

A case of granuloma in the occipital lobe of a patient with Wegener's granulomatosis

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Abstract We report a case of Wegener's granulomatosis (WG) with central nervous system (CNS) involvement in a woman who complained of bilateral visual disturbance. The intracranial necrotizing granulomatous lesion was confirmed by MR imaging and brain biopsy. After high-dose oral corticosteroid treatment, not only clinical manifestations but also laboratory tests improved. Moreover, the CNS lesion completely regressed. This suggests that high-dose corticosteroid alone might be effective in treating WG with CNS involvement.

Keywords Central nervous system involvement · High-dose corticosteroid therapy · Intracranial granuloma · MR imaging · Wegener's granulomatosis

Introduction

Wegener's granulomatosis (WG) is a chronic systemic inflammatory disease of unknown etiology. It is characterized by necrotizing granulomatous vasculitis that mainly affects the upper and lower respiratory tracts and the kidney. Neurological involvement is not infrequent and has been described in 22–54% of all cases [1, 2]. Most neurological involvement is associated with the peripheral nervous system (in 10.6–21.2% of patients [3]), typically mononeuritis multiplex. Central nervous system (CNS) involvement is uncommon (only 2–8% of patients) [3, 4]. In particular, intracranial granuloma is quite rare. Here, we report a case of WG with the granulomatous lesion in the occipital lobe successfully treated with high-dose oral corticosteroid alone.

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Case report

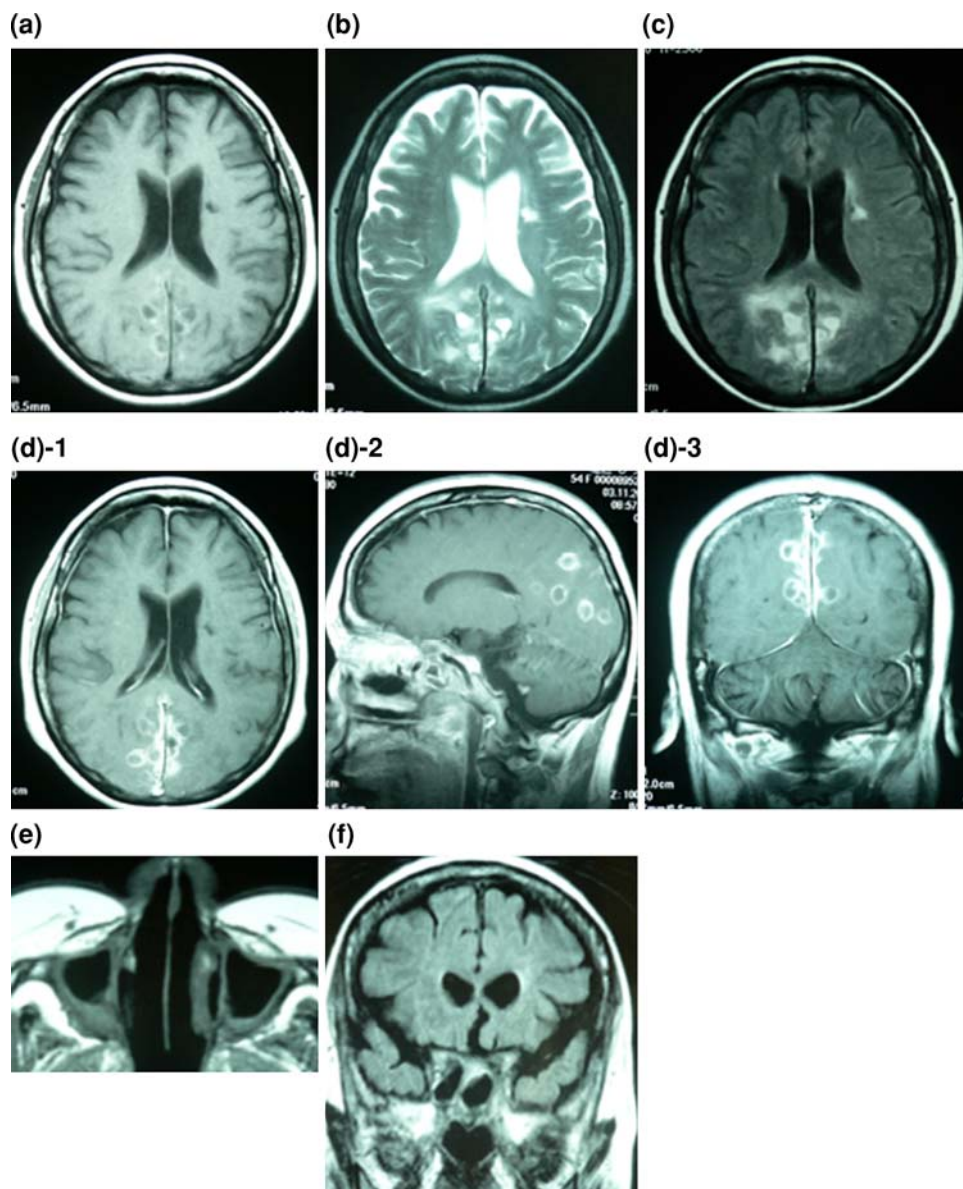
In May 2004, a 54-year-old woman presented to her family doctor with complaints of nasal bleeding and mild hearing loss. Saddle nose deformity was noted and suspected WG was diagnosed. Corticosteroid therapy was started [oral prednisolone (PSL); initial dose of 45 mg per day and then tapered]. The detail of clinical course after the initiation of PSL was unknown because of her willful discontinuation of receiving regular outpatient treatment. In February 2005, she complained of visual disturbance and consulted a local eye doctor who noted bilateral papilledema. She was

admitted to Rinku General Medical Center for further examination. Ophthalmological consultation confirmed bilateral papilledema, left inferior quadrant hemianopia, and enlargement of the blind spot of Mariotte. Gadolinium (Gd)-enhanced MR imaging study revealed a ring-like enhanced mass in the occipital lobe on T1-weighted images (Fig. 1). She was transferred to our hospital on 18 March 2005 for further examination.

On admission, her consciousness was clear and vital signs were normal. A saddle nose deformity and nasal mucus were present. Neither abnormal cardiac nor respiratory sounds were audible. Although eye movements and pupil reflexes were normal, bilateral peripheral visual field defects were noted. On neurological examination, left hemiparesis was observed but not sensory disturbance or meningeal irritation.

On complete blood count, mild microcytic anemia (red blood cell count $3.29 \times 10^6/\mu\text{l}$ and hemoglobin 10.3 g/dl) was noted; however, white blood cell count ($7.950 \times 10^3/\mu\text{l}$) was within the normal range—as were serum potassium (5.2 mEq/l), sodium (139 mEq/l), and chloride (101 mEq/l). Blood urea nitrogen and creatinine were elevated (54.0 and 6.33 mg/dl, respectively). Mild elevation of C-reactive protein (CRP) (1.05 mg/dl) and positive proteinase-3-anti-neutrophil cytoplasmic antibody (PR3-ANCA) (14 EU: cut off <10 EU) were noted. Neither anti-nuclear antibody (ANA), myeloperoxidase-ANCA (MPO-ANCA), nor rheumatoid factor (RF) was positive. Urinalysis could not be performed because of anuria. Serum β -D-glucan was within normal range (<3.2 pg/ml) and the result of tuberculin test was negative. She had undergone regular hemodialysis for 3 years to treat chronic renal failure. The

Fig. 1 Brain MR images (March 2005): **a** T1-weighted image, **b** T2-weighted image, **c** FLAIR image, **d** T1-weighted Gd-enhanced images (1 horizontal, 2 sagittal, 3 coronal): ring-like enhanced masses are shown in the occipital lobe. **e** Mucosal thickening of bilateral maxillary sinus and destruction of conchae. **f** Deviation of nasal septum



cerebrospinal fluid was clear with normal cell count. Although both the levels of glucose and chloride were within normal range and cultures for bacteria, fungi and mycobacteria were negative, levels of protein (48 mg/dl) and IgG (7.5 mg/dl) were mildly elevated. The index of IgG was elevated at 0.93, but no oligoclonal bands were detected. On chest X-ray and computed tomography (CT), no abnormal lesions were noted. In brain MR imaging study (Fig. 1), a low-intensity lesion with peripheral high-intensity linear signal was detected at the occipital lobe on T1 weighted images. The lesion had high-intensity on T2 weighted images and on fluid-attenuated inversion recovery (FLAIR) images. Moreover, Gd-enhanced MR imaging showed lesions with multiple ring-like enhancement in the occipital lobe on T1-weighted images. Mucosal thickening of bilateral maxillary sinus and destruction of conchae were also noted. Gallium (Ga) scintigraphy (Fig. 2) revealed abnormal accumulation of radioisotope in the bilateral maxillary sinus and parotid glands, and the occipital lobe. These Ga accumulations were coincidentally located in lesions detected by MR imaging. Although Ga uptake increased in parotid glands, physical symptoms were not presented. For the purpose of differential diagnoses, brain biopsy was performed with the patient's informed consent. Histopathological examination showed necrotizing granulomas with epithelioid cells, and stains for fungi and mycobacteria were negative (Fig. 3). The histopathological findings were compatible with those of WG. There were no signs of acute inflammatory changes, neoplasm, or metastasis, and CNS infections were excluded

by CSF data, histological findings and other specific studies. Finally, WG with CNS involvement was diagnosed. Then she was started on high-dose oral PSL at the initial dose of 1 mg/kg/day. Thereafter, the brain mass decreased promptly and serum levels of PR3-ANCA became normalized, and visual disturbance and bilateral papilledema disappeared. Moreover, no signs of recurrence were observed on Gd-enhanced MR imaging for 2 years and over during the period of PSL tapering (Fig. 4).

Discussion

Wegener's granulomatosis with neurological manifestations is not uncommon (representing 22–54% of all WG cases) [1, 2]. The most frequent neurological manifestations are peripheral neuropathies (10.6–21.2% [3]), such as mononeuritis multiplex. CNS involvement is uncommon (only 2–8%) [3, 4]. Nishino et al. [5] reported neurological involvement in 109 (33.6%) of 324 WG patients, including 53 (16%) with peripheral neuropathy, 21 (6%) with cranial neuropathy, 16 (5%) with external ophthalmoplegia, and 13 (4%) with cerebrovascular events. No CNS granulomatous lesions have been described, and only one thickening of the right tentorium cerebelli was reported. Drachman [2] divided the 104 WG cases with neurological involvement into three groups as follows: (1) necrotizing vasculitis of the cerebral, spinal, and radicular vasculature (28% of all cases); (2) contiguous extension from extravascular granulomas in the paranasal sinuses, nasal cavities, or orbits

Fig. 2 Ga Scintigraphy (March 2005): **a** total body: abnormal accumulations were revealed (arrow). Brain: **b** transverse, **c** sagittal, **d** coronal. Accumulations on the occipital lobe, bilateral maxillary sinus, and bilateral parotid glands were coincidentally located in the lesions detected on MR images

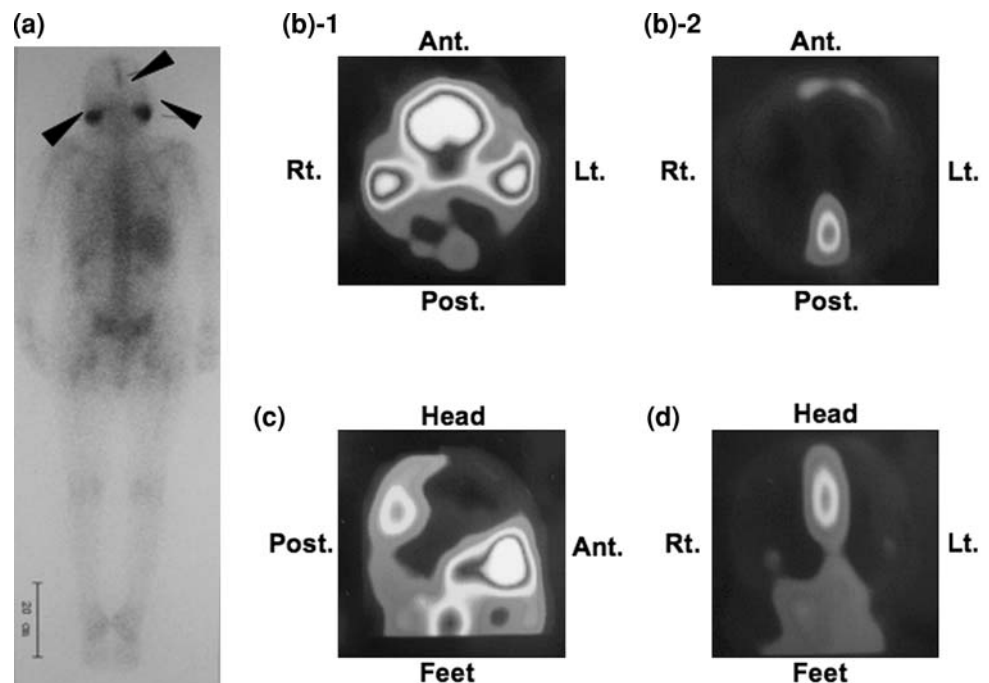
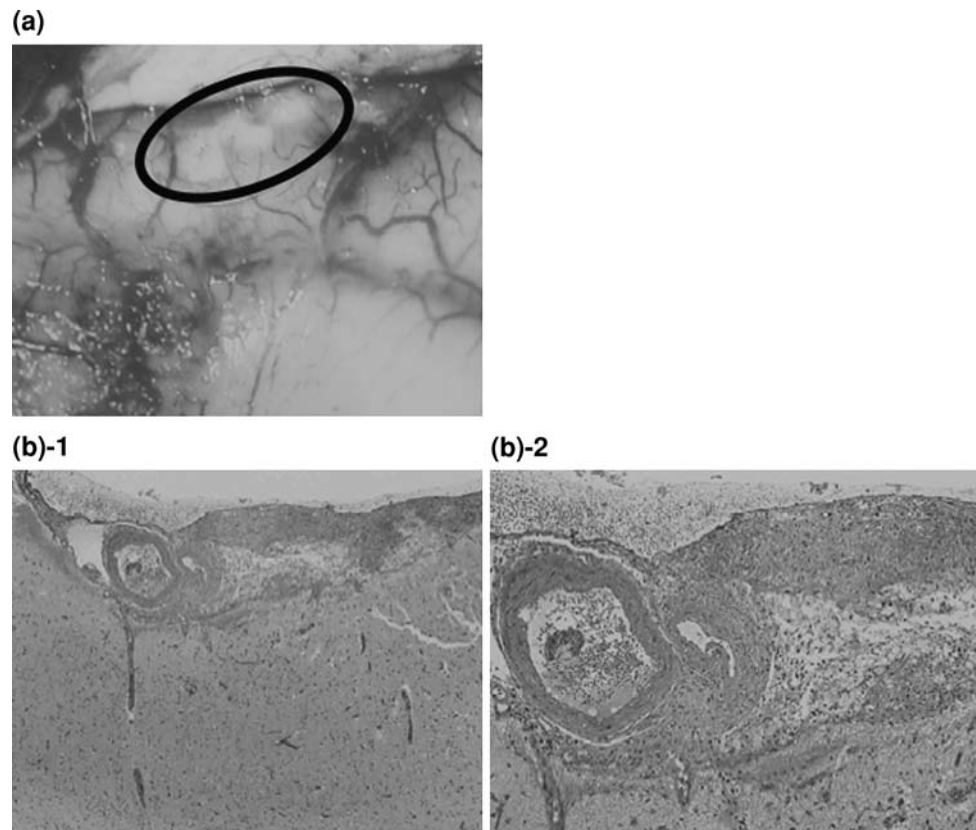


Fig. 3 Brain biopsy: **a** macroscopic aspect of the occipital lobe. The yellowish white granulomatous lesions are demonstrated (in *ellipse*). **b** Histological examination ([b]-1 H&E staining, $\times 100$, [b]-2 H&E staining, $\times 200$); necrotizing epithelioid granulomatous lesion was formed around the vessel on the subarachnoid space and occupied the subarachnoid space. Lymphocytes and epithelioid cells (CD68 positive in immunostaining) were aggregated in granulomatous lesion, and necrotizing lesion with many types of cells was located under the granulomatous lesion



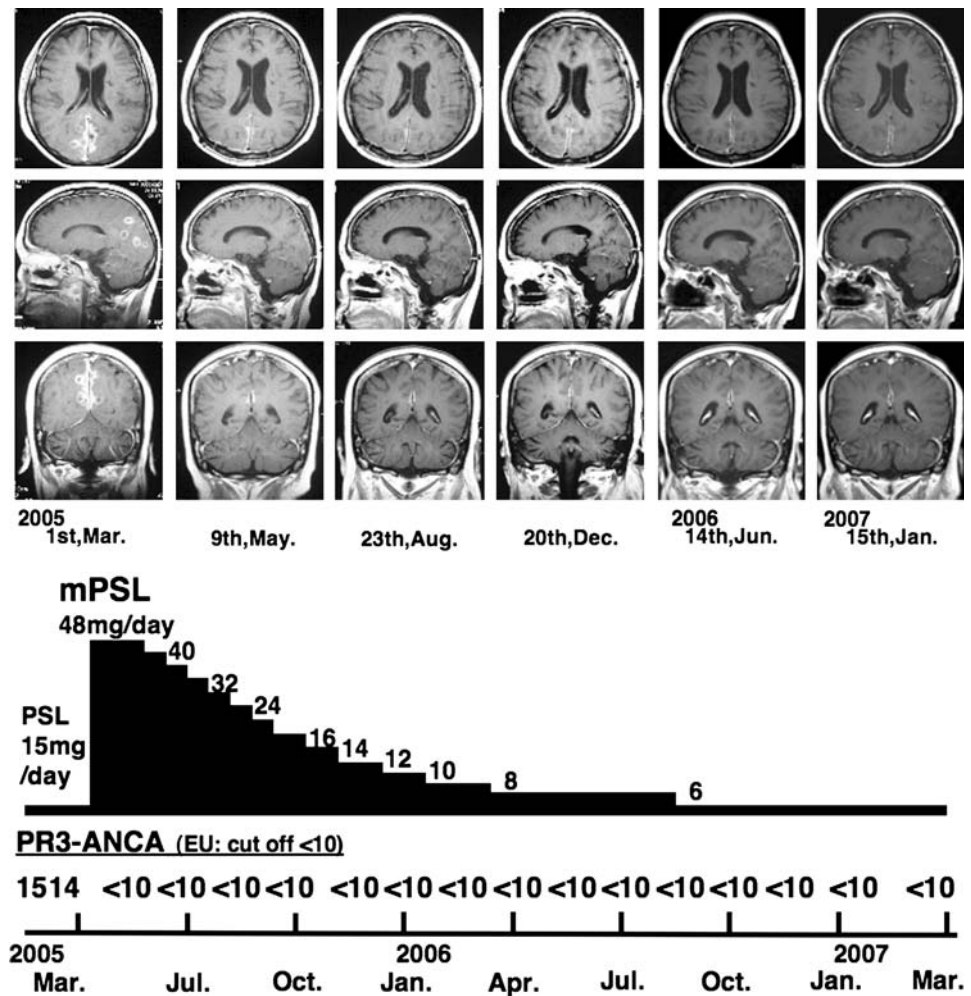
(26%); (3) primary necrotizing granulomas in the skull, meninges, cranial nerves, or brain (4%). In a study of 19 cases, Murphy et al. [3] found that meningeal thickening was the most common CNS involvement (occurring in 11 of the 19 patients) and that this thickening was adjacent to nasal, orbital, or sinus lesions in 5 of these 11. However, thickening that is non-adjacent to CNS granulomatous lesions (such as occurred in our case) has been observed only once and is quite rare. In addition, to our knowledge, WG with CNS granulomatous lesion in the occipital lobe has not been reported.

In this case, the CNS lesions appeared as multiple ring-like structures in T1-weighted Gd-enhanced MR imaging. Since MR imaging of brain abscesses, neoplasms, and metastases can result in similar patterns, the diagnosis required confirmation, and so brain biopsy was performed. Although an invasive procedure, the biopsy was helpful for the differential diagnosis in this case. CNS lesions of WG on MR images have been characterized as either homogeneous-enhancing or ring-enhancing lesions on Gd-enhanced T1-weighted images or as hyperintense signal lesions contrasting with white matter on T2-weighted images [3, 6, 7]. Thus, brain MR imaging is also useful for differential diagnosis. Whereas, in this case, Ga accumulations were coincidentally located in lesions detected by MR

imaging, few reports of Ga scintigraphy in patients with WG have been published [8] and the value of the study in detecting the disease is uncertain.

Our patient was treated with corticosteroid alone because of severe chronic renal failure and frequent recurrence of bacterial pneumonia. The CNS lesions responded well and regressed quickly. We succeeded in tapering the dose of corticosteroid without any recurrence. Although conventional treatment for WG is the combination of corticosteroid and cyclophosphamide (CPA), in some cases of WG with CNS lesions [9–11], only high-dose corticosteroid was administered as the induction therapy, and each clinical conditions and MR imaging ameliorated dramatically by the therapy. This suggests that CNS involvement in some cases of WG might be reversible and that high-dose corticosteroid therapy alone might be effective, although experience with more cases is needed to confirm this possibility. But, in some previous cases, the CNS lesion relapsed during tapering the dose of corticosteroid, therefore CPA and other immunosuppressant were required. Recently, the utility of plasma exchange [12] or intravenous immunoglobulin (IVIG) [13] have been reported in cases of WG that the use of immunosuppressant is undesirable, and it will be necessary to consider those use at the time of the recurrence in future.

Fig. 4 Clinical course: these Gd-enhanced T1-weighted images (*upper* transverse, *middle* sagittal, *lower* coronal) showed that the granulomatous masses in the occipital lobe regressed promptly and serum level of PR3-ANCA was normalized after starting high-dose corticosteroid therapy. PSL prednisolone, mPSL methylprednisolone



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