. Lung hemorrhage, pleural effusion and pulmonary infiltrates may occur. Other features of this syndrome include renal involvement<sup>13</sup> (from 16 to 49%), dermatological manifestations<sup>3</sup> (purpura and subcutaneous nodules) and nervous system involvement<sup>3</sup> (peripheral neuropathy or central nervous system involvement with

disorientation, convulsions and coma). Patients with CSS may experience fever, weight loss, general malaise, or abdominal pain due to vasculitis of the mesenteric circulation,<sup>13</sup> and death secondary to cardiac complications (congestive heart failure, cardiomyopathy and pericardial effusion) is not uncommon.

This rare syndrome can present with various ocular manifestations<sup>4-12</sup>, ranging from bilateral upper eyelid swelling and bloody ocular discharge as described by Meissler et al,<sup>8</sup> to episcleritis and uveitis as described by Cury et al<sup>9</sup>. Chumbley and associates<sup>14</sup> found marginal ulcerative keratitis in one of their 30 patients with CSS, and Bawazeer and colleagues<sup>10</sup> also reported marginal ulcerative keratitis in a patient with CSS. In both cases the ocular symptoms resolved fully after systemic corticosteroid therapy. Posterior segment involvement can include severe panuveitis with retinal infarction, branch retinal artery occlusion and optic disc vasculitis.<sup>14</sup> Bosch-Gil et al described one patient with definite CSS and another possible case, both of whom developed orbital pseudotumor.<sup>11</sup> Neuro-ophthalmologic manifestations in CSS patients include ischemic optic neuropathy, amaurosis fugax and cranial nerves palsies.<sup>7</sup>

Lanham and associates<sup>15</sup> emphasized the clinical approach for the diagnosis of CSS. Although our patient fulfilled only 3 of the major CSS criteria (severe asthma, sinus abnormality, polyneuropathy) she also developed other impressive <sup>TM</sup>minor criteria: pleural and pericardiac effusion, fever, abdominal pain, renal involvement, dermatologic and ocular manifestations. The very high dose of prolonged systemic steroid treatment may have accounted for her lack of peripheral eosinophilia.<sup>15</sup>

We advised immunomodulatory treatment in order to achieve a steroid sparing effect, since the patient had been steroid dependent for 20 years. According to Churg and Strauss, allergic granulomatosis is often a fatal disease.<sup>1</sup> Guillevin et al.<sup>16</sup> reported an increase in the survival of patients with CSS since the advent of steroid therapy from 10% to 55%. However they also reported serious side effects (severe diffuse osteoporosis, cataract, diabetes and nervous breakdown) with prolonged systemic high-dose steroid use<sup>16</sup>. Renal, gastrointestinal and nervous system involvement are indicators of poor prognosis for CSS and treatment with a combination of cyclophosphamide and oral steroids is often beneficial<sup>16-17</sup>.

There are no reports in the ophthalmic literature describing successful treatment of both ocular and extravascular inflammatory manifestations of CSS with cyclophosphamide. Shields et al<sup>5</sup> described a case of a patient who received cyclophosphamide and systemic steroid treatment for CSS with conjunctival involvement but with no description for the exact dose and duration of treatment. Another report describes treatment of anterior ischemic optic neuropathy in a patient with CSS with cyclophosphamide and high dose steroid (80mg).<sup>12</sup> We managed to control the inflammatory component in our patient with a combination of cyclophosphamide and a relatively low dose of prednisone (17.5mg). Although CSS is known to be controlled with high dose steroid treatment, the combination of lower dose steroids and cyclophosphamide can offer an alternative treatment for this otherwise fatal disease.

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