



A 67-Year-Old Woman With Asthma, Word Finding Difficulty, and an Abnormal Chest Radiograph

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A 67-year-old woman presented to the ED of a tertiary hospital with sudden onset of difficulty expressing words, associated with a frontal headache. She reported general malaise, muscle weakness, and a persistent abnormal sensation in her legs in the preceding couple of weeks. These symptoms presented on a background of refractory asthma, which had been diagnosed in early childhood. She had been on maintenance therapy of 10 mg prednisolone daily (which she titrated based on her exacerbations), in addition to fluticasone/salmeterol 250 µg/50 µg metered-dose inhaler, two puffs bid. There was no history of rhinosinusitis or nasal polyposis. Two years prior, she had an episode of amaurosis fugax, which was treated as temporal arteritis (no histology was undertaken), with oral steroids.

Physical Examination Findings

On examination, the patient's heart rate was 95 beats/min, respiratory rate was 28 breaths/min, and BP was 130/77 mm Hg. Oxygen saturation was 94% on 8 L/min oxygen. Chest examination indicated increased work of breathing, widespread wheeze, and coarse crackles. Cardiovascular and abdominal examinations were normal. CNS examination identified receptive and expressive dysphasia, dyscalculia, and loss of right and left discrimination. Peripheral ner-

vous system examination revealed peripheral sensory loss in stocking distribution.

Diagnostic Studies

Full blood count showed a normal hemoglobin level, WBC count of $18.5 \times 10^9/L$ (normal range, $4-11 \times 10^9/L$), slightly elevated neutrophil count of $9.92 \times 10^9/L$ (normal range, $1.8-7.5 \times 10^9/L$), and markedly elevated eosinophil count of $5.92 \times 10^9/L$ (normal range, $0.02-0.50 \times 10^9/L$). C-reactive protein level was elevated at 120. Renal function and liver function test results were normal. Urine microscopy did not reveal any active sediments. An autoantibody screen showed negative antineutrophil cytoplasmic antibody (ANCA), weakly positive antinuclear antibody, and negative extractable nuclear antigen results.

The chest radiograph (Fig 1) showed features of alveolar shadowing with areas of dense consolidation.



FIGURE 1. Anteroposterior chest radiograph taken at the time of presentation.

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What is the diagnosis?

FIGURE 2. CT scan of the brain.

A CT scan of the brain (Fig 2) showed features consistent with acute cerebral infarct involving the left middle cerebral artery. A CT scan of the thorax (Fig 3) confirmed the patchy alveolar shadowing and consolidation. The patient subsequently underwent bronchoscopy and transbronchial biopsy.

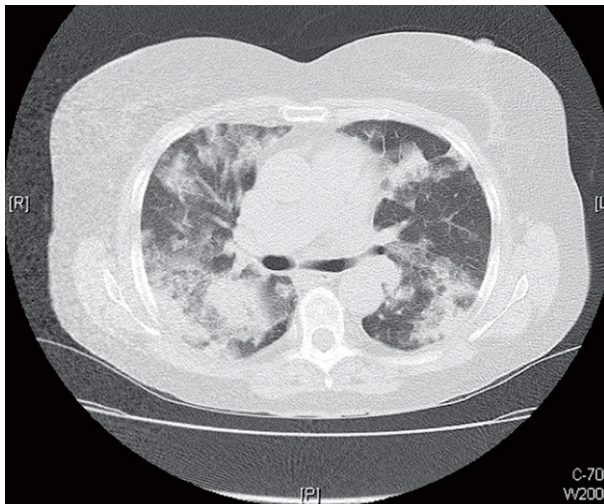


FIGURE 3. CT scan of the thorax.

DISCUSSION

Churg-Strauss syndrome (CSS) is characterized by vasculitis of small to medium arteries and veins and is associated with extravascular eosinophilia. It is closely related to granulomatosis with polyangiitis (Wegener) and microscopic polyangiitis. CSS is rare, with a reported incidence of 0.11 to 2.66 cases per million population per year internationally.

CSS is characterized by three stages. The prodromal phase consists predominantly of asthma, rhinosinuitis, and nasal polyposis, followed by a second phase, which is characterized by peripheral blood and tissue eosinophilia, and then develops into the advanced vasculitic phase. Asthma is considered a unifying feature, reported in up to 96% of cases. From the onset of asthma, there is a latency period to the vasculitic phase, which is reported as 3 to 9 years, on average. Around the time of CSS onset, patients commonly experience constitutional symptoms of malaise, diffuse myalgia, and polyarthralgia. During the eosinophilic and vascular phases, the disorder involves multiple systems, including neurologic, cardiovascular, renal, gastrointestinal, and skin manifestations of the disease.

The American College of Rheumatology established that the diagnosis of CSS requires that at least four of the following criteria are met: asthma, eosinophilia >10% of normal, paranasal sinusitis, pulmonary infiltrates on the chest radiograph, histologic evidence of vasculitis with extravascular eosinophils, and mononeuritis multiplex or polyneuropathy. Temporal arteritis is a rare manifestation and has only been reported in a few, isolated case reports. A negative ANCA status does not influence the diagnosis because a positive ANCA result is reported in approximately only 40% of CSS cases. Therefore, a positive ANCA result has low predictive value. A transbronchial biopsy specimen can be used to confirm the diagnosis. It is less invasive than a surgical lung biopsy; however, a negative transbronchial biopsy result in the context of high clinical suspicion of CSS would then indicate a surgical lung biopsy, because a transbronchial biopsy could miss a positive diagnosis.

Peripheral nervous system involvement is common in CSS (55% to 75% of cases), but CNS involvement is rare (<10%). CSS presenting in association with a stroke is unusual, particularly in a patient with few cardiovascular risk factors. A few case reports identify patients diagnosed with CSS and stroke, but it is unclear whether the etiology of the stroke can be attributed to the underlying CSS, as eosinophilia affecting the cerebral vasculature can only be proven

with a biopsy specimen. One case report identified cerebellar infarction in association with a relapsing purpuric rash that contained eosinophils on histologic examination, and it was suggested that patients with deteriorating CSS could be more susceptible to a stroke.

Primary therapy of CSS is with corticosteroids (0.5-1 mg/kg of prednisolone). Additional immunosuppressive therapy (typically cyclophosphamide) is used in patients with advanced/refractory disease. High-dose steroids are typically given for 6-12 weeks depending upon clinical response. Maintenance immunotherapy is recommended for 12-18 months, but some patients may require life-long immunosuppression. Individual case reports have stated cyclophosphamide and azathioprine have led to recovery of neurologic complications of CSS; however, there is limited literature reporting effective treatment of CNS complications because they are rare.

Clinical Course

Our patient met five of the six criteria required for a diagnosis of CSS, including past history of asthma, eosinophilia >10% of normal, pulmonary infiltrates on chest radiograph, eosinophilic vasculitis, and polyneuropathy. She had a history of amaurosis fugax, which was attributed to temporal arteritis because the condition responded to corticosteroid treatment, although a temporal artery biopsy was not performed. The transbronchial biopsy specimen was crucial to identify eosinophilic vasculitis on the lung parenchyma, which indicated the advanced vasculitic phase of CSS. While it is possible our patient had a coincidental thrombotic stroke, it is also possible in this scenario that vasculitis was the cause of the stroke.

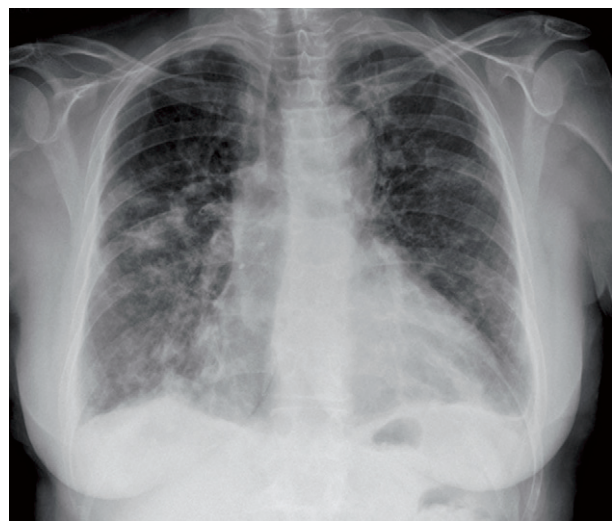


FIGURE 4. Anteroposterior chest radiograph demonstrating improvement of bilateral alveolar infiltrates and consolidation.

Our patient commenced treatment on prednisolone (1 mg/kg) with rapid clinical and radiographic improvement (Fig 4). To manage the stroke, antiplatelet therapy was initiated, and the patient's speech improved. She was discharged home with a plan to reduce the steroid therapy under close observation.

CLINICAL PEARLS

1. Patients presenting with stroke and hypereosinophilia on biopsy specimen should be investigated for underlying CSS, even though CNS complications of CSS are rare.

2. CSS could be masked in patients with chronic, refractory asthma who have been managed with long-term corticosteroids, particularly as asthma characterizes the prodromal phase of CSS.

3. A positive ANCA result is reported in approximately only 40% of CSS cases and, hence, has a low predictive value to diagnose CSS.

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