Churg Strauss Syndrome after Polypectomy in Asthmatic and Allergic Patients

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Received: 14 June 2008; Received in revised form: 30 September 2008; Accepted: 23 November 2008

ABSTRACT

Churg Strauss Syndrome (CSS) is a form of primary vasculitis that is characterized by severe eosinophilia and often granulomatous inflammation as well as history of asthma or allergy. Previously, the association between cysteinyl leukotrien receptor antagonists (LTRAs), corticosteroid withdrawal or a sudden change in its used method and CSS had been established.

We report three cases that have been referred because of dyspnea, wheezing and cough with a history of allergic rhinitis and nasal polypectomy. After polypectomy, disseminated skin purpuric rashes appeared on their forelegs, abdomen and all of them had experienced neuropathic signs in their extremities. Clinical findings, marked eosinophilia in blood and skin biopsies finally led to the diagnosis of CSS. The patients have been free of symptoms after receiving prednisolone; routine examinations and blood tests have rended regular results.

Here, we report a probable occurrence of an association between nasal polypectomy and CSS on the basis of our findings. Further, extended researches are required to establish this correlation.

Key words: Allergic angiitis; Bronchial asthma vasculitis, Churg Strauss; Rhinitis

INTRODUCTION

Allergic angiitis and granulomatosis, Churg Strauss syndrome (CSS), is a rare combination characterized by eosinophilia and systemic vasculitis of the small arteries and veins in patients with asthma and/or allergic rhinitis.^{1.2} The pathogenesis of CSS has not been clarified, but it involves autoimmune mechanisms in which leukocytes and endothelial cells play a role. It may mimic other autoimmune diseases like Wegener Granulomatosis (WG).³ Like other types of multisystemic diseases, CSS involves variable organs including lungs, skin, nerves and gastrointestinal tract.⁴ The clinical presentation depends on the organ affected. The most prominent symptoms and signs are those related to pulmonary, cardiac, dermatologic, renal, and peripheral nerve involvement.⁴ The diagnosis of CSS can be achieved by a clinical examination accompanied with laboratory studies, especially antineutrophil cytoplasmic antibodies (ANCA) and imaging studies

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such as chest x ray and CT scan, in combination with histologic findings. According to published reports, treatment of patients with asthma with cysteinyl leukotriene receptor antagonists (LTRAs).^{5,6} and also corticosteroid withdrawal or sudden change of oral steroid to inhaler, have been associated with the development of CSS.^{3,7} Dourakis et al. and Sirbu et al. have indicated that CSS had occurred in patients with a history of nasal polypectomy.^{10,11} To our knowledge, no association has yet been detected between nasal polypectomy and CSS.

Here, we report three cases of asthma and allergic rhinitis that after nasal polypectomy, had experienced skin purpuric lesions and peripheral neuropathic signs which finally led to the diagnosis of CSS. In the present report, we raise the notion of whether a probable association exists between nasal polypectomy and CSS.

CASE REPORTS

Case 1

A 35-year-old man was admitted to *Masih Daneshvari Hospital (NRITLD)* with dyspnea, wheezing, cough and also skin rashes on his forelegs. He had a twelve-year history of bronchial asthma and allergic rhinitis and a one-week history of nasal polypectomy. Before admission the patient was under therapy with inhaled bronchodilator, 5 mg oral prednisolone per day, and beclomethasone nasal spray.

Physical examination demonstrated skin purpuric lesions on his forelegs. Laboratory report studies revealed a high white blood cell count (WBC) 12600/mm³ with an eosinophil count of 12%, platelet count (Plt) 256000/mm³ and erythrocyte sedimentation rate (ESR) of 42 mm/hr. A chest x ray showed bilateral infiltration. On the third hospital day, he was affected by left foot numbness and weakness and also right foot drop.

Laboratory indices for autoimmune disease were absent. Electromyography (EMG) and nerve conduction studies of lower extremities revealed moderate neuropathy. According to these findings, diagnosis of CSS could be established; therefore, methyl prednisolone pulse therapy at a dose of 1 gr was started and continued for three days. Then the patient was set on oral prednisolone 40 mg/daily and azathioprine 50mg/daily, the former tapered within four weeks. He was symptom free one month after discharge from hospital.

Case 2

The patient was a 48-year-old farmer. He was referred to our center (NRITLD) because of exacerbation of wheezing, dyspnea and cough. He had several years history of wheezing, allergic rhinitis and one month history of nasal polypectomy. Before hospitalization, he just used salbutamole spray from time to time.

After surgery, skin purpuric rashes had appeared on his chest and abdomen. In laboratory tests, WBC was 7400/mm³ with an eosinophilic count of 6%, platelet count was 380000/mm³, and coagulation tests were normal. A chest x ray showed no signs of pulmonary disease. Treatment with oral prednisolone at a dose of 60 mg per day and inhaled bronchodilator was prescribed and skin biopsy of rashes was done. The biopsy revealed vasculitis with small vessel granulomatosis. Two weeks later, during tapering off prednisolone, he suffered from right foot tingling and pain. EMG showed lower extremities' neuropathy.

These findings raised the suspicion of CSS therefore, the patient was switched over to 60 mg oral prednisolone per day, and after a few days he was set on a tapering dose. Three weeks later, he was fully recovered.

Case 3

The patient was a 28-year-old man, with a 3-year history of allergic rhinitis and frequent otitis. He was hospitalized because of dyspnea, wheezing and coughs. He had a year and a week history of polypectomy. Before his admission, 100mg/day hydrocortisone was injected for him for three days but no improvement was seen.

After hospitalization, treatment with 60 mg oral prednisolone per day was started, and he improved. On the sixth hospital day, skin purpuric lesions on his abdomen and forelegs accompanied with extremity swelling and tingling, appeared. Laboratory indices for autoimmune and coagulation diseases were absent. Eosinophilia was detected in his laboratory tests. His chest radiogragh was normal. The biopsy of skin showed vasculitis accompanied with eosinophilic infiltration near the vessels. These findings led to the possible development of CSS. Then he received a course of pulse therapy with cyclophosphamide (1 gr) and oral prednisolone (60 mg/daily). One week after treatment, he was discharged with oral prednisolone (30mg/d). Two weeks later he was asymptomatic (Table 1).

Churg Strauss Syndrome after Polypectomy

Case	Age (years)	Gender	Symptoms	History of Asthma & Allergy	Time interval between nasal polypectomy & CSS diagnosis	New symptoms after hospitalization	Treatment
1	35	Male	Dyspnea, Wheezing, Cough, Skin rashes on his forelegs	A-12-year history	<u>1</u> week	Left foot numbness & right foot drop	Methyl orednisolone Pulse therapy (1gr for 3 days) Oral prednisolone (40mg/daily) Azathioprine (50mg/daily)
2	48	Male	Exacerbation of wheezing, dyspnea, cough,skin purpuric rashes on chest & abdomen	Several year history	<u>1</u> month	Right foot tingling & pain	Oral prednisolone (60mg/daily)
3	28	Male	Dyspnea.wheezi ng,cough	A-3-year history	<u>1</u> year & <u>1</u> week	Skin purpuric lesions on abdomen & forelegs, extremity swelling & tingling	Cyclophosphamide Pulse therapy (1 gr) Oral prednisolone (60mg/daily)

Table 1. Summary of reports of the three cases.

 Table 2. Laboratory tests of the three cases

Case number	Age (Year)	White blood cell count (WBC)	Eosinophil count	Platelet count	Chest x ray	Biopsy
1	35	12600/mm ³	12%	256000/mm ³	Bilateral infiltration	_
2	48	7400/mm ³	6%	380000/mm ³	Normal	vasculitis with small vessel granulomatosis
3	28	10400/mm ³	7%	300000/mm ³	Normal	vasculitis accompanied with eosinophilic infiltration near the vessels

DISCUSSION

CSS is an eosinophil associated, small vessel granulomatous vasculitis, characterized by late onset asthma and/or allergy, eosinophilia, upper airway disorder and clinical manifestations of systemic vasculitis.^{8,9} It may mimic other autoimmune diseases like Wegener Granulomatosis (WG).³ CSS has been recognized in patients who were treated with cysteinyl leukotriene receptor antagonists and weaned off systemic corticosteroids.^{3,7} Physical examination in

combination with laboratory studies, imaging studies, and histologic findings are important to lead to CSS diagnosis. The patients discussed in this report were admitted because of dyspnea, wheezing and cough exacerbation. They all suffered from allergic rhinitis and/or asthma and they all had a history of nasal polypectomy. After nasal polypectomy, they developed disseminated purpuric rashes and extremity neuropathy. In these cases laboratory indices showed no findings of coagulation and autoimmune diseases. Eosinophilia was observed in all 3 cases. Electromyography (EMG) and nerve conduction studies in all of them revealed neuropathy due to neuro-axonal conductive disorders. Skin biopsy revealed vasculitis with eosinophil infiltration near the vessels and small vessel granulomatosis. These findings raised the diagnosis of CSS therefore we set all of them on prednisolone and after a few days, symptoms were relieved and clinical examinations, imaging studies and laboratory tests returned to normal.

These findings raise the question of whether a correlation between CSS and nasal polypectomy exists. In the two articles, development of CSS after polypectomy have been explained regardless of their association.^{10,11}

According to the articles and other findings, we have concluded that nasal polypectomy can unmask CSS in patients who have a history of asthma or allergy on the basis of the following hypothesis:

1) Nasal polypectomy and other surgeries increase cytokines as tumor necrosis factors (TNFs), interleukins (ILs) and interferones (IFN),^{12,13} thus, immune regulatory disorders such as CSS can appear.

2) Colonization by microorganisms, mainly staphylococci, plays an important role in inducing formation of specific IgE and stimulation of IL-5 production.¹⁴ IL-5 is one of the essential survival factors for human eosinophils.^{15,16} According to presence of microorganisms in nasal cavity in patients with allergic rhinitis,^{17,18} we have raised the notion that nasal polypectomy can predispose the nasal cavity to colonization of staphylococci stimulating hyper responsiveness to antigens of these microorganisms leading to CSS.¹⁹

3) Nasal polyposis in the setting of allergic asthma increases leukotrien C4 (LTC4) synthesis and causes overproduction of cysteinyl leukotriens (Cys-LTs) leading to bronchoconstriction,^{20,24,25} thus, probably, nasal polypectomy can decrease the release of Cys-LTs such as LTRAs and lead to CSS manifestation

4) CSS may be a T helper type 2 (Th2) mediated disease,¹⁹ because of releasing Th2 cytokines such as IL-5, the most potent stimulator of eosinophil production and functional of mature eosinophils which play an important role in CSS.²¹ Nasal polypectomy increases Th2, therefore it can develop CSS.¹³

5) Some studies have indicated that a large number of patients who suffered from asthma and got improved with treatment were then able to diminish their systemic steroid therapy therefore, CSS had been unmasked by weaning off steroid,³ also nasal polypectomy associate with asthma improvement.^{22,23,26,27} Thus, on the basis of these reports a correlation between nasal polypectomy and CSS manifestation should be considered.

Based on this data, besides treatment with LTRAs and systemic steroid withdrawal, nasal polypectomy should be considered as a cause of CSS development in asthmatic and allergic patients, hence, patients with a history of asthma or allergy, should be monitored and closely observed for CSS manifestations after nasal polypectomy.

To our knowledge, no correlation has been yet detected between nasal polypectomy and CSS development.

Dourakis et al. and Sirbu et al. have just pointed to the development of CSS after nasal polypectomy^{10,11} but they have explained no association between them.

In this report, on the basis of our findings and other studies, we have raised the idea that CSS will be unmasked after nasal polypectomy. One of the most important limitations of this hypothesis is the small number of patients. Also, lack of evaluation of the role of chemical mediators in the development of CSS is another limitation of the present study.

We offered a variety of hypothesis to explain the possibility of high prevalence of CSS after nasal polypectomy but more investigations are needed to confirm it.

CSS is a form of primary vasculitis in patients with asthma or allergic rhinitis. Several cases of CSS have been recognized in patients treated with LTRAs and weaned off systemic steroids. According to our findings, CSS seems to develop after nasal polypectomy; however more investigations should be done.

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