

# Pulmonary manifestation in churg-strauss syndrome: clinical case

## Abstract

**Aims:** Although diffuse pulmonary disorders are very common in daily practice the main disease mechanism in each case commonly remains undetermined. Systemic inflammatory diseases preferably ANCA-associated vasculitis could be one of the possible causes for respiratory system affection. In this report we present typical clinical case of pulmonary manifestation in the form of ANCA vasculitis known as Churg-Strauss syndrome.

**Methods and results:** Clinical data obtained from 54 years old pts who had been managed for a long period due to asthma were analyzed in term to verify the diagnosis of systemic vasculitis. Further investigations including specific immunologic tests were performed, and there results confirmed the autoimmune nature of lung affection. Diagnosis of Churg-Strauss polyangiitis (a type of ANCA-associated systemic vasculitis) was established on the basis of patient complaints, clinical picture of the disease, and obtained laboratory findings. Rational treatment with glucocorticoid and cyclophosphamide was effective in systemic and pulmonary symptoms abolishing.

**Conclusion:** In case of asthma associated with constitutional symptoms Churg-Strauss syndrome should be ruled out as a possible cause of pulmonary affection. Clinical findings must be confirmed by specific immune markers. Precise diagnosis and rational therapy are critical in the prevention of disease progression and improving outcome.

**Keywords:** churg-strauss syndrome, pulmonary, antineutrophil cytoplasmic antibodies, asthma, erythrocyte sedimentation rate

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Babaeva AR,<sup>1</sup> Kalinina EV,<sup>1</sup> Solodenkova KS<sup>2</sup><sup>1</sup>Volgograd State Medical University, Volgograd, Russia<sup>2</sup>IM Sechenov First Moscow State Medical University, Moscow, Russia

**Correspondence:** Aida Rufatovna Babaeva, Volgograd State Medical University, Volgograd, Russia, Tel: +79053929400, Email arbabaeva@list.ru

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## Introduction

Systemic connective tissue disorders still remain one of the great diagnostic challenges in real practice because they often begin with nonspecific symptoms and signs and progresses slowly over months and even years. Vasculitis refers to a heterogeneous group of disorders that is characterized by inflammatory lesion of blood vessels. Depending on size, distribution, and severity of the affected vessels, vasculitis can result in clinical syndromes that vary in severity from a minor self-limited rash to a life-threatening multisystem disorder. Current clinical classification of primary vasculitides is based on clinicopathologic features: they can be separated by the size of affected vessels (large, medium, small).<sup>1</sup> Small-vessel vasculitides are associated with antineutrophil cytoplasmic antibodies (ANCA), which can be detected in plasma.<sup>2,3</sup> One of the common clinical types of ANCA-associated vasculitis is Churg-Strauss syndrome (CSS) reported at first time by Churg and Strauss in 1951. Asthma, eosinophilia, and systemic vasculitis are the hallmarks of the Churg-Strauss syndrome. The Chapel Hill Consensus Conference defined CSS as a disorder characterized by eosinophil-rich, granulomatous inflammation of the respiratory tract and necrotizing vasculitis of small- to medium vessels with asthma and eosinophilia.<sup>1,4</sup> Since lung involvement is a frequent clinical feature of ANCA-associated vasculitides the differential diagnosis should be made to verify systemic vasculitis in patients with pulmonary disorder.<sup>3,5</sup> General clinical clues suggesting the presence of systemic vasculitis are constitutional symptoms, signs of inflammation, subacute onset, joint pain, multisystem disease evident. Establishing the diagnosis of vasculitis requires confirmation by laboratory test, biopsy, and/or serology. In term to demonstrate the typical natural history of ANCA-

associated vasculitis and diagnostic difficulties in real clinical practice we present observed clinical case.

## Methods and results

Patient ZTF, male, 54 years old, has been managed by general practitioner at out-patient clinic due to diagnosed asthma since the September 2012. Disease started one year before and presented with episodes of allergic rhinitis, conjunctivitis and dry cough in the summer season preferably at rural area. Later the patient was suffering from episodic shortness of breath, wheezing attacks and loading chest. These symptoms occurred 2-3 times per week and occasionally during the night. The patient joined out-patient clinic and was observed in term to verify respiratory system disease. On the basis of clinical features and instrumental data (peak expiratory flow charts which confirmed reversible bronchial obstruction) the diagnosis of persistent asthma was set up and treatment with bronchodilators was started. Two years later despite the treatment the episodes of breath shortness, paroxysmal cough and wheezing became oftener about 2-3 times a day usually worst during the nights with poor effect from inhaled short-acting beta2-agonist. As repeated spirometry revealed reduced peak expiratory flow (PEF=70% from sufficient levels), uncontrolled asthma was confirmed and treatment was modified. Combination of long-acting beta2-agonist and inhaled glucocorticoid was effective. Asthma attacks were less than once a week.

In February 2017 at first time patient experienced low back pain and arthralgia in upper and low limbs. Patient has been taking analgesics and non-steroidal anti-inflammatory drugs for a few months. In May 2017 joint swelling occurred: hands, wrists, feet and ankles were affected. At the same time there was subfebrile

fever, anorexia, progressive weakness. Patient was referred to rheumatologist and was admitted at in-patient clinic with preliminary diagnosis “undifferentiated arthritis”. Laboratory tests revealed moderate anemia, increased erythrocyte sedimentation rate (ESR), elevated creatinin levels (300mkmol/l) and mildly raised antibodies against cyclic citrullinated peptide. In term to determine systemic rheumatic disorder pts was admitted at rheumatology ward for further investigation and for choosing treatment strategy.

On examination the pts general condition was qualified as moderate in severity. The skin was pale. Small (hands, feet) and medium-size (wrists, ankles) joints were painful and swollen. Pain increased in movement and in palpation. Respiratory rate was 18 per min. Auscultation detected wheezing bilateral pulmonary rules. Heart sounds were clear, rhythmic, no murmurs were found out, heart rate was 88 per min. Blood pressure was 150/90mm Hg. No abnormalities were registered on abdominal palpation. Blood analysis demonstrated normochromic anemia (Hb = 79g/l), mild eosinophilia 6%, increased ESR – 64mm/h, creatinin levels accounted for 913mkmol/l, estimated glomerular filtration rate (GFR) was 5ml/min, total cholesterol – 6.7mmol/l. Urine analysis revealed proteinuria (0.3 g/l), microhematuria (10-15 er in f/v), cylinderuria (granular cylinders 2-4 in f/v).

Since the disease had presented with obvious systemic manifestation, associated with constitutional (fever, weight loss)

symptomes, joint, lung, kidney lesions, anemia, mild eosinophilia systemic vasculitis was suggested. On 9.06.17 an antineutrophil cytoplasmatic antibodies (ANCA) and antinuclear antibodies (ANA) tests were performed. The results showed increased level of proteinase-3 antibodies (PR3 - 124 units; positive control - 102 units), as well as a high level of anti-nuclear antibodies (ANA titer was 1:1280, normal range up to 1:80). In addition, the patient underwent chest tomography on 28.06.17 - focal and infiltrative changes in the lungs were not detected. X-ray of the paranasal sinuses have shown thickening of mucosa. Otorhinolaryngologist has diagnosed chronic hyperplastic rhinosinusitis. Abdominal ultrasound examination on 15.06.17 detected diffuse changes in the kidneys. Echocardiography from 15.06.17 revealed aortic valve and aortic walls compaction, normal systolic function.

Thus, diagnosis of ANCA-associated systemic vasculitis (PR3 antibodies in high titer): Churg-Strauss polyangiitis, subacute course with the damage of lungs (bronchial asthma), paranasal sinuses (chronic hyperplastic rhinosinusitis), kidneys (diffuse glomerulonephritis, chronic renal disease stage 5), anemia of moderate severity was established on the basis of patient complaints, clinical picture of the disease, and obtained laboratory and instrumental data. Therapy with Prednisolone i.v., antiplatelet agents, calcium channel antagonists, was performed. The dynamic of clinical and laboratory data during the patient’s observation is presented in Table 1-3.

**Table 1** Laboratory data

Parameter	Hb (120-160g/l)	WBC (4-9 10*9/l)	RBC (4,2-5,6 10*12/l)	PI (180-320 10*9/l)	Eosinophils (0-5%)	ESR (2-15mm/h)	TC (3,5-5,0mmol/l)	Creatinine (71-115mkmol/l)	GFR (80/120ml/min)
baseline	79g/l	7,2	2,8	280	6%	64mm/h	6,7	913	5ml/min/1,73
after treatment	117g/l	4,8	3,76	210	0%	12mm/h	5,4	150	45ml/min/1,73

WBC, white blood cells; RBC, red blood cell; PI, platelets; ESR, erythrocyte sedimentation rate; TC, total cholesterol; GFR, glomerular filtration rate (CKD-EPI ml/min/1,73)

**Table 2** Immunological markers

Parameter	ANCA		ANA (1:80 – normal)	CRP (0-10 mg/l)	RF (0-15 IU/l)	ACCP (0-20 IU/l)
	Anti-PR-3 (positive control- 102)	Anti-MP (positive control 102)				
baseline	124	64	0.930556	68	25	45
after treatment	34	12	0.152778	12	15	24

ACCP, antibodies against cyclic citrullinated peptide; CRP, C-reactive protein; RF, rheumatoid factor; ANCA, anti-neutrophil cytoplasmic antibodies; Anti-PR-3, proteinase-3 antibodies; Anti-MP, myeloperoxidase antibodies; ANA, antinuclear antibodies

**Table 3** Urine analysis

Parameter	Gravity	Protein (absent)	WBC (1-2 f/l)	RBS (absent)	Cylindruria (absent)
baseline	1012	0,3g/l	4-6f/l	10-15f/l	2-4f/l
after treatment	1015	0,03g/l	2-4f/l	0-1f/l	0

As obtained data suggest there was laboratory improvement on the background of treatment: creatinine level decreased up to 352 $\mu$ mol/L, hemoglobin level increased, ESR decreased, general urine analysis parameters become normal. Also the improvement of the patient's well-being was observed: pain in joints disappeared, the body temperature was stably normal, there were no pulmonary symptoms. The patient underwent pulse therapy with methylprednisolone and cyclophosphamide at a standard dose once a month after reaching a level of creatinine of 300 $\mu$ mol/L.<sup>2,3</sup> After 3 months of therapy there were no symptoms and signs of disease activity: the patient did not present any complaints, there were no attacks of suffocation. The level of hemoglobin was 117g/L, creatinine - 150 $\mu$ mol/L, ESR -12mm/h. Urine analysis became normal. The work ability was preserved.

## Discussion and conclusion

Patient's disease history and clinical picture suggest that CSS occurring is characterized by the presence of allergic disease (typically allergic rhinitis and asthma). More than 90% of patients with CSS have histories of asthma. This phase often lasts for several years. Eventually systemic disorder due to vasculitis affecting a wide range of organs presents with non-specific constitutional or musculoskeletal symptoms and signs of internal organ damage.<sup>2,5</sup> Eosinophilia before treatment is the initial clue for suspicion of CSS. But it must be taken into account that in case of previous glucocorticoids treatment eosinophilia might be moderate or even mild (like in observed patient treated with inhaled glucocorticoids). Laboratory findings are essential tool in CSS diagnosis verification because of high diagnostic value of ANCA antibodies. Antibodies in high titers to either PR-3 or MPO (but not to both) are typical immune marker of CSS. In presented clinical case anti-PR-3 antibodies were detected in sera. On one hand this finding proves the CSS diagnosis and can be considered as a specific prognostic marker. On the other hand anti-PR-3 antibodies reflect disease severity and can be used for further CSS activity evaluation during the treatment.<sup>5,6</sup> Delayed diagnosis of this uncommon disease results in progressive vital organ damage.<sup>7</sup> In observed patient the most sever complication was renal failure due to typical kidney involvement characterized by glomerulonephritis. Since kidney damage in ANCA-vasculitis requires therapy with cytotoxic agent<sup>6-8</sup> cyclophosphamide was used in combination with methylprednisolone i.v. Since used approach was effective and well tolerated the patient could reach clinical remission.

Thus, presented clinical case confirms the concept, that respiratory system disorders are typical features of ANCA-associated vasculitis,

moreover, upper and lower respiratory tract lesions could be the first manifestation of the disease. Concerning Churg-Strauss polyangiitis on the base of presented observation one can conclude that asthma is very common disease onset consequently associated with constitutional symptoms, anemia, joint and kidney lesions. Early diagnosis and rational therapy are critical for improving outcome.

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## Conflict of interest

Author has declared there is no conflict of interest.

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