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Childhood Churg-Strauss syndrome: report of a case

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Churg-Strauss syndrome (CSS) (allergic granulomatosis and angitis) is an uncommon form of systemic vasculitis, which is rare in children. It is characterized by peripheral blood hypereosinophilia, systemic necrotizing vasculitis, and a preceding history of bronchial asthma. We described a boy with initial presentation of poorly controlled bronchial asthma, allergic rhinitis, recurrent sinusitis and several episodes of hemoptysis since the age of 9. He then developed purpuric skin lesions, generalized soreness, and symptoms of mononeuritis multiplex at age 11. On admission to our hospital at the age of 12, he developed marked pericardial effusion. After a series of studies including chest computed tomography (CT), skin biopsy, nerve conduction study, and serological tests for autoantibodies, CSS was diagnosed. Thereafter, he received regular corticosteroid therapy, and his symptoms were generally well-controlled with occasional acute exacerbation. The clinical characteristics, diagnosis and management of CSS in children are also reviewed.

Key words: Churg-Strauss syndrome, children

Systemic vasculitis in children includes a wide variety of inflammatory disease entities and different etiologies. Autoimmune processes, infection, and malignancy can all be initiating factors. Churg-Strauss syndrome (CSS) or allergic granulomatosis and angiitis, originally described by Churg and Strauss in 1951 [1], is characterized by the development of hypereosinophilia and systemic necrotizing vasculitis with multiple organs involvement in patients with a previous history of asthma and allergic rhinitis. This widespread small artery and vein involvement [2,3] in CSS accounts for its varying clinical manifestations. Although several large series of studies of adult CSS have been reported [3-7], only 10 reported cases of childhood CSS had been reported prior to 1999 according to a review article by Louthrenoo *et al* [6]. Here we report an additional case of pediatric CSS.

Case Report

A 12-year-old boy had suffered from frequent asthmatic attacks since the age of 9 despite regular medication. At age 11, recurrent purulent nasal discharge developed, and paranasal sinusitis was diagnosed by skull roentgenogram and head computer tomography (CT).

He was admitted to a medical center in January 1999 because of an episode of dyspnea, hemoptysis and intermittent fever. Chest roentgenogram and CT disclosed interstitial infiltration with air-bronchogram predominantly over the right lower lung field and bilateral pleural effusion (Fig.1). The skull Water's view revealed opacification of the left maxillary sinus. A hemogram showed a hemoglobin of 14.5 g/dL and a white blood cell count of 20.5 x 10^9/L with 70% neutrophils, 7.5% lymphocytes, 20.5% eosinophils and 2% monocytes. The IgE was 1822 KU/L (normal range, below 150 KU/L). Chest CT revealed interstitial infiltration with air-bronchogram. Under the impression of acute exacerbation of bronchial asthma complicated with pneumonia and paranasal sinusitis, he received antibiotics and intravenous corticosteroid, and the symptoms improved. However, recurrent pulmonary infiltration persisted and he was admitted again 1 month later with the same symptoms and signs. Leukocytosis with eosinophil count up to 4096 x 10^9/L was still noticed. Right calf soreness and severe abdominal pain occurred during admission. Endoscopy was done and only duodenal mucosal erosion was detected. The respiratory symptoms improved again under prednisolone and antibiotic therapy.

One month later, maculopapular rash with some vesicular lesions over bilateral feet developed and then evolved to purpuric rash and spread to bilateral axilla and upper extremities. Several pustule-like lesions and nodules over the wrist were also observed. He was also disturbed by a sensation of numbness over the medial aspect of the left forearm and generalized migratory

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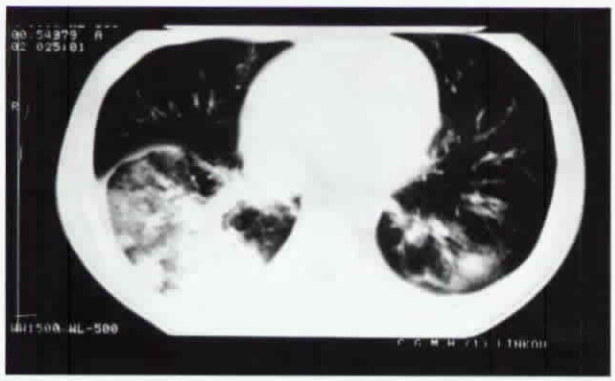

Fig.1. Chest CT demonstrates consolidation with air-bronchogram formation predominantly over right lower lung.

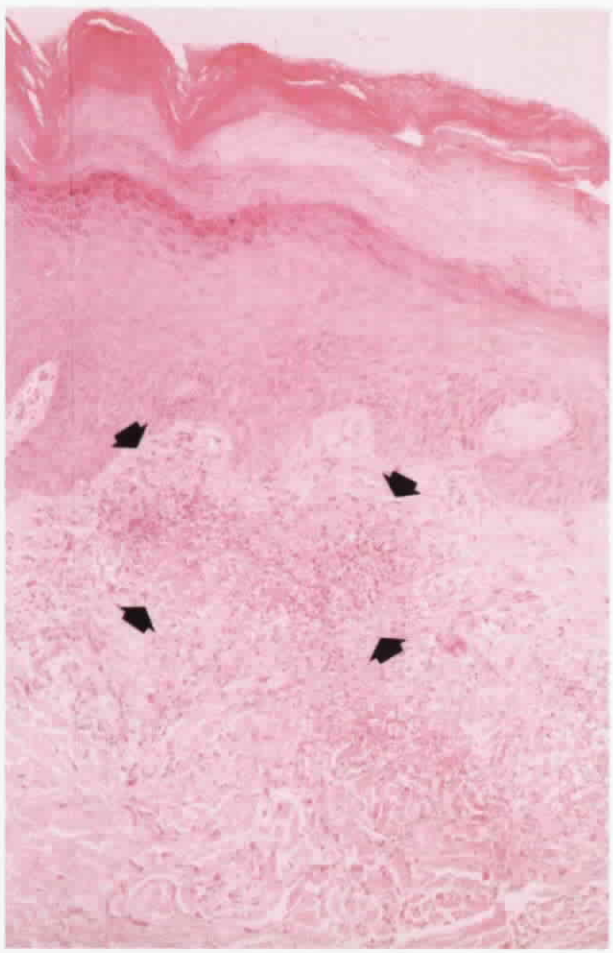

Fig.2. Histopathological picture of skin lesion showing extravascular granuloma (arrows) composed of palisaded histiocytes around degenerated collagen (H&E, original magnification x 100).

soreness, especially in back and lower legs, also disturbed him. Productive cough, hemoptysis, and occasional nasal bleeding persisted. He visited our emergency service in April 1999. On admission,

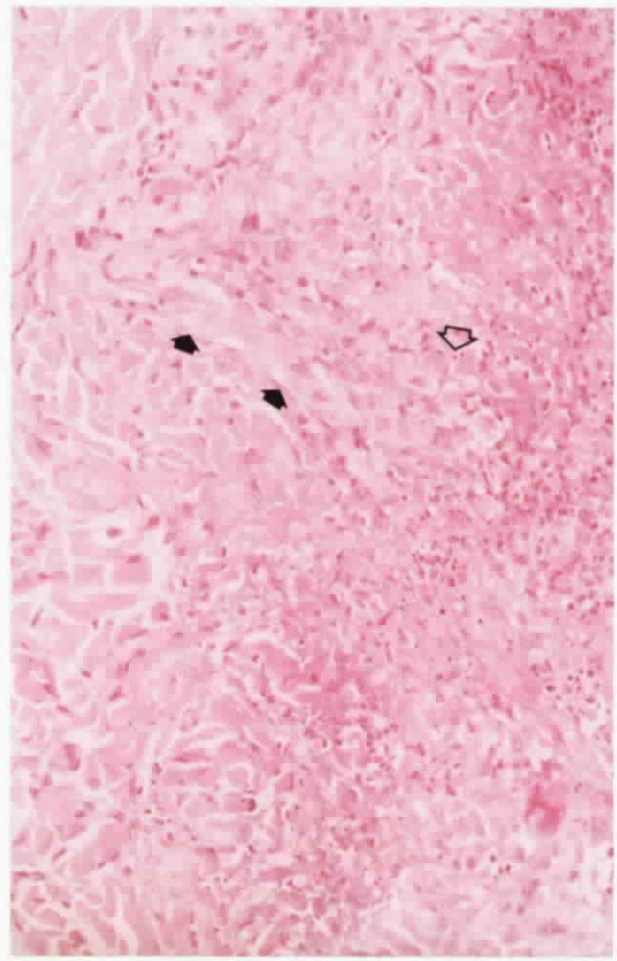

Fig.3. Histopathological picture showing leukocytoclastic vasculitis (solid arrows) with nuclear dust formation (hollow arrows) (H&E, original magnification x 400).

physical examination revealed multiple purpura and hyperpigmentation scars over bilateral feet and erupted interdigital vesicles over bilateral hands. Breathing sound was clear and no heart murmur was found. Neurological examination disclosed decreased light touch and pain sensation over the fourth and fifth fingers of the left hand and the first to fourth toes of the left foot. Decreased muscle power over the left hand and left foot dorsiflexion were also found. Chest roentgenogram revealed interstitial infiltration and cardiomegaly. Echocardiography disclosed pericardial effusion from 1.8 to 2.27 cm with thick and bright pericardium, and right ventricle diastolic dysfunction. The white blood cell count was 15.44 x 10^9/L with 25.5% eosinophils. Histopathology of skin biopsy showed leukocytoclastic vasculitis. P-ANCA (perinuclear-antineutrophil cytoplasmic antibody) was positive. Nerve conduction velocity study showed left ulnar and sural nerve neuropathy, which was compatible

with mononeuritis multiplex. Under the impression of CSS with impending cardiac tamponade, methylprednisolone pulse therapy was started. Pericarditis subsided echocardiographically and another hemogram revealed a dramatic drop in eosinophil count. He was discharged in improved status and kept on low dose oral prednisolone and inhaled corticosteroid. All of his symptoms were under control except for occasional asthmatic attacks.

Six months after discharge, pea-sized nodules and vesicles over hands and feet developed again and he complained of recurrence of the previous peripheral neuropathy and attacks of dyspnea and severe cough. Chest auscultation revealed diffuse wheezing. Repeated chest CT showed emphysematous change and an ill-defined soft tissue density in the left lung. Skin biopsy of the nodule-like vesicle revealed extravascular necrotizing granuloma and leukocytoclastic vasculitis (Figs. 2,3). Dyspnea and skin rash subsided gradually with intravenous corticosteroid and supportive management. This patient was then followed up in our out patient clinic after he was discharged.

Discussion

In 1951, Churg and Strauss reported a group of 13 patients developing severe asthma, fever, hyper-eosinophilia, followed by symptoms of systemic vasculitis with a terminal fatal illness involving multiple organs 3 months to 5 years later. From the 13 patients, a histopathologic entity including tissue infiltration by eosinophils, necrotizing vasculitis, and extravascular granuloma was first described [1]. While the clinical features of adult CSS have been well illustrated [3-7], the features of childhood CSS are less clear [6]. CSS typically develops in male patients, with the age distribution was mostly from 14 to 74 years old [3-5]. From a series of 16 patients and a review of another 138 patients reported in the literature, Lanham *et al* proposed a diagnostic criteria for CSS including asthma, peripheral eosinophil counts in excess of 1.5×10^9/L, and systemic vasculitis involving two or more extrapulmonary organs [4].

The typical prodromal phase of CCS is characterized by late-onset asthma preceded by allergic rhinitis in patients usually without family atopic history. A second phase of tissue and peripheral eosinophilia with recurrent pulmonary infiltration or eosinophilic gastroenteritis then follows. The third phase is characterized by systemic vasculitis with multiple organs involvement including pulmonary, cutaneous, musculoskeletal systemic, central and peripheral nervous system, gastrointestinal and renal disease [4-6]. The first phase usually lasts for 3 to 10 years before the development of systemic vasculitis. In our patient, the duration from initial asthma to recurrent pulmonary infiltration was about 3 years, with subsequent rapid progression to fulminant systemic vasculitis. All of the clinical characteristics (asthma, eosinophilia, mononeuropathy multiplex , non-fixed pulmonary infiltrates, and paranasal sinusitis) of our patient fulfilled the diagnostic criteria for CSS proposed in 1990 by the American College of Rheumatology (ACR). The presence of four or more of these six criteria yielded a diagnostic sensitivity of 85% and a specificity of 99.7% [7].

Pulmonary disease is a central feature of CSS and presents with Löffler syndrome, transitory patchy pulmonary infiltrates, nodular infiltrates, or pleural effusion, which often antedate and coexist with the systemic vasculitis [3-6,8]. Asthma develops in all patients and is preceded or sometimes develops concomitantly with the onset of systemic vasculitis [4-6]. Although recurrent asthma attacks usually complicate the clinical course, only the symptoms of systemic vasculitis are representive of acute disease exacerbation [5]. In our patient, initial recurrent patchy and interstitial pulmonary infiltrates both heralded all the other clinical symptoms of systemic vasculitis. In addition, a soft-tissue density lesion was disclosed on chest CT during the second relapse of systemic vasculitis with acute exacerbation of asthma.

Our patient had typical cutaneous manifestations including palpable purpura, skin nodules, urticaria rash, and other rarely reported skins lesion such as finger tip vesicles, infiltrated papules, and aseptic pustules [4,5, 9]. The histopathological findings of skin biopsy included leukocytoclastic vasculitis and extravascular necrotizing granuloma were found in this patient. The three major histopathologic features of eosinophils infiltration, necrotizing vasculitis and extravascular granuloma mentioned by Churg and Strauss rarely coexist temporally and spatially, and are only found together in a minority of CSS patients [4].

Pericardial effusion with impending cardiac tamponade was another striking finding in our patient. Methylprednisolone pulse therapy was initially given for this critical condition, and the pericarditis improved dramatically. Under regular oral corticosteroid therapy, cardiac complications did not recur. Cardiac manifestations of CSS include acute pericarditis, constrictive pericarditis, and myocardial infarction, and accounts for the majority of mortality (45-48%) in CSS [4,5]. In a review of 10 patients with cardiac manifestations of CSS, Harvey *et al* found six patients

with pericardial disease and nine patients with myocardial disease. Only one of the patients died of congestive heart failure. Most of the patients responded well to oral prednisolone [10]. When such cardiac complications develop, early initiation of corticosteroid therapy is life-saving.

The major manifestation of neurological involvement in CSS is mononeuritis multiplex, as was found in our patient. Cranial nerve palsies develop infrequently [4,5,11-13]. The reported incidence of neurologic disease in CSS has ranged from 62% to 66% [4,11]. Typical pathologic findings includes epineurial necrotizing vasculitis and lymphocyte or eosinophil infiltration [12]. There was no evidence of renal involvement in our patient. Renal disease in CSS is usually benign and rarely progresses to renal failure [3-5]. In their review literature, Louthrenoo *et al* found two documented cases of renal disease and another two with proteinuria among 10 reported pediatric patients [6].

The diagnosis of CSS is mainly based on clinical features and other supportive information including histopathological and imaging studies. In our patient, additional serologic evidence was antineutrophil cytoplasmic antibody (ANCA). ANCA is a group of autoantibodies against various constituents of polymorphonuclear leukocytes, and has been associated with several vasculitis syndromes such as Wegener's granulomatosis, microscopic polyarteritis, drug induced vasculitis, and CSS [2,14]. According to the series of Guillevin *et al*, ANCA was detected in 47.6% patients with CSS, with a perinuclear fluorescence pattern in 15, cytoplasmic in one and unspecified in four [5].

Patients with CSS usually respond well to corticosteroid therapy, and survival was rare in the presteroid era. The acute exacerbation of the vasculitic phase usually requires treatment with high doses of steroids for several weeks [3,4]. Several trials including cyclophosphamide, plasma exchange, and azathioprine have been reported useful in controlling disease progression or reducing relapse [16].

In summary, the clinical picture of our patient was typical for CSS. The presentation of poor control asthma and other vasculitis symptoms lead to the final diagnosis. A five-factor score determining the poor prognosis of CSS as described by Guillevin *et al* includes renal failure, severe proteinuria, severe gastrointestinal involvement, cardiomyopathy and central nervous system involvement [16]. Short duration from the onset of asthma to the onset of systemic vasculitis was also another poor prognostic factor. Considering the relapsing nature of CSS, further close follow-up the clinical course of our patient was mandatory.

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