AN UNUSUAL CASE OF MULTIPLE CRANIAL NERVE PALSIES IN WEGENER'S GRANULOMATOSIS

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We describe an unusual case of Wegener's granulomatosis, which initially caused fulminant palsies affecting cranial nerves II, V, VI, VII, and VIII during a brief episode of the disease. The patient was successfully treated with immunosuppressive therapy. Wegener's granulomatosis should be suspected when multiple cranial nerves are initially affected. (*J Natl Med Assoc.* 2000;92:455–457.)

Key words: Wegener's granulomatosis ♦ antineutrophil cytoplasmic antibody ♦ cyclophosphamide ♦ glucocorticoids

First described by Frederick Wegener in 1936,[1] Wegener's granulomatosis is a vasculitic disease that affects the upper and lower portions of the respiratory tract and the kidneys.[2,3] Characteristic pathology consists of necrotizing vasculitis, granulomatous in the small and midsized arteries.[3] Neurologic complications, including peripheral neuropathy, cranial neuropathy, cerebrovascular events, and seizure were found in 22%–33.6% of patients who had Wegener's granulomatosis.[4–6] Cranial nerves were affected in 2%–4.4% of patients affected with the disease.[4,6,7] In one series, only 2.5% of patients had multiple cranial nerves affected (unilaterally in most) and only 2.2% had cranial nerves affected when first evaluated.[6] Indeed, neurologic involvement as the initial symptom is rare. To our knowledge, this is the first unique case of this disease wherein it affects multiple cranial nerves fulminantly on initial presentation. Our review of the literature located no other article that has reported this kind of presentation. In addition, this is a pioneering case in which tissue biopsy and, subsequently, the antineutrophil cytoplasmic antibody (ANCA) immunologic test were used to verify its diagnosis.

CASE REPORT

A 63-year-old, married, right-handed male painter was well until 2 months before admission to the hospital, when infection was seen in the right ear. He was treated with antibiotics and decongestant medication only, and the only preoperative procedures were radiographic. One month before admission, facial weakness developed on the right side, as did double vision and inability to close the right eye, and the right side of the tongue was ageusic. Computed axial tomography (CAT) showed no abnormality. Mastoiditis prompted mastoidectomy on the right side. Three weeks before admission, although no tumor or cholesteatoma was reported, the facial weakness remained unchanged and pain developed in the right side of the face, for which phenytoin (300 mg per day) was given. Hear-

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ing in the right ear subsequently decreased. A few days before admission, the patient again complained of double vision and progressive blurring of vision in the right eye. Just before admission, the patient became blind in the right eye. The patient denied smoking or alcohol use and his only child (a daughter) was healthy.

At physical examination, vital signs were normal, as were mentation and speech. Neurologic examination showed the right eye to have a pale fundus, visual acuity of 20/400, and paralysis of the right abductor muscle; decreased sensation on the right side of the face; peripheral eyelid weakness; decreased taste in the right side of the tongue; and decreased hearing in the right ear. Motor function, sensory function, and deep tendon reflexes were normal. Babinski's sign was not seen on either side. No incoordination or ataxia was seen.

Initial laboratory studies showed a white blood cell count of 11,600/mm^3 (11.6 $\times$ 10^9/liter; hemoglobin level of 11.8g/dL (118 g/liter); platelet count of 676 $\times$ 10^3/mm (676 $\times$ 10^9/liter), and erythrocyte sedimentation rate of 72. Results were normal also for Sequential Multiple Analyzer (SMA)-16, veneral disease research laboratory (VDRL), antinuclear antibody factor, rheumatoid factor, and thyroid function tests. An electrocardiogram did not show abnormalities. A tuberculin skin test gave a negative result. Chest x-ray films showed multiple soft-tissue nodules (i.e., densities in the left and right lower lung fields). Sinus x-ray films showed air fluid level in the right maxillary sinus consistent with acute sinusitis. An intravenous pyelogram was normal. A repeat CAT scan of the brain showed no abnormality except for soft-tissue density in the right mastoid area. Magnetic resonance imaging of the brain showed no abnormality except in the maxillary sinus. Nuclear magnetic resonance imaging showed osteoblastic activity in the right mastoid bone and in the adjacent sphenoid bone. A gallium study of the skull showed increased activity in the eyelid-mastoid region. Cerebrospinal fluid studies showed normal pressure, seven mononuclear cells, glucose level of 78 mg/dL (4.3 mmol/L), and total protein level 25 mg/dL (0.25 g/liter). India ink capsule stain and cerebrospinal fluid cultures for bacteria, tuberculosis, and fungus showed negative results. No malignant cells were seen. Needle aspiration of one of the soft-tissue masses in the right lung showed inflammatory cells and indistinct epithelial cells. Pathologic examination yielded inconclusive results; however, Wegener's granulomatosis was suspected when sinusitis was found. Biopsy specimens from the right maxillary sinus showed multifocal necrotizing areas characterized by fibrinoid material surrounded by palisaded fibrohistiocytic cells. Discrete granulomas with multinucleated giant cells were also present. Vasculitis was identified and was characterized by infiltration of inflammatory cells into the vessel walls. Overall histomorphology of the lesion in conjunction with the clinical history confirmed the diagnosis of Wegener's granulomatosis. Subsequently, an ANCA immunologic test was performed to verify the diagnosis. The patient was treated with prednisone and cyclophosphamide. Neurologic examination showed no further deterioration. The patient still had right optic nerve atrophy and right sensorineural hearing loss when seen 24 months later.

DISCUSSION

Wegener's granulomatosis affects the nervous system by spreading contiguous granulomatous lesions to nerves through the paranasal sinus (when the condition accompanies vasculitis affecting the nervous system) or from a remote granulomatous process to small vessels. Wegener's granulomatosis can be spread intracranially as a result of thrombosis or hemorrhage; and if spread extracranially, Wegener's granulomatosis can cause peripheral neuropathy.[4,5] Cranial nerves can also be affected via ischemic arteries, causing cranial nerve palsy.[4] Our patient was unusual because he had progressive cranial nerve involvement on the right side, initially affecting the seventh cranial nerve and then spreading to the fifth, eighth, sixth, and second cranial nerves.

The cause of Wegener's granulomatosis is unknown. However, recent discovery of ANCA in patients affected with Wegener's granulomatosis confirms that immune mechanisms, termed pauciimmune because of the lack of demonstrable immune complexes, may be involved in the pathogenesis.[8,9] As a multisystem disease, Wegener's granulomatosis can mimic collagen vascular disease, tuberculosis, fungal infection, sarcoidosis, and neoplasm. Because Wegener's granulomatosis is treatable, early diagnosis of this disease is important. Without proper diagnosis and treatment, patients affected with Wegener's granulomatosis can die within 2 years.[10]

Our patient was successfully treated with prednisone and oral cyclophosphamide; glucocorticoids and cyclophosphamide have yielded complete remission in >90% of patients affected with Wegener's granulomatosis.[11] Recently, trimethoprim and sulfamethoxazole were used in combination to treat non-life-threatening Wegener's granulomatosis.[12,13] Higher-dose trimethoprim used alone has also given good results and may allow rapid tapering of prednisone dosage.[14] Pulsed dosing with cyclophosphamide has produced remission in certain groups of patients affected with severe disease, but more data are needed to clarify its use because of recent evidence of increased relapses with pulse therapy.[11,15,16] Other alternatives, including methotrexate and cyclosporin, may also be effective in refractory cases of Wegener's granulomatosis.[17–19] Plasmapheresis has also been employed to treat this condition, although the mechanism for putative benefit in pauci-immune disease such as Wegener's is unclear.[20] Surgical management is indicated for nasolacrimal duct obstruction and subglottic stenosis accompanying Wegener's granulomatosis.[21]

In conclusion, Wegener's granulomatosis is a multisystem disease of unknown etiology. The disease affects the upper respiratory tract, lungs, kidneys, and central nervous system and should be suspected when multiple cranial nerves are affected. Delay in diagnosis can lead to further organ involvement and may cause irreversible damage to affected organs. If diagnosed early with ANCA and tissue biopsy, the condition can be treated with cyclophosphamide, prednisone, and possibly trimethoprim-sulfamethoxazole.

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