

Churg-Strauss Syndrome in a Seven Year Old Boy-A Case Report

Abstract:

Churg-Strauss syndrome (CSS) is a vasculitis of small to medium sized vessels. This syndrome is known by a history of bronchial asthma with systemic necrotising vasculitis and peripheral blood hypereosinophilia. It is now called eosinophilic granulomatosis with polyangiitis (EGPA). This disease affects both genders and all age groups but it is very rare among children. CSS diagnosis is based on clinical findings such as asthma, eosinophilia, rhinosinusitis and signs of vasculitis in major organs. In cases which Steroids alone or in combination with other immunosuppressive agents are used as treatment, the outcome and long-term survival is usually satisfying. In comparison with other systemic vasculitis, the mortality rate of this syndrome is low.

The case that we report is a 7 year old boy who had a poorly controlled bronchial asthma since he was 3. Then he developed purpuric skin lesions, sinusitis, arthritis and weakness of limbs with symptoms of mononeuritis multiplex at the age of 7. After being admitted to our hospital, a series of studies including CBC-diff, chest X-Ray, paranasal sinus radiographies, brain MRI, nerve conduction study, spirometry and serological tests for autoantibodies, were performed and he was diagnosed as Churg-Strauss syndrome. Thereafter, he received regular corticosteroid therapy in combination with methotrexate and his symptoms were generally well-controlled with the beginning of the treatments. The clinical characteristics, diagnosis and management of CSS in children are also reviewed.

Keywords: Asthma, Churg-Strauss syndrom, Mononeuritis multiplex, vasculitis

Introduction:

Churg-Strauss syndrome (CSS), is a vasculitis that affects small to medium sized vessels and is described as “allergic granulomatosis and angiitis,”(1) or “eosinophilic granulomatosis with polyangiitis (EGPA)”(2). This syndrome is a vasculitis that is associated with anti-neutrophil cytoplasmic antibody (ANCA). The histopathologic findings of CSS are eosinophilic inflammation, extravascular granulomas and necrotizing vasculitis that affects multiple organs (3).

The main clinical feature of the disease is asthma and this problem happens in almost 90% of patients (3). The incidence rate of CSS is up to 67 per million among patients with asthma (4, 5). Because of the vasculitis that affects the central nervous system (CNS) or the epineurial vessels of peripheral nerves, neurological manifestations are common in these patients. Mononeuritis multiplex occurs in up to 76% of patients with CSS (3). Skin involvements are also common and occurs in about 30 to 50 % of patients and includes tender subcutaneous nodules, macular or popular erythematous rash, petechiae and palpable purpura (3). ANCA are positive in about 40% of patients (6,7).

American College of Rheumatology (ACR) has described six criteria for diagnosis of CSS, four or more criteria should be positive to be classified as having CSS. These criteria are: [1] asthma, [2] eosinophilia (more than 10% on differential white blood count), [3] mono- or polyneuropathy attributable to a systemic vasculitis, [4] migratory or transient pulmonary infiltration, [5] paranasal sinus abnormalities and [6] extravascular eosinophils on a biopsy including arteries, arterioles, or venules (8).

However CSS affects all age groups but it is a rare syndrome among children and could have different clinical presentations. This syndrome should be considered in any patient with poorly controlled asthma that receives moderate doses of inhaled corticosteroids as treatment (3).

Case presentation:

A seven-year-old boy was referred to our hospital with complaints of fever and rash which has been started two weeks before admission. Then he developed weakness of limbs and gait disturbance, with pain and swelling in the joints of hands and feet. During admission he had a fever up to 38.5 degree, with stable vital signs, normal heart and lung auscultation findings and normal abdominal examination. Widespread erythematous rash was observed as purpura, petechiae and hives with priority on the side of his leg. In joint examination we detected effusion and tenderness of wrists, ankles and knees. On neurologic examination there was Mononeuritis multiplex leading to gait disturbance as “foot slapping gait”. Distal muscle weakness of right upper limb and left lower limb, as well as right “wrist drop” and left “foot drop” were observed. Cerebellar test and cranial nerve examination were normal. He also had a history of asthma that had been poorly controlled with inhaled corticosteroid (ICS) since the age of 3.

In Complete blood count with differentiation (CBC-diff) test Eosinophil count was observed 1012(11%). Immunoglobulin E- levels (IgE), Erythrocyte sedimentation rate (ESR), and C - reactive protein levels (CRP) were markedly elevated. Serum chemistries and urine microscopy were performed to detect any evidence of renal involvement which were normal. ANCA , Anti - nuclear antibody (ANA) and Rheumatoid factor (RF) were negative. The results of laboratory examinations are shown in table 1.

As shown in figure 1, the chest x-ray showed hyperinflation of both lungs and flattening of diaphragm. The radiography of paranasal sinuses showed a thickness of the mucosa of the right maxillary sinus in paranasalsinus views, (as seen in figure 2).

He had normal Brain Magnetic Resonance Imaging (MRI), but his Spirometry showed severe reversible airflow obstruction. In Nerve conduction study, early stages of immune mediated process was highly suspected. Close observation was recommended.

According to clinical presentation of a poorly controlled asthma, mononeuritis multiplex, paranasal sinusitis and skin rash in addition to eosinophilia (more than 10% in CBC), the diagnosis of Churg-Strauss syndrome was suggested. Montelukast tablets (every night half of tablets) had been prescribed for his severe cough, about 2 weeks before admission. Corticosteroids pulse therapy with methylprednisolone was prescribed with the dose of 30 mg / kg daily for 3 days and then prednisolone tablet was started with the dose of 2 mg / kg daily and was tapered within 3 months. Methotrexate was started with dose of 15 mg / M² and tapered within 1 year.

Fortunately with the initiation of treatment, all symptoms resolved immediately and no adverse events were noted. After one and half year, he was asymptomatic in follow up with normal physical examination, and his spirometry findings had been significantly improved.

Discussion:

Churg -Strauss syndrome is a primary systemic vasculitis affecting small- and medium-sized vessels. The key features in these patients are asthma and severe eosinophilia that is presented with h. The pathogenesis of CSS may include damage in vascular and perivascular tissues by activated eosinophils that secretes enzymes directly(10, 11). The severe and sustained eosinophilia

observed in the blood and organs of patients with CSS is caused by chemokines such as eotaxin 3 (CCL26) (12).

Churg -Strauss syndrome usually occurs at the age between 14 and 75 years, with a mean age of 50 years. In a recent review Louthrenoo reported that CSS has been observed in children as young as 4 years (13).Wilkinson reported that although CSS is mostly observed in middle-aged individuals with asthma, it can develop in children too. (14). Also, Ozen suggested that physician knowledge of the clinical features of children with CSS can lead to an earlier diagnosis of the children with this disease (15). According to Lanham and coworkers, the disease is categorized into three phases (16). The prodromal phase, consisting of allergic disease, including allergic rhinitis, nasal polyposis, and asthma, this phase may last for years. The second phase is characterized by the peripheral blood and tissue eosinophilia that causes clinical presentations resemble to Loffler's syndrome, chronic eosinophilic pneumonia or eosinophilic gastroenteritis. Finally, the third phase is a life-threatening systemic vasculitis. The vasculitis phase may be presented with nonspecific constitutional symptoms and signs, especially fever, weight loss, and malaise, and lassitude. Usually 8 to 10 years are there between first and third phase of disease (16). In our presented case, this period of time was 4 years. He had asthma and was treated with ICS since 3 years old (phase1), But despite appropriate dose of medications,his symptoms were poorly controlled. At the age of 7 he was referred to our hospital with the manifestations of mononeuritis multiplex, arthritis and skin symptoms (phase 3).

Zwerina et al. had reported interesting findings in 33 cases with CSS. At the time of clinical presentation, most children had a history of asthma (91%) and sinusitis (77%).Although pleural effusion was rarely observed (12%), pulmonary involvement presenting as nonfixed infiltration was very common (85%) (17). The key features in these patients, were asthma and severe

eosinophilia in combination with vasculitic organ manifestations (17). In accordance with previous studies, our presented case had asthma, sinusitis as first phase and eosinophilia, mononeuritis multiplex, arthritis and skin symptoms as second and third phase. In contrast to other literatures pulmonary involvement such as infiltration or pleural effusion was not observed.

Reports of Churg-Strauss syndrome in the past, primarily focused on the incidence of this disorder in the general population(1,2). However, recent studies have examined the incidence of CSS in asthmatic populations, particularly in patients with resistant asthma who has received various forms of therapy. Increase in CSS cases was observed after taking the leukotriene receptor antagonists (18,19) . Wechsler and Drazen reported three patients with asthma who showed evidences of CSS after receiving Montelukast or Zafirlukast . They suggested that this vasculitis syndrome develops in patients who had an underlying eosinophilic disorder which was being suppressed by corticosteroid treatment .Symptoms and signs of CSS had been appeared with taking of leukotriene modifiers and reducing corticosteroids (19). The improvement of anti-asthmatic medications caused a better control on asthma symptoms that reduced the need of patients to oral corticosteroids (OCS) and as a result, more cases of CSS are unmasked and diagnosed (18,19). In consistent with previous studies, our presented case showed presentations of CSS vasculitis phase (e.g. mononeuritis multiplex, arthritis and skin involvement), two weeks after initiation of Montelukast.

Churg-Strauss syndrome is a form of vasculitis that is associated with ANCA (20). Comarmond C, et al performed a cohort study in a large population and have found that ANCAs are present in only about 40% of cases. They suggested that CSS has two clinical subsets or phenotypes: one that is an ANCA-associated process and mainly has the features of small-vessel vasculitis (such as glomerulonephritis and mononeuritis multiplex), and the other that is ANCA-negative and more related to eosinophilic tissue infiltration; this type predominantly leads to cardiopulmonary

manifestations and fever (21). In our patient findings confirmed that ANCA were negative and he had features of both ANCA- negative and ANCA-positive process. At presentation he had fever and mononeuritis multiplex in associated with other manifestations.

Cardiac involvement is relevant to advanced disease because terminal cardiac events have been reported in 50% of autopsy cases (22). Our patient did not have any cardiac manifestations, probably due to early stage of his disease. In the future he may develop cardiac involvement, so he should be kept under observation for the possible occurrence of this event. Zwerina J et al. reported that cardiorespiratory manifestations were seen more frequently in children, while peripheral nerve and musculoskeletal symptoms were less common (17). In contrast to this article, peripheral nerve and musculoskeletal involvements were observed in our patient but cardiorespiratory manifestations were not detected.

Mononeuritis multiplex is the most common type of neurologic manifestations. Peripheral nerve involvement can also be as the result of either vasculitis of vasa nervorum or perineural eosinophilic infiltrate (22,23). Numerous central nervous system involvements such as cerebrovascular diseases, cranial nerve palsy, convulsion and encephalopathy have been reported (24). In confirmation of previous studies, Mononeuritis multiplex was observed as the neurologic involvements in our presented case.

Gastrointestinal (GI) manifestations associated with CSS were reported in the latest studies (22, 23). Gastrointestinal tract involvement is common and usually appears in the vasculitic phase. Abdominal pain is the main manifestation. Multiple mucosal ulcers in the colon secondary to local ischemia have been described (25). An eosinophilic gastroenteritis with the presentation of bloody diarrhea may lead to intestinal perforation. Pancreatitis and cholecystitis, also have been

reported (26). In contrast with the previous studies, GI manifestations was not observed in our presented case.

Conclusion:

Churg-Strauss syndrome is a rare disease in children and manifestations of this disease depend on the age of the patient. CSS should be considered in every patient with poor controlled asthma who does not respond properly to moderate doses of inhaled corticosteroid. It should be considered especially when there are neurologic, dermatologic, GI or other organ involvements. Physicians should be aware of this disease because with early diagnosis and appropriate treatment, can lead to satisfactory improvement and decrease complications of the disease.

Acknowledgments:

Non.

Legends of table and figures:

Table 1. The laboratory finding of presenting patient

Fig1: Hyperinflation of both lungs and flattening of diaphragms are obvious

Fig2: Para-nasal sinuses radiographies: Mucosal thickening in the right maxillary sinus

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