Wegener’s Granulomatosis with Multiple Cranial Nerve Involvements as the Initial Clinical Manifestations

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Wegener’s granulomatosis (WG) is a disease of unknown origin characterized by necrotizing granulomas of both the upper and lower respiratory tracts and glomerulonephritis. A 62-year-old woman presenting unusual neurological manifestations is reported. The patient suffered from palsies of multiple cranial nerves without manifestation of respiratory tracts in the initial clinical course. Seven years after the onset, pulmonary consolidations appeared on the chest X-ray study. A diagnosis was made by a needle biopsy of the lung. Palsies of cranial nerves suspected to be due to meningeal involvement of WG. During the entire clinical course, no finding of glomerulonephritis was observed. (Internal Medicine 34: 1110-1113, 1995)

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Introduction

Wegener’s granulomatosis (WG) is a disease of unknown origin characterized by necrotizing granulomas of the both upper and lower respiratory tracts and glomerulonephritis. Involvement of the cranial nerve is not rare, but it is usually accompanied by other organ involvement including respiratory tracts.

We treated a patient with WG with unusual neurological manifestation. The patient suffered from palsies of multiple cranial nerves without manifestation of respiratory tracts in the initial clinical course. Almost seven years after the onset of neurological symptoms, pulmonary consolidations appeared on the chest X-ray study. The diagnosis of WG was made by needle biopsy of the lung. During the entire clinical course, no finding of glomerulonephritis was observed. Palsies of the cranial nerves were suspected to be due to meningeal involvement of WG. The details of this patient are described, together with discussion on the clinical manifestations of WG.

Case Report

A 62-year-old housewife suffered from ringing of her left ear accompanied by low grade fever in April 1981. Her past history was remarkable for hyperthyroidism and partial thyroidectomy in her twenties (though no details were obtained), and suspected rheumatoid arthritis in her fifties. She was admitted to an otorhinolaryngological clinic, because of progressive bilateral hearing disturbance and left-sided facial palsy in November 1981, then she underwent surgery for probable otitis media on both sides. Her facial palsy and low grade fever regressed several months after the operation.

She enjoyed daily life until August 1983, when decreased sense of smell and hoarseness of voice developed. She was subsequently noted to have difficulty in swallowing and left facial palsy, and entered another hospital in October 1983. At the time of admission, neurological examination revealed multiple cranial nerve palsies on the left side. Nasopharyngeal examination and chest X-ray studies were normal. Possible diagnosis of epidural abscess on the temporal region was made based on radiological studies, then she underwent exploration of the mastoid process. Although she was subsequently treated with antibiotics administration, she progressively deteriorated to a bed-ridden state, and required tube feeding. She was discharged from the hospital in February 1984 without remarkable improvement.

Because of persistent headache and low grade fever, she was admitted to another hospital in April 1984. On admission, neurological examination revealed palsies of the multiple cranial nerves, including the first, seventh, eighth, ninth and tenth, cranial nerves bilaterally with left side predominance. Examination of nasopharynx was negative, and chest X-ray studies...
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Figure 1. Computed tomography in 1984, revealing narrowing of the left lateral ventricle. Abnormal enhancement along the Sylvian fissure and cerebellar tent on the left side is also noted.

were interpreted as normal. Significant results of laboratory studies included pleocytosis of cerebrospinal fluid and inflammatory findings from blood examinations. Computed tomography of the head revealed narrowing of the left lateral ventricle, and abnormal enhancement along the Sylvian fissure and cerebellar tent on the left side (Fig. 1). Gallium scintigram showed positive uptake extending from the skull base to the cerebral hemisphere on the left side (Fig. 2).

A presumed diagnosis of chronic pachymeningitis with infectious origin secondary to mastoiditis was made. After treatments with high-dose of antibiotics and low-dose of prednisolone (10 mg/day), she regained the ability of oral intake and walking without aid. Her left facial palsy improved slightly, though other cranial nerve palsies remained unchanged. She then had maintained a stable condition until April 1985, when she developed vocal cord obstruction due to bilateral recurrent nervous palsies, for which tracheostomy was required. In May 1988, low grade fever and general malaise developed. Chest X-ray studies revealed abnormal shadows, requiring admission to our hospital.

On admission, physical examination revealed mild emaciation, fever, and deformity with swelling of bilateral proximal finger joints without pain. Lungs were clear. No finding was observed in the nasopharyngeal region. Neurological examination revealed multiple cranial nerve palsies unchanged from previous studies. Results of laboratory studies were as follows: Urinalysis was normal, erythrocyte sedimentation rate was 117 mm/h, white blood cell count was 13,600/mm³, hemoglobin concentration was 11.8 g/dl, C-reactive protein was 14.6 mg/dl, and the rheumatoid factor was positive. Staphylococcus aureus and pseudomonas aeruginosa were cultured by the sputum obtained from the tracheostomy. No acid fast bacilli were cultured. Chest X-ray and computed tomography series demonstrated bilateral pulmonary air space consolidations and nodules (Figs. 3, 4). Antineutrophil cytoplasmic antibodies could not be measured at that time.

Despite administration of antibiotics, she continued to have fever, with subsequent development of bloody sputum and hemoptysis. She underwent a transbronchial lung biopsy, which showed nonspecific inflammatory findings. A percutaneous
Figure 3. Chest X-ray in 1988, showing several consolidations bilaterally.

Figure 4. Computed tomography in 1988, revealing pulmonary air space consolidations and nodules in right upper and middle lobes.

lungs biopsy was performed, which demonstrated granulomas including multinucleated giant cells of the Langhans with necrotic foci and vasculitis (Figs. 4, 5). These findings indicated Wegener’s granulomatosis, though the affected vessels were generally smaller in size compared to the typical types of this disorder.

Repeated urinalysis and renal function tests failed to reveal any abnormalities. Renal biopsy showed no findings of glomerulonephritis. Combination chemotherapy with prednisolone (1 mg/kg) and cyclophosphamide (2 mg/kg) was begun, resulting in dramatic reduction of fever, hemoptysis and chest X-ray abnormalities. Unfortunately, she died early in 1986 due to

Figure 5. Biopsy specimen of the lung demonstrating granulomas including multinucleated giant cells (HE stain, ×10).

Figure 6. Necrosis of small blood vessel surrounded by inflammatory cells suggestive of vasculitis (HE stain, ×20).
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pneumonia in another hospital, although no details were obtained. ANCA, which was measured by the frozen serum obtained three months after the chemotherapy was started, was negative. The serum prior to the combination chemotherapy was not preserved and therefore ANCA at that time could not be measured.

Discussion

The clinical course of this patient was unique in that multiple cranial nerve palsies due to meningeal involvement were the initial clinical presentation, about seven years prior to development of the respiratory tract manifestations. The diagnosis of Wegener’s granulomatosis (WG) was made based on percutaneous lung biopsy. The diagnosis is consistent with the 1990 criteria of the American College of Rheumatology (1).

It has been reported that symptoms like otitis media could appear as the initial clinical symptom in WG (2). Nervous system involvement is rare at the initial stages, but not infrequent during its entire clinical course (3). Although peripheral neuropathy is the most common neurological involvement, cranial nerve palsies are also reported in this disease (3–6).

In 1962, Drachman (4) reviewed neurologic complications of WG in the literature and found that 56 out of 103 patients (54%) had some forms of neurologic involvement. He classified the three patterns of neurologic involvement of this disease as follows: (1) granulomatous lesions encroaching on the nervous system by direct invasion from nasal or paranasal granulomas, (2) vasculitis of the cranial nerves, and (3) granulomatous lesions remote from the nasal granuloma. In the present patient, results of the computed tomography and gallium scintigram study strongly suggested the presence of chronic meningitis. Although cranial nerve neuropathy is the most common cause of cranial nerve involvement in WG in the literature (3–6), the mechanism causing the present patient’s cranial nerve palsies was most likely due to direct extension of the granulomatous inflammation into the basilar meninges probably from the mid ear, with nerve damage due to mechanical compression or vascular compromise (7, 8).

Recently, Nishino and coworkers (6) studied 324 patients in whom the diagnosis was made at the Mayo Clinic; 100 patients (33.6%) had some form of neurological involvement. Peripheral neuropathy occurred in 53 and cranial neuropathy in 21, however meningeal involvement were observed in only two patients. Although there are no detailed data regarding meningeal involvement, development of this presentation is usually observed in the late course of this disease. From this respect, this case is very unusual.

Analysis of antineutrophil cytoplasmic antibody (ANCA) (which was not available at that time) might have facilitated earlier detection of this disease. It was difficult to evaluate the negative result during the treatment when the disease was controlled. Other reports suggest that meningeal biopsy is useful for diagnosis of meningeal involvement of WG (9, 10).

In summary, Wegener’s granulomatosis must be included in the differential diagnosis of the diseases presenting refractory otitis media and cranial nerve palsies, even without the manifestations of the upper and lower respiratory tracts and kidneys.

References