

CHOREA IN A CHILD WITH
CHURG-STRAUSS SYNDROME

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Abstract

Introduction: Churg-Strauss syndrome (CSS) is a systemic granulomatous vasculitis rarely described in children, particularly associated with neurological involvement, exceptionally chorea. To our knowledge there are only 35 children and adolescent patients with CSS described in the literature. During a 25-year period 5283 patients were followed up at the Pediatric Rheumatology Unit of our University Hospital and only one (0.02%) presented CSS.

Case report: A 7-year-old boy suffered from severe asthma, eosinophilia, history of allergy, recurrent non-fixed pulmonary infiltrates, several nodular lesions in both lungs and maxillary sinusitis. Thoracic biopsy of the right lung revealed necrotizing extravascular eosinophilic infiltrates and the diagnosis of CSS was established. During the follow-up he had persistent vasculitis skin lesions and hemichorea. Despite the treatment with immunosuppressive drugs and intravenous immunoglobulin, he died because of pulmonary abscess and sepsis.

Discussion: A rare case of CSS with chorea was reported, reinforcing the possibility of this disease in children with asthma, allergic rhinitis, hypereosinophilia and cutaneous vasculitis.

Keywords: Churg-Strauss syndrome; Chorea; Eosinophilia; Asthma.

Introduction

Churg-Strauss syndrome (CSS) is a rare systemic granulomatous vasculitis of medium and small vessels, characterized by a long history of asthma, chronic allergic rhinitis and hypereosinophilia¹. This disease is very rare in the pediatric population and to our knowledge there are only 35 children and adolescent patients described in the literature²⁻⁴. It is important to note that peripheral neurological involvement occurs in 37% of pediatric CSS, particularly mononeuritis multiplex²⁻⁴. In addition, other neurologic manifestations are infrequently described in children and adult patients^{5,6}.

From January 1983 to December 2008, 5283 patients were followed up at the Pediatric Rheumatology Unit of Instituto da Criança da Faculdade de Medicina da Universidade de São Paulo. Only one (0.02%) of them fulfilled criteria for CSS according to the American College of Rheumatology (ACR)¹. We described this patient's case, which presented hemichorea and died despite the treatment. The Local Ethical Committee of our University Hospital approved this study.

Case Report

A 10-month-old male infant was born of normal pregnancy and had history of allergy with recurrent wheezing ever since 4 months of age. He gradually developed recurrent infections and respiratory allergy of the upper and lower respiratory tract (chronic maxillary sinusitis, allergic rhinitis, tonsillitis and pneumonia) and progressive obstructive airway symptoms (asthma) that demanded innumerable hospitalizations. The asthma was treated with inhalation of beclomethasone propionate (750 µg daily). No consanguinity was observed, and no family history of asthma and adverse events after vaccination were found. At 6-years-old, he had anorexia, loss of 20% of total body weight, failure

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Figure 1. Chest x-ray showed pulmonary infiltrates in both lungs.

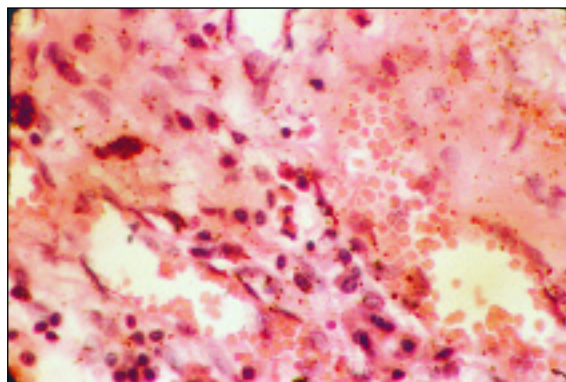


Figure 2. Biopsy of the right lung showing accumulation of extravascular eosinophilic infiltrates.

to thrive, fever, dyspnea and wheezing since 10 months of age. The head circumference was on the percentile 2. The laboratory exams showed hemoglobin of 7.4 g/dL (normochromic and normocytic chronic anemia), white blood cell count of 28.100 cells/mm³ (69% eosinophilia) and platelet count of 350.000 cells/mm³. Erythrocyte sedimentation rate (ESR) was high (54 mm 1st/hour), as C-reactive protein (CRP) levels were 35 mg/dL. The serum complement (C3 and C4), urinalysis, renal and liver function tests were normal. Serum IgE detected by solid phase radioimmunoassay was elevated (2.500 UI/mL) and allergic tests for inhalants and food antigens were not reactive. Serologies were negatives: hepatitis A and B, mononucleosis, toxoplasmosis and rubella. Antinuclear antibodies, antineutrophilic cytoplasmic antibody, anti-double stranded DNA antibody, anticardiolipin antibodies, lupus anticoagulant and rheumatoid factor were all negative. A chest x-ray showed non-fixed pulmonary infiltrates (Figure 1) and a chest computed tomography (CT) revealed several nodular lesions in both lungs. Pulmonary function tests were not performed. Transthoracic biopsy of the right lung revealed necrotizing extravascular eosinophilic infiltrates (Figure 2). Stool examinations for parasites were negative. At that moment, the diagnosis of CSS was established according to 5 of 6 ACR criteria for this disease (asthma, eosinophilia, history of allergy, non-fixed pulmonary infiltrates, maxillary sinusitis and biopsy with extravascular eosinophils)¹. Prednisone (2.0 mg/kg/day) was administered for two weeks, with rapid improvement within one month (ESR 18 mm 1st/hour and CRP 4 mg/dL) and the dosage was progressively decreased to 10 mg/day. At 7-year-old, he was hos-

pitalized with bilateral otitis, acute pneumonia, persistent vasculitis skin lesions (palpable purpura and subcutaneous nodules) in lower limbs, with increased ESR 76 mm 1st/hour and CRP 52 mg/dL. At that time, the patient developed persistent involuntary movements in left upper and lower limbs compatible with hemichorea. The symptoms did not disappear during sleep. Neurologic examination revealed hypotonia, motor impersistence and choreic movements of left upper and lower limbs. This patient did not present any pyramidal sign. Cerebrospinal fluid, electroencephalogram and echocardiography were normal. Antistreptolysin O titers were also normal (200 UI) and throat culture for group A Streptococcal infection was negative. A magnetic resonance imaging (MRI) of the brain revealed bilateral lesions isointense on T1-weighted and hyperintense on FLAIR and T2-weighted at the subcortical white matter and semioval center suggesting gliosis, associated to cortical/subcortical atrophy with non-hypertensive dilatation of the lateral brain ventricles (Figure 3). The patient underwent for three consecutive days intravenous pulse therapy with methylprednisolone (30mg/kg/day) in combination with intravenous cyclophosphamide (500 mg/m²/month) on the third day. These drugs were administered for 3 consecutive months and cutaneous vasculitis improved. However, the choreic movements improved only after one dose of intravenous immunoglobulin (2g/kg) combined with third pulse therapy with methylprednisolone and intravenous cyclophosphamide. At the age of 7 years and 3 months, he was hospitalized in the intensive care unit (ICU) due to pulmonary abscess and sepsis by *Citrobacter freundii*. Despite the precocious use of antibio-

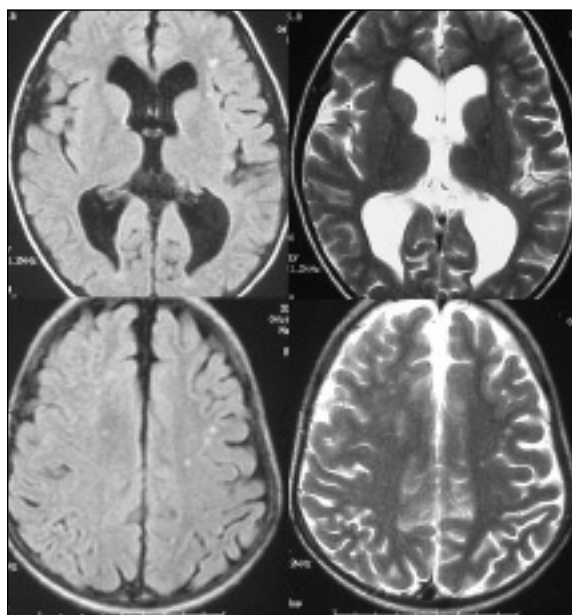


Figure 3. Magnetic resonance imaging (MRI) of the brain revealed on FLAIR and T2-weighted axial resonance imaging, lesion at the subcortical white matter and semioval center suggesting gliosis, associated to cortical/subcortical atrophy with non-hypertensive dilation of the lateral brain ventricles.

tics (vancomycin and ceftazidime) in ICU, he died after two weeks.

Discussion

A rare prevalence of CSS in children was observed in our population of a tertiary Pediatric University Hospital for a period of 25 years. Moreover, this is the first case reporting chorea in a CSS patient fulfilling the ACR criteria.

Primary vasculitis in children and adolescents are rare diseases and can involve the central and peripheral nervous system in the form of mono or polyneuropathies in polyarteritis nodosa⁷, cerebral vascular accident in Takayasu arteritis⁸ and Henoch-Schölein purpura as previously reported in our population⁹.

CSS is a primary vasculitis that has rarely been reported in children and adolescents and only 35 cases were described in the medical literature²⁻⁴. CSS occurred predominantly in girls with a male:female ratio of 1:1.5, mean age at diagnosis 12 years (2-18 years) and clinical manifestations that rarely started before one year of age, as it was

observed in our patient²⁻⁴. A clinical comparison between children and adult patients with CSS showed that pulmonary infiltrates and cardiomyopathy were frequent in children and multiplex mononeuritis and myalgias in adult population².

The usual presentation of this primary vasculitis includes fever, pulmonary infiltrates, sinusitis, skin lesions vasculitis, peripheral eosinophilia (generally higher than 1.500/mm³), elevation of acute phase reactants and hyper-IgE in a child who has had asthma². Histopathologic studies with eosinophilic infiltrates confirm vasculitis¹, as observed in this case.

It should be noted that the neurologic manifestations were reported in 36% of adult patients with CSS, especially multiple mononeuropathy and distal symmetric polyneuropathy. The vasculitis of CSS generally involves the vasa vasorum of the peripheral nerves. Radiculopathies, ischemic optic neuropathy and bilateral trigeminal neuropathy were rarely described in adults with CSS⁵. Neurologic involvement was described in 40% of children with CSS, particularly multiple mononeuropathy (35%) and orbital pseudotumor (3%)²⁻⁴. Interestingly, asthma preceding the onset of neurologic involvement was reported in all the adult patients with a mean duration of 6.7 years⁵. In the pediatric population, the occurrence of asthma before the diagnosis of CSS was evidenced in 91% of the patients, as in our CSS patient²⁻⁴.

Chorea is an extrapyramidal disorder, which can be isolated as observed in our patient, or associated with other neurological signs, such as pyramidal tract dysfunction. The most frequent etiology of acute choreiform movements in children and adolescents is post infectious, named rheumatic fever generally associated with movement improvement during sleep as it was previously described by our group¹⁰. In addition, the association of vasculitis, asthma and eosinophilia was not evidenced in rheumatic fever. Chorea can be also associated with other vasculitis and/or vasculopathy of central nervous system, specially neuro-Behçet's disease, antiphospholipid syndrome and systemic lupus erythematosus possible due to antineuronal and antiphospholipid antibodies^{11,12}.

In patients with CSS, chorea was described just in a 13-year-old girl with a probable CSS disease based on incomplete ACR criteria (3 out of 6: asthma, eosinophilia and sinus abnormalities). The MRI of the latter patient showed hyperintense in T2 images in globus pallidus and subcortical whi-

te matter⁶, but in ours, the only abnormality disclosed was only subcortical white matter and semioval center lesion and cortical/subcortical atrophy probably related to steroid therapy. The MRI was performed 2 days after the onset of chorea and before the beginning of intravenous cyclophosphamide. The MRI aspects observed herein suggest vasculitis in subcortical white matter.

The treatment of CSS includes high doses of corticosteroids. The use of immunosuppressive drugs and intravenous cyclophosphamide should be restricted to severe cases². Intravenous immunoglobulin was also administered in this patient, as it was previously used for leukocytoclastic vasculitis and giant cells arteritis in our pediatric population⁸⁻⁹. Moreover, intravenous immunoglobulin is a treatment option in patients with CSS with neuropathy¹³. Despite the treatment, this is a serious and life-threatening disease, with a mortality rate of 6/35 (17%) in the pediatric cases reported²⁻⁴. The most frequent causes of mortality in these patients are cardiac failure and intestinal perforation².

In conclusion, we report a rare case of CSS with chorea and we would like to reinforce the importance of the possibility of CSS diagnosis in children with asthma, allergic rhinitis, hypereosinophilia and cutaneous vasculitis.

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