

Simultaneous Churg-Strauss Syndrome and Cryoglobulinemia Presenting as Subarachnoid Hemorrhage

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Citation

T Yamaguchi, K Kinjo, M Kinjo. *Simultaneous Churg-Strauss Syndrome and Cryoglobulinemia Presenting as Subarachnoid Hemorrhage*. The Internet Journal of Neurology. 2006 Volume 7 Number 2.

Abstract

Churg-Strauss syndrome (CSS) is a small vessel vasculitis characterized by asthma and eosinophilia. CSS rarely manifests with central nervous system involvement, and only a few cases of overlapped vasculitis have previously been reported. We describe a case of CSS which presented with an acute subarachnoid hemorrhage and features of essential cryoglobulinemia, suggesting an uncommon primary vasculitis overlap syndrome.

INTRODUCTION

Churg-Strauss Syndrome (CSS) is a vasculitis of small to medium vessels, first described in 1951. CSS presents with prominent asthma and eosinophilia, which distinguishes it from other vasculidites. Although peripheral neuropathy is common in CSS, central nervous system involvement is rare. Many types of vasculitis present in tandem, but only a few cases of CSS combined with another primary vasculitis have been reported. We present a case of CSS with a cerebral artery aneurysm dissection and subarachnoid hemorrhage (SAH), in whom a catastrophic vasculitis had features of both CSS and essential mixed cryoglobulinemia.

CASE REPORT

A 55-year-old male presented with coma and anisocoric pupils. Computed Tomography (CT) scan of the brain revealed a large subarachnoid hematoma in the left Sylvian fissure. At craniotomy, the cerebral vessels were stenotic and irregular, and a ruptured dissecting aneurysm of the left middle cerebral artery (MCA) was clamped and bypassed. After surgery, he had persistent fever and leukocytosis with increasing eosinophilia. Multiple intermittent episodes of wheezing required frequent administration of bronchodilators. Progressive renal failure developed by the 37th day of hospitalization. He remained comatose and respirator-dependent thereafter.

He had been diagnosed with asthma 4 years prior to presentation, and had required both inhaled and oral corticosteroids. He had never taken leukotriene receptor

antagonists. He had sustained multiple episodes of sinusitis and rhinorrhea in the past. He had no cardiovascular risk factors. He had used no regular medication but occasional oral and inhaled corticosteroids. He was an office worker. He rarely drank alcohol and did not smoke.

Temperature was 38.7°C, blood pressure was 110/85mmHg, heart rate was 110/min, and respirations were 36/min. Examination revealed diffuse wheezes in all lung fields. Multiple palpable purpura were present. The physical examination was otherwise unremarkable. Babinski sign was positive bilaterally, and neurologic assessment was limited by coma. Meningeal signs were absent.

The peripheral leukocyte count was 25,100/mm³ with 45% eosinophils. Hemoglobin was 11.0 g/dl, and the platelet count was 312,000/mm³. Electrolytes and liver function tests were normal. BUN and creatinine were 38.2 and 1.4 mg/dl, respectively. C-reactive protein was elevated to 21.6 mg/dl (< 0.6mg/dl). Urine dipstick revealed proteinuria and hematuria, and there were dysmorphic red blood cells, white blood cells, and white blood cell casts in the urinary sediment. Hansel stain showed eosinophils in both urine and sputum. Chest x-rays and cerebrospinal fluid analysis were unremarkable. Cultures of blood, urine, sputum and cerebrospinal fluid were negative. C3 and C4 were 150 mg/dl (80-140 mg/dl) and 17.2 mg/dl (11-34 mg/dl); and CH50 < 5 mg/dl (30-45 U/ml). Anti-nuclear antibodies were undetectable. Peri-nuclear anti-neutrophil cytoplasmic antibody (p-ANCA) was positive with an myeloperoxidase

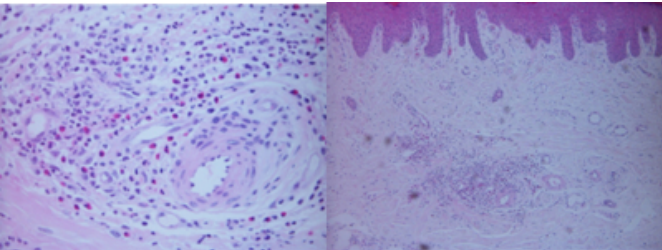
(MPO) titer of 1,455 U/ml (<8.9 U/ml); cytoplasmic-ANCA was negative. A qualitative test for cryoglobulins was positive, as was a rheumatoid factor (RF). Tests for hepatitis B and C were negative for antigen or antibody. The bone marrow was packed with mature eosinophils. Skin biopsy of a palmar purpura revealed an eosinophilic small vessel vasculitis (Figure 1, 2).

Churg-Strauss Syndrome was diagnosed. Intravenous methylprednisolone, 1000 mg/day, was administered initially, followed by oral prednisolone 60 mg daily. Renal failure, wheezing and eosinophilia resolved. MPO-ANCA levels decreased as complement levels normalized, and cryoglobulins became undetectable in his serum in the first few weeks.

Despite serologic recovery, coma persisted. Steroids were tapered gradually, without relapse of vasculitis. The hospitalization was complicated by several bouts of pneumonia, with increasingly antibiotic-resistant organisms. He sustained recurrent renal failure in the absence of an active urinary sediment, and died of multiorgan system failure on the 162nd hospital day.

Figure 1

Figure 1: Patient's skin biopsy specimen (a) 200 $\tilde{A}$ — magnification. (b) 400 $\tilde{A}$ — magnification. Infiltration of small vessels and perivascular tissues in dermis by eosinophils and neutrophils with fragmentation of neutrophil nuclei. This finding is characteristic of leukocytoclastic vasculitis with dominant infiltration by eosinophils, which is consistent with Churg-strauss syndrome.



DISCUSSION

This report documents a case of CSS with two unique and previously unreported manifestations: SAH as a presenting manifestation of CSS, and coexisting cryoglobulinemia.

Neurological symptoms complicate CSS in 62-75% of patients^{2,3,4,5,6}, and these are predominantly peripheral neuropathies. Central nervous system (CNS) involvement is rare, less than 6%^{4,5,6}, although CNS involvement is associated with poorer outcome. Among patients with CNS involvement, nearly all have cerebral infarction. Only 4

cases of SAH in CSS have been reported (Table 1). Almost all cases of SAH in CSS were due to a dissecting aneurysm^{7, 9, 10}. Dissecting aneurysm in CSS may be due to fragility of vessels which are involved by vasculitis. Previous cases of SAH in CSS were preceded by eosinophilia and signs of vasculitis in skin or peripheral nerves^{7,8,9,10}. In our patient, except for pre-existing asthma, typical features of CSS did not become apparent until the first few weeks after the CNS event. Rapid development of eosinophilia, palpable purpura and renal insufficiency suggested the explosive onset of an autoimmune catastrophe.

Figure 2

Table 1: Summary of reported cases of SAH in CSS

Case	Age/Sex	Affected site	Diagnostic procedure	Asthma History	WBC count (Eos %) at presentation	Treatment
1 ⁹⁾	47yo F	Vessels of choroid plexus	Autopsy	20yrs	29000/ μ l (76%)	Dead
2 ⁹⁾	59yo M	Rt thalamic hemorrhage	MRI/CT	39yrs	104800/ μ l (91.1%)	Oral PSL
3 ⁷⁾	47yo F	Basilar Artery	AG	6yrs	32600/ μ l (46.6%)	Oral PSL+CPA
4 ¹⁰⁾	36yo F	Rt Vertebral Artery	AG	8yrs	24780/ μ l (38.4%)	Oral PSL

AG denotes angiography, PSL denotes prednisolone, CPA denotes cyclophosphamide.

Transient expression of a serum cryoglobulin was another remarkable feature of this case. Cryoglobulins precipitate in vitro when the serum is cooled to 4°C, indicating the presence of immunoglobulins or immune complexes in the serum¹¹. CSS is an ANCA-associated vasculitis illustrating 'pauci-immune' immunohistology and normal complement levels, whereas complement consumption and positive rheumatoid factor are characteristic of immune-complex vasculidities such as cryoglobulinemia. Essential mixed cryoglobulinemia (EMC) is diagnosed when there are no underlying diseases inducing cryoprecipitable immunoglobulins. CSS typically presents in characteristic clinical patterns that do not overlap with other vasculitic syndromes. Overlap of CSS and cryoglobulinemia with or without HCV is extremely rare¹². Although more than 90% of EMC is associated with chronic hepatitis C virus (HCV) infection¹¹, tests for hepatitis B and C were negative in this case. Moreover, hypocomplementemia and positive rheumatoid factor, common in EMC but not CSS, were present in this case. Although presence of rheumatoid factor or immune complex in the vasculitic phase of CSS is recognized^{13,14,15}, it is not well understood what initiates progression of CSS. Both serological abnormalities resolved after immunosuppressive therapy.

The presentation of systemic vasculitis as an intracranial

bleed is unusual, and may suggest an awareness of vasculitis as an unusual cause of SAH. In addition, this case illustrates a rare 'overlap' vasculitis, with features of both Churg-Strauss Syndrome and essential mixed cryoglobulinemia.

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