

cephalic chorea was mild in comparison to the intensity of respiratory muscle involvement, the presenting complaint, and because the patient also had asthma.

Increased awareness of the potential for respiratory dyskinesia to be confused with other causes of respiratory distress is necessary not only to avoid potentially harmful treatments, as exemplified in the present report, but to allow effective management to be instituted. One must keep in mind the spectrum of causes, in particular the use of neuroleptics, and the possibility that choreiform movements of limb or trunk may be mild and may not necessarily precede the onset of respiratory symptoms.

#### REFERENCES

- 1 Weiner WJ, Goetz CG, Nausieda PA, Klawans HL. Respiratory dyskinesias: extrapyramidal dysfunction and dyspnea. *Ann Intern Med* 1978; 88:327-31
- 2 Yassa R, Lal S. Respiratory irregularity and tardive dyskinesia. *Acta Psychiatr Scand* 1986; 73:506-10
- 3 Turner WA, Critchley M. Respiratory disorders in epidemic encephalitis. *Brain* 1925; 48:72-104
- 4 Wiholm BE, Mortimer Ö, Boethius G, Häggström, JE. Tardive dyskinesia associated with metoclopramide. *BMJ* 1984; 228:545-47
- 5 Klawans HL. Pharmacology of extrapyramidal disorders. Basel: S Karger, 1973

## Wegener's Granulomatosis Presenting as a Primary Seizure Disorder with Brain Lesions Demonstrated by Magnetic Resonance Imaging\*

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Since the earliest attempt by Klinger in 1931 to describe the systemic vasculitis subsequently characterized in 1936 by Wegener as Wegener's granulomatosis, this disorder has been reported to present in a number of differing fashions. No previous description relates Wegener's presenting as a seizure disorder, and no reports of MRI of the brain in such patients exists. We relate such a case, along with MRI findings, prior to and after treatment, with a review of neurologic manifestations of the disorder.

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WG = Wegener's granulomatosis

Wegener's granulomatosis is characterized by widespread necrotizing granulomatous lesions and an associated systemic vasculitis. The disease usually involves the upper and lower respiratory tract and kidneys.<sup>1</sup> Since its original description, multiple organ system involvement and alternative presenting manifestations have been described. Although seizures during treatment of WG have been recognized, no case of a patient initially presenting as a seizure disorder has been reported.<sup>2-4</sup> This case report describes a patient seen primarily for a convulsion. The

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diagnosis was uncovered by CT and MRI, which revealed intracranial lesions thought to be the etiology of the seizures, and by open lung biopsy, which demonstrated the classic pathologic changes of WG.

#### CASE REPORT

A 34-year-old white man presented to the Trident Regional Medical Center after working outside all day in the summer heat. His original complaint to the triage nurse was fatigue and heat exhaustion. After a 30-min wait, a tonic-clonic seizure witnessed by the medical staff occurred and the patient was transferred to an examination room. A second seizure minutes later prompted administration of intravenous diazepam and phenytoin. He was then maintained on phenytoin without further seizures.

He had been in good health until eight weeks prior to admission, when gradual weight loss and a cough productive of foul-smelling yellow sputum, mixed occasionally with blood, was noted. Drenching sweats had occurred nightly for several weeks, and one hard shaking chill was noted four weeks prior to admission. A fall from a ladder had led to a fracture of the left hand three weeks before presentation. This was treated surgically with an uneventful recovery.

A history of chronic recurring headaches was obtained but they had not changed in character or frequency. Symptoms of sinusitis, arthritis, or prior neurologic problems were denied by the patient. A remote exposure to tuberculosis without prophylaxis was noted and he was an active smoker with a 40-pack-year history. He denied specific risk factors for HIV infection. Physical findings, including funduscopic and neurologic examinations, were within normal limits. The sinuses and lungs were without abnormality. The fingers were not clubbed. The white blood cell count was 14,400 without a left shift, and the hemoglobin value was 11 g/dl. The creatinine level was 0.7 mg/dl, and urinalysis disclosed 3 to 5 WBC and 10 to 15 RBC without casts per low-power field. Drug and alcohol screenings were negative. A left upper lobe thick-walled cavity without an air fluid level and a right middle lobe infiltrate and small cavity were

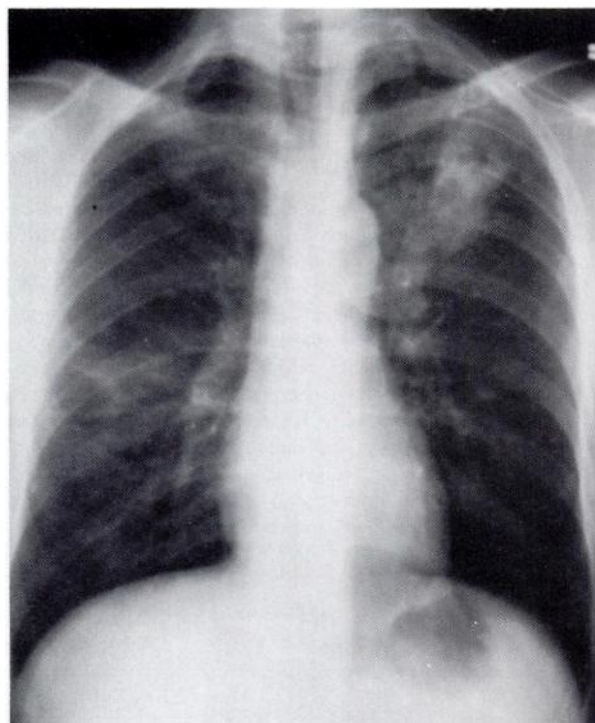


FIGURE 1. Admission posteroanterior chest radiograph revealing left upper lobe and right middle lobe cavitory lesions.

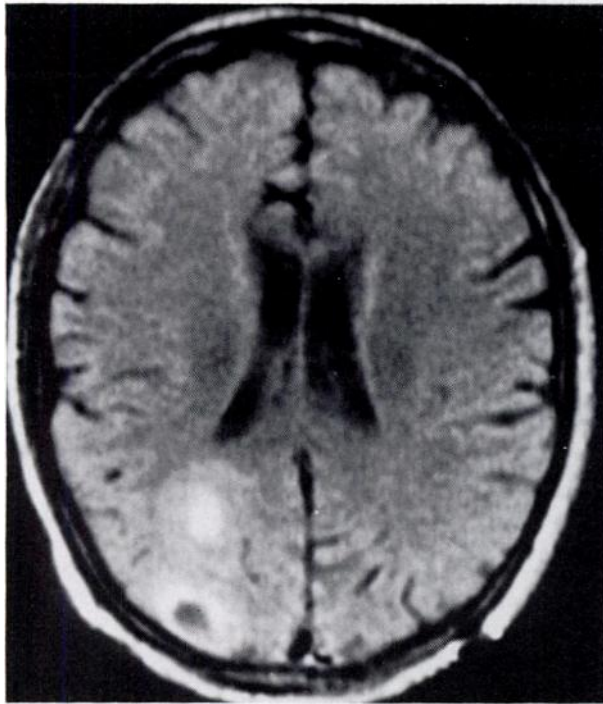


FIGURE 2. A T1 weighted gadolinium-enhanced MRI scan of the brain on admission revealing one ring-enhancing granulomatous lesion and the edge of a second similar lesion in the right occipital area. A third left temporal lesion is not seen on this image.

noted on the chest roentgenogram (Fig 1). Microscopic sputum examination revealed the presence of polymorphonuclear cells but no pathogenic bacteria. A CT scan of the brain with contrast revealed two ring-enhancing masses in the posterior portion of the right occipital lobe. Subsequent MRI revealed the same two masses and an additional lesion which was enhanced with gadolinium administration in the left temporal area (Fig 2). Neither the CT nor MRI revealed any sinus abnormality. Sputum cultures were negative for acid-fast bacilli or fungi, and transbronchial lung biopsy results were suspicious for malignancy. On the day an open-lung biopsy was performed, a qualitative anticytoplasmic neutrophil antibody test was positive in a cytoplasmic staining pattern. Open biopsy disclosed the classic changes associated with WG. Cyclophosphamide, prednisone and trimethoprim with sulfamethoxazole were administered orally, and the patient clinically improved. A second MRI eight weeks later showed almost total resolution of two of the three lesions, and a chest roentgenogram was normal (Fig 3).

#### DISCUSSION

The patient exhibited several unusual manifestations of WG. Seizure as a primary symptom in WG makes it singular in the literature. In addition, the absence of paranasal sinus involvement, confirmed by CT and MRI imaging, in a disease where the sinuses are affected 90 percent of the time, is atypical.<sup>1</sup> The use of MRI as a method of examination of the CNS in WG has not been reported.

Although initially described by Klinger<sup>5</sup> in 1931, in 1936 Wegener, with a recounting of three patients who had nasal granulomas, isolated what is now known as WG from the other systemic vasculidites.<sup>6</sup> Recognition that neurologic complications may occur has become evident in the intervening years. Drachman,<sup>7</sup> the first physician to analyze the spectrum of neurologic manifestations, separated these into peripheral and CNS abnormalities. He and others point out

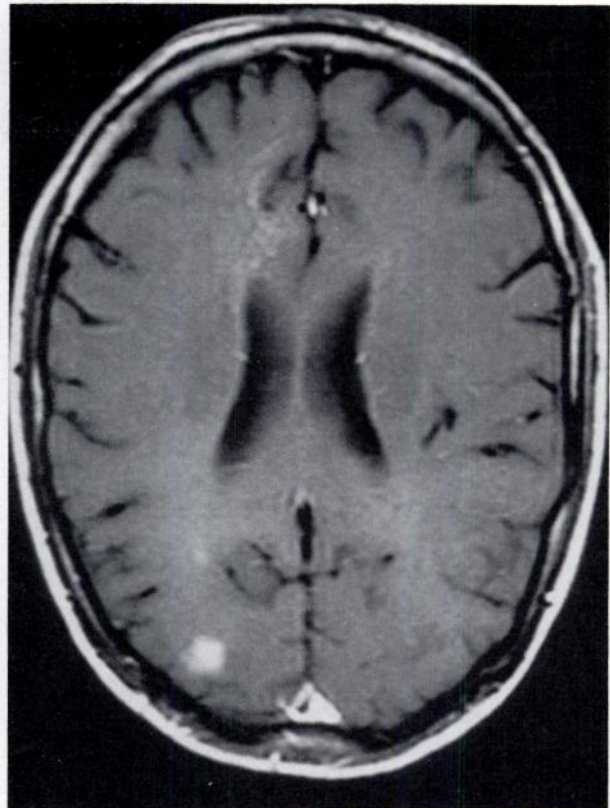


FIGURE 3. A T1 weighted gadolinium-enhanced MRI scan obtained two months after treatment reveals a marked decrease in both previously identified granulomas. The third left temporal lesion was not apparent on the second MRI scan.

that peripheral neuropathy, or mononeuritis multiplex, is the most common neural manifestation of WG and occurs in about 30 percent of all cases.<sup>7,8</sup> Drachman<sup>7</sup> also described three basic CNS pathologic processes. First was the contiguous invasion of the brain by granulomatous lesions in the paranasal sinuses. The reported frequency in this initial review was 26 percent and still remains today as the most common CNS manifestation of WG. Second was the development of a vasculitis of the nervous system, with necrotizing angitis of small arteries and veins of the peripheral nerves or the CNS leading to one of several clinical complications. Although 28 percent of Drachman's<sup>7</sup> original cases included a neural vasculitis, only 9 percent involved the CNS. These lesions included intracranial hemorrhage, subarachnoid hemorrhage, subdural hematoma, and cerebral artery and venous thrombosis.<sup>7,8</sup> These hemorrhagic syndromes are believed to be secondary to weakening of vessel walls by an inflammatory angitis with subsequent rupture and bleeding. Conflicting prognostic reports exist, but most of these patients do poorly.<sup>9</sup> The use of steroids and cyclophosphamide is more beneficial than the administration of steroids alone, as shown by the uniformly fatal results achieved by steroids alone noted by Hearne and Zawada.<sup>4</sup> Central nervous system vasculitis should be suspected in patients with WG who develop changing levels of consciousness. The third form of CNS involvement is the formation of individual or multiple granulomatous lesions in the brain or cranial nerves, which occurred in only 3 percent of Drachman's<sup>7</sup> series. This figure probably underrepresented the true

incidence of CNS granulomas, since reports of such granulomas have increased with the advent of CT scanning.<sup>3,4,10</sup> This patient most likely developed these multiple granulomatous lesions as evidenced on CT and MRI. These lesions have been described by CT as areas of low density that have ring-enhancing properties with contrast administration. The MRI scan in this patient revealed lesions with ring-enhancing properties similar to those seen on CT scan, and was sensitive enough to discover an additional lesion not suspected on CT scan. The increased sensitivity of MRI in demonstrating CNS lesions, as evidenced in this case, coupled with the avoidance of potentially nephrotoxic contrast agents necessary for CT, suggests MRI is a superior test in this disorder. Oimomi et al<sup>11</sup> described these CNS lesions, found at surgery, as dark brown, scarred, indurated and poorly demarcated. Tissue sections contained granulomatous foci with plasma cells, lymphocytes, occasional histiocytes and giant cells. Evidence of a necrotizing angiitis was rarely noted. Since these lesions may disappear on serial CT examinations, and on MRI in this patient's case, they appear to be amenable to treatment.<sup>3,4,11</sup>

This patient was treated with cyclophosphamide and prednisone, the medications usually prescribed for WG. He also received trimethoprim with sulfamethoxazole (320 mg and 1,600 mg, respectively) on a daily basis. This commonly utilized antibiotic has been reported as effective for the treatment of WG, even if used alone.<sup>12,13</sup> Although not yet a conventional drug for the treatment of WG, the severity of CNS involvement in this case, coupled with low toxicity profile of trimethoprim with sulfamethoxazole, prompted its administration in this case.

Logic suggests that the space-occupying brain lesions in this patient precipitated the seizures. Recovery over a period of hours was consistent with the diagnosis of a true seizure disorder. The lack of alcohol and drugs as precipitating agents confirm this view. Additionally, suppression of the seizure state was readily achieved by treatment.

In summary, a primary seizure occurrence in a patient having a disorder associated with protean manifestations is presented. The MRI of the intracranial lesions is novel. It appears to be more sensitive in the detection of intracranial

lesions in this disorder and avoids the complications of contrast agents. The suggestion to include WG in the differential diagnosis in patients with cavitory pulmonary disease and symptoms related to an intracranial disturbance seems worthy. These lesions in the brain and other organ systems respond to therapy with cyclophosphamide, prednisone and trimethoprim with sulfamethoxazole.

#### REFERENCES

- 1 Fauci AS, Haynes BF, Katz P, Wolf SM. Wegener's granulomatosis: Prospective clinical and therapeutic experience with 85 patients for 21 Years. *Ann Intern Med* 1983; 98:76-85
- 2 Hearne CB, Zawada ET. Survival after intracerebral hemorrhage in Wegener's granulomatosis. *West J Med* 1982; 137:431-34
- 3 Satoh J, Miyasaka N, Yamada T, Nishido T, Okuda M, Kuroiwa T, et al. Extensive cerebral infarction due to involvement of both anterior cerebral arteries by Wegener's granulomatosis. *Ann Rheum Dis* 1988; 47:606-11
- 4 Payton CD, Jones JMB. Cortical blindness complicating Wegener's granulomatosis. *Br Med J* 1985; 290:676
- 5 Klinger H. Grenzformen der periarteritis nodosa. *Frankfurt Z Pathol* 1931; 42:455-80
- 6 Wegener F. Über generalisierte, septische Gefässerkrankungen. *Verh Deutsch Ges Pathol* 1936; 29:202-10
- 7 Drachman DA. Neurologic complications of Wegener's granulomatosis. *Arch Neurol* 1963; 8:145-55
- 8 Aita JA. Neurologic manifestations of Wegener's granulomatosis, 1972. *Nebraska Med J* 1973; 58:335-37
- 9 Dwyer J, Janzen VD. Wegener's granulomatosis with otological and nervous system involvement. *J Otolaryngol* 1981; 10:476-80
- 10 Yamashita Y, Takahashi M, Bussaka H, Miyawaki M, Tosaka K. Cerebral vasculitis secondary to Wegener's granulomatosis: computed tomography and angiographic findings. *CT: J Comput Tomog* 1986; 10:115-20
- 11 Oimomi M, Suehiro I, Mizuno N, Baba S, Okada S, Kanazawa Y. Wegener's granulomatosis with intracerebral granuloma and mammary manifestation. *Arch Intern Med* 1980; 140:853-54
- 12 DeRemee RA, McDonald TJ, Weiland LH. Wegener's granulomatosis: observations on treatment with anti-microbial agents. *Mayo Clin Proc* 1985; 60:27-32
- 13 Israel HL. Sulfamethoxazole-trimethoprim therapy for Wegener's granulomatosis. *Arch Intern Med* 1988; 148:2293-95