Churg-Strauss syndrome: A case report

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Abstract

Introduction. Churg-Strauss syndrome (CSS) is an allergic granulomatous angiitis, a rare disease of small and medium arteries and veins, associated with the presence of perinuclear antineutrophil cytoplasmic antibodies (p-ANCA). According to the American College of Rheumatology (ACR), there are four or more criteria out of six for the diagnosis: asthma, eosinophilia (> 10% in peripheral blood), paranasal sinusitis, pulmonary infiltrates, histological evidence of vasculitis with extravascular eosinophils, and mononeuritis multiplex or polyneuropathy. Case report. We reported a female patient, aged 80 years, with asthma for many decades and repeatedly verified eosinophilia in peripheral blood, in which CSS was suspected only after the occurrence of skin changes in the form of vesicles, vesiculopustule, purpuric macula, papule and petechiae. Further tests verified pulmonary infiltrates, paranasal sinusitis, extravascular eosinophils on histopathologic sample of skin tissue, and polyneuropathy. The treatment started with methylprednisolone (60 mg/d, with decreasing doses), and continued with pulse doses of cyclophosphamide (800 mg once monthly), also corticosteroid ointment for skin lesions. Conclusion. Despite long-standing pulmonary symptoms and laboratory findings of eosinophilia, the appearance of skin changes raised suspicion of possible CSS. Skin changes resolved and the patient was referred to rheumatologist. Key words: churg-strauss syndrome; diagnosis; skin diseases; histological techniques.

Introduction

Churg-Strauss syndrome (CSS) is a systemic vasculitis involving small vessels, affecting several organs. Asthma is usually the first clinical sign of CSS. It is often accompanied by allergic rhinitis and sinusitis. CSS progress to peripheral and tissue eosinophilia, eventually resulting in necrotizing vasculitis with extravascular granulomas. About 60% of CSS patients have skin lesions in the active phase of the disease, but the skin lesions may appear also in its early stage. Most common are palpable purpura and nodules, usually located on the limbs and scalp. Less usual skin features are livedo reticularis, vesicles, aseptic pustules, ecchymoses and urticarial wheals. Also maculopapular erythematous eruption resembling erythema multiforme has been described. Papular and nodular lesions may turn in necrotic-ulcerative evolution. All of these
features can appear at the same time or in the different stages of CSS. Histopathology examination reveals a leukocytoclastic vasculitis, commonly involving venules; sometimes, the vessel wall reveals fibrinoid changes surrounded by granulomatous inflammation; finding of numerous eosinophils in the infiltrate, in addition to neutrophils, lymphocytes and macrophages, is of diagnostic importance. We presented a female patient with suspected CSS due to cutaneous features which corresponded to lesions described in the literature. It was confirmed by histopathologic report.

Case report

A 80-year-old female was admitted to hospital with few vesicles, vesiculopustules, purpuric maculas, papules and petechiae on the skin of her hands, feet, extremities and trunk (Figures 1, 2 and 3). Skin changes occurred a year and a half before, with fatigue and weight loss (about 10 kg of body weight), without neurological and other symptomatology. Data from the personal history revealed repeated eosinophilia in recent decades; diagnosed bronchial asthma was treated with beclomethasone, salbutamol and salmeterol xinafoate inhalation powder; arterial hypertension was not regularly treated.

On admission, laboratory analyses revealed increased erythrocyte sedimentation rate (ESR) (54 mm/h), fibrinogen 6.83 g/L; eosinophilia 45.8% was evident (with normal count of leukocytes $9.57 \times 10^9/L$), with relative neutropenia 31.4%, lymphopenia 14.5%, as well as elevated rheumatoid factor of 66.4 U/L and increased immunoglobulin (Ig) E concentration 741 IU/L. Other complete blood count parameters, electrolytes, urea, creatinine, total bilirubine, creatine phosphokinase, protein electrophoresis, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gama-glutamyl transferase ($\gamma$GT), IgG, IgA, IgM, C3 and C4 were within normal range. Urinalysis was normal. ELISA test for echinococcus, toxocara, HIV, HBsAg and HCV tests were negative. Other infective causes of eosinophilia were also ruled out [stool sample test for intestinal parasites and Strongyloides stercoralis, sputum for acido-resistance bacilli (ARB) direct examination and Löwenstein cultivation]. In peripheral blood smear increased number of leukocytes was evident ($11.7 \times 10^9/L$), as well as elevated percentage of eosinophiles (61%). The concentration of proteins in 24-h urine (Biuret method, in 3 times) was normal; albumin in 24-h urine: normal findings. Antinuclear antibodies (ANA) (tissue-type substrate) $+1$ : 10; perinuclear antineutrophil cytoplasmic antibodies (p-ANCA), cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA) and anticyclic lipoprotein antibodies (ACA) within the physiologic range. Autoantibodies against basement membrane zone (ABMZ) were not detected. Lung function test: normal spirometry finding, transfer factor for carbon monoxide (CO) and transfer coefficient were slightly reduced; oxygen saturation was 96%.

Multislice scanning (MSCT) of the chest revealed changes of partly honeycomb appearance in the lungs bilaterally and in the upper and lower lobe, in favor of fibrosis, in particular mediastinal lymph nodes up to 1 cm in diameter at the level of tracheal carina in the right hilus and below the aortic arch (Figure 4). Bronchoscopy was planned but refused by the patient. Radiologic (X-ray) findings on paranasal sinuses revealed thickened lining of the left frontal and maxillary sinuses (Figure 5). Ultrasound examination of the heart, abdomen and pelvis revealed normal findings.
Skin biopsy was taken and histopathologic analysis revealed infiltrate of lymphocytes, many neutrophils and eosinophils around capillaries and collagen fibers between the upper dermis, with clustered eosinophils at some places; the presence of cariorexic debris and fresh erythrocytes extravasated; periodic acid schiff (PAS) staining revealed segments of the microvascular wall space with fibrinoid necrosis (Figure 6a and b). Deposits of immunoreactants were not found on direct immunofluorescence (DIF) examination of the skin specimen. Neurologic examination revealed sensorimotor neuropathy.

Considering the changes in the lungs, asthma, hyperesinophilia, thickened mucosa of frontal sinus and sensorimotor neuropathy (consulted specialists were rheumatologist, neurologist, pulmologist, otolaryngologist, hematologist and infectologist) diagnosis of CSS was established and the therapy with methylprednisolone (60 mg daily iv, with decreasing doses), pulse dose of cyclophosphamide (800 mg) once monthly, was started, with vitamine B complex and tocopherol recommended by neurologist, bronchodilators recommended by pulmologist and local therapy with momethasone furot 0.1% ointment once daily until skin changes resolved; then the patient was referred to the rheumatologist.

Discussion

Churg and Strauss first described this disorder in 1951 when they reviewed 13 autopsy cases that were previously classified as polyarteritis nodosa. These cases were atypical in that asthma and eosinophilia preceded the systemic vasculitis. They named the syndrome “allergic angiitis and allergic granulomatosis”, also known as CSS. CSS is an allergic granulomatous angiitis; a very rare disease of small and medium arteries and veins, associated with p-ANCA. p-ANCA directed predominantly against a myeloperoxidase was initially reported in as many as 75–80% of patients with CSS, but in one study showed that only 13% had positive p-ANCA findings. Allergic granulomatosis and angiitis is a disorder characterized by extravascular granulomas, hypereosinophilia, and pulmonary and systemic small-vessel vasculitis. The American College of Rheumatology (ACR) has proposed 6 criteria for the diagnosis of CSS. The presence of 4 or more criteria are enough for diagnosing CSS. These criteria include: asthma, eosinophilia (> 10% in peripheral blood), paranasal sinusitis, pulmonary infiltrates, histological evidence of vasculitis with extravascular eosinophils, and mononeuritis multiplex or polyneuropathy. The differential diagnosis of CSS includes at first place diseases associated with pulmonary infiltrates and eosinophilia (eosinophilic pneumonia, eosinophilic granuloma, infections and Wegener granulomatosis). Corticosteroids are the mainstay of treatment in CSS. The addition of other medications...
(cytotoxic agents) may be necessary in cases of life- or organ-threatening vasculitis. The survival rate of CSS ranges from 68% to 100% at 5 years. 

Cutaneous findings occur in 60% of CSS patients, and include palpable purpura, subcutaneous nodules (typically on the scalp or extremities), and less often, vesicles, urticaria, livedo reticularis, retiform purpura and papulonecrotic lesions. They usually present on the limb surfaces, but can affect any part of the body. In our patient, few vesicles, vesiculopustules, purpuric macules, papules and petechiae on the skin of her hands, feet, extremities and trunk were found. In differential diagnosis autoimmune bullous dermatosis was observed, but immunopathology test did not approve it. Also, in hypereosinophilic syndrome, skin pattern is angioedematous with urticaria and dermographismus, erythematous pruritic papules, plaques and nodules, less common erythoderma and erythema annulare, but skin changes and thickened mucosa of frontal sinus of our patient with the absence of severe cardiac and neurologic manifestations (embolic or thrombotic), which are usual in primary hypereosinophilic syndrome, made clinical distinction. In our patient, skin changes were insufficient for making diagnosis by clinical examination, but histopathologic finding of skin specimen with perivascular eosinophils confirmed diagnosis of CSS cutaneous manifestation. The changes in the lungs, asthma, hypereosinophilia, thickened mucosa of frontal sinus, sensorimotor neuropathy and skin lesions established diagnosis of CSS.

**Conclusion**

Despite long-standing pulmonary symptoms and laboratory findings of eosinophilia, the appearance of skin changes raised suspicion of possible CSS. Skin changes correspond to changes in this syndrome have been described in the literature.

**REFERENCES**

1. Marzano AV, Vezzoli P, Berti E. Skin involvement in cutaneous and systemic vasculitis. Autoimmun Rev 2013; 12(4): 467–76.

2. Cox NH, Jorizzo JL, Bourke JF, Savage CO. Vasculitis neutrophilic dermatoses and related disorders. In: Burns I, Breathnach S, Cox N, Griffiths CC, editors. Rook’s textbook of dermatology. Oxford: Wiley-Blackwell; 2010. p. 2360–454.

3. Ljote F, Cohen P, Guillemin L. Polyarteritis nodosa, microscopic polyangiitis and Churg-Strauss syndrome. Lupus 1998; 7(4): 238–58.

4. Gota CE, Mandell BF. Systemic necrotizing vasculitis. In: Wolff K, Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Leffell DJ, editors. Fitzpatrick’s Dermatology in General Medicine. New York: McGraw Hill; 2008. p. 1606–16.

5. Himmisch B, Eikens S, Caronk E, Gross WL. Update on the pathogenesis of Churg-Strauss syndrome. Clin Exp Rheumatol 2003; 21(6 Suppl 32): 69–7.

6. Grau RG. Churg-Strauss syndrome: 2005-2008 update. Curr Rheumatol Rep 2008; 10(6): 453–8.

7. Masi AT, Hunder GG, Lie JT, Michel BA, Bloch DA, Arend WP, et al. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). Arthritis Rheum 1990; 33(8): 1094–100.

8. Phillip R, Lugmani R. Mortality in systemic vasculitis: a systematic review. Clin Exp Rheumatol 2008; 26(5 Suppl 51): S94–104.

9. Chung L, Kea B, Fiorentino DF. Cutaneous vasculitis. In: Bolognia JL, Jorizzo JL, Rapini RP, editors. Dermatology. Philadelphia: Mosby Elsevier; 2008. p. 361–2.

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