

# Microscopic Polyangiitis Nodosa: A Rare Cause of Cerebral Hemorrhage

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## Abstract

Microscopic polyangiitis nodosa (MPA) is a necrotizing vasculitis that affects small vessels, typically associated with myeloperoxidase anti-neutrophil cytoplasmic antibody. Cerebrovascular diseases are rarely reported to be associated with MPA. A 41-year-old male patient presented to the emergency room with complaints of speech difficulty and loss of strength on the left upper extremity, and MPA was detected with cerebral hemorrhage and renal failure. The case report, just as we first defined with this case in the national literature, was presented to emphasize that MPA may be rarely demonstrated with symptoms of cerebrovascular involvement except for commonly seen organ involvement.

**Keywords:** Cerebral hemorrhage, renal failure, microscopic polyangiitis nodosa

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## INTRODUCTION

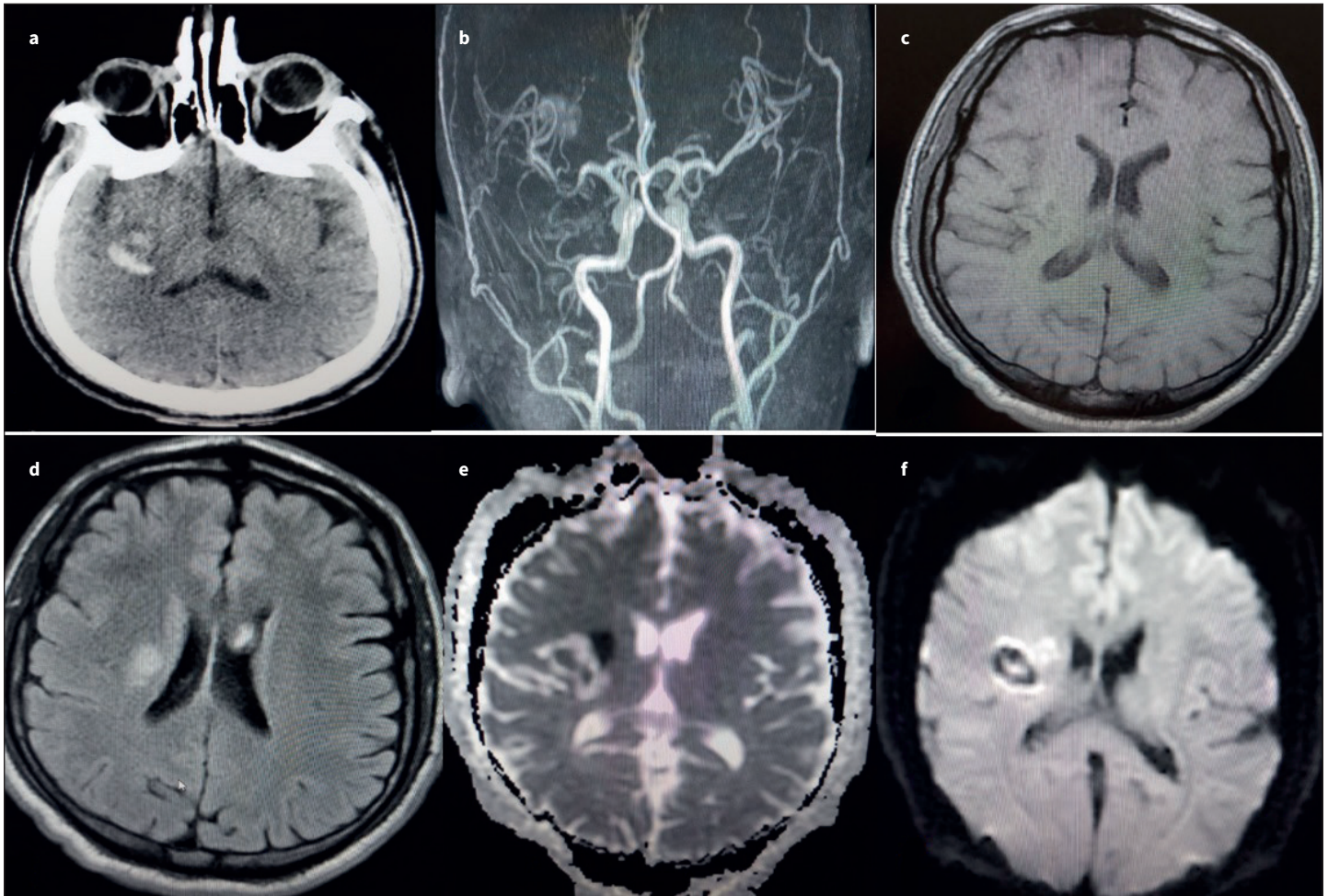
Microscopic polyangiitis nodosa (MPA) is a necrotizing vasculitis affecting small vessels, typically associated with myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA). Neurological involvement, characterized by rapid progressive glomerulonephritis, pulmonary hemorrhage, and interstitial pneumonia in this disease, is often seen as mononeuritis or symmetric distal polyneuropathy but can rarely cause cerebral artery thrombosis or cerebral hemorrhage (1-3). MPA-associated hemorrhagic stroke case, because it is a rare entity not previously defined in the national literature, has been presented to emphasize its importance.

## CASE PRESENTATION

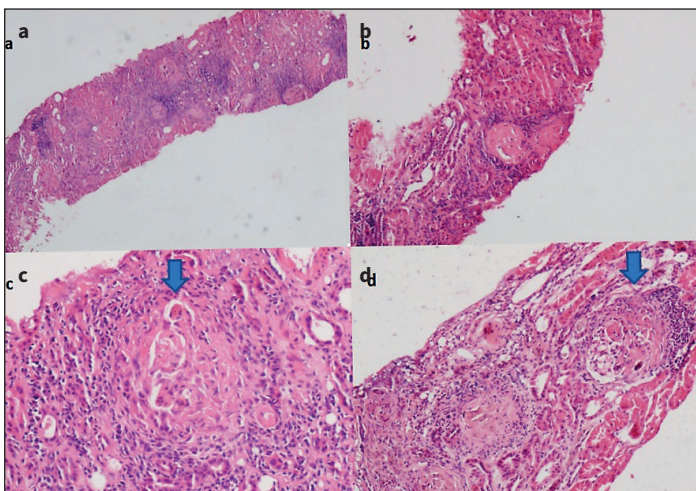
A 41-year-old male patient presented to the emergency room with acute complaints of loss of strength on the left upper extremity and speech difficulty. The patient was hospitalized due to renal dysfunction and detection of right cerebral hemorrhage on brain computed

tomography (Figure 1a). The patient was examined retrospectively through the hospital information system. Fatigue and weakness, which started 2 weeks ago, were detected. There was no history of chronic disease, drug use, and substance dependence. The patient's blood pressure was 110/80 mmHg, body temperature was 36.8 °C, heart rate was 92 beats/min, and heart rate was rhythmic. On physical examination, the patient had pale appearance, dysarthria, and loss of strength (4/5) on the left upper extremity. Laboratory results were as follows: leukocyte: 9280/mm<sup>3</sup>, hemoglobin: 8.7 g/dL, mean corpuscular volume: 82 fl, platelet: 31,910/mm<sup>3</sup>, prothrombin time: 14.3 s, activated partial thromboplastin time: 33.1 s, erythrocyte sedimentation rate: 60 mm/h (normal interval <15 mm/h), C-reactive protein: 21.3 mg/dL (normal interval <0.3 mg/dL), creatinine: 4.9 mg/dL, urea: 122 mg/dL, total serum protein: 5.9 g/dL, albumin: 2.8 g/dL, calcium: 8.2 mg/dL, phosphorus: 4.0 mg/dL, uric acid: 7.0 mg/dL, sodium: 134 mmol/L, potassium: 5.3 mmol/L, pH: 7.31, HCO<sub>3</sub>: 18.9, pCO<sub>2</sub>: 37 mmHg, (negative)





**Figure 1. a-f:** (a) In brain computed tomography (axial), extending to the external capsule in the right temporal lobe, around edema, minimal pressure of the lateral ventricular body, hyperdense appearance of approximately 20 mm size compatible with cerebral hematoma. (b) Magnetic resonance (MR) angiography (coronal) detected no evidence of arteriovenous malformation, aneurysm, and stenosis (c, d) in brain MR imaging (axial), right lentiform nucleus posteriorly uniformly restricted, edematous, T1A hyperintense and hypointense on T2 and FLAIR, compatible appearance with 19×4 mm hematoma, (e, f) in diffusion-weighted MR imaging (axial), in the right basal ganglion area, the appearance of significant diffuse restriction in favor of acute-subacute ischemia-infarction localization taking place in the right ventricular cortex.



**Figure 2. a-d:** (a) Significant global sclerosis in the glomeruli (hematoxylin and eosin, H&E ×40), (b) glomeruli with global sclerosis (H&E ×200), (c) with arrow, fibrocellular crescentic glomeruli and fibrinoid necrosis in the focal area (H&E ×200), (d) with arrow, fibrocellular crescentic glomeruli and glomerular solidified candidate to become global sclerosis (H&E ×100).

BE: -6, ferritin: 256 ng/dL, transferrin saturation: 9%, parathormone: 47 pg/mL, vitamin B12: 178.2pg/mL, and folate: 3.34 ng/mL. In the sediment microscopy of urine, 10-25 red blood cells/high-power field (hpf) and 5-10 WBCs/hpf were counted, and proteinuria was detected at 1.96 g/day. Renal length and echogenicity were normal on abdominal ultrasound examination. On serological tests, viral marker, immunoglobulin, light chain, serum immunofixation, antinuclear antibody (ANA), and serum complement values were within the normal reference interval. MPO-ANCA value was measured as 52.9 U/mL, and it was higher than the normal reference interval of <20 U/mL (negative). Anti-proteinase 3-ANCA was measured as 2.79 U/mL with a normal range of <20 U/mL (negative). The presence of hemorrhagic foci and cerebral ischemia was also compatible with necrotizing vasculitis on magnetic resonance imaging of the brain (Figures 1b-f). Pauci-immunocrescentic glomerulonephritis and global glomerulosclerosis (60%) were detected in renal biopsy due to unexplained renal failure and MPO-ANCA positivity (Figure 2). The patient had normal chest computed tomography and echo-



cardiography findings and was diagnosed with MPA with acute hemorrhagic stroke. Intravenous (iv) pulse 1 g/day and maintenance 1 mg/kg/day prednisolone treatment for 3 days/week and 0.5 g/m<sup>2</sup>iv cyclophosphamide treatment every 4 weeks were started. Because the patient's neurological symptoms and findings obviously improved, he did not need dialysis, and serum creatinine level was 3.9 mg/dL at discharge. The patient was scheduled for 6 doses of cyclophosphamide treatment at 4-week intervals. MPO-ANCA level was detected as 18.53 U/mL after the third dose intake. Following the fourth dose of cyclophosphamide, lobar pneumonia therapy was initiated, and then the patient was given 1 mg/kg/day oral azathioprine and 0.1-0.2 mg/kg/day prednisolone maintenance treatment. On the last follow-up, serum creatinine level was measured as 4.2 mg/dL, and the follow-up of the patient, who is clinically stable, has been ongoing. Informed consent was obtained from the patient who participated in this study.

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## DISCUSSION

Although respiratory and renal involvements are quite common in MPA, cerebrovascular involvement is seen at approximately 4% (1, 4). The most common form of MPA is infarction, but rarely cerebral and subarachnoid hemorrhage. It is suggested that thromboembolism-associated infarct or vascular rupture, observed in necrotizing vasculitis, may cause cerebral hemorrhage (5). The authors mostly emphasize that thromboembolism-associated ischemia develops during the active phase of the disease, after then, the addition of cerebral hemorrhage adversely affects the prognosis (1, 2, 6). In the present case report, serological findings, comorbidity of cerebral ischemia and hemorrhage, and presence of pauci-immunocrescentic glomerulonephritis support MPA-associated small vessel vasculitis.

Central nervous system involvement is also common in Wegener granulomatosis (WG), which causes small vessel vasculitis, but typical respiratory tract involvement, which is seen in WG, was not seen in the present case report. However, WG has mostly anti-proteinase 3-ANCA positivity instead of MPO-ANCA (7, 8). The other small vessel vasculitis causes, systemic lupus erythematosus (SLE) and Churg-Strauss syndrome, were excluded by using some diagnostic criteria. In the present case report, SLE was excluded with normal complement level, absence of ANA, and absence of renal biopsy-specific immunohistochemical staining. Churg-Strauss syndrome was excluded with absence of asthma history and absence of eosinophil in renal biopsy.

In the management of MPA with cerebrovascular involvement, long-term neurological recovery has been demonstrated with azathioprine or mycophenolate maintenance treatment after pulse IV steroid and cyclophosphamide induction (9). In the case reports, it has been indicated that the use of pulse steroid and cyclophosphamide in the initial treatment provides significant improvement in neurological findings (9, 10). However, it has been indicated that adding plasmapheresis to immunosuppressive treatment can accelerate neurological improvement

(11). This case report was evaluated according to the Kidney Disease: Improving Global Outcomes clinical guideline on glomerulonephritis. Although nearly 60% of glomerulosclerosis was observed in renal biopsy, steroid and cyclophosphamide treatments were preferred because of non-renal involvement (12). Neurological involvement was controlled by steroid and cyclophosphamide treatments without plasmapheresis. We believe that early diagnosis and treatment play an important influence to control MPA-associated neurological involvement.

## CONCLUSION

It should be considered that MPA may be rarely presented with cerebrovascular involvement symptoms, except for common organ involvement. MPO-ANCA positivity is helpful for early diagnosis. In addition, early treatment is important for improving neurological involvement and prognosis.

**Informed Consent:** Informed consent was obtained from the patient who participated in this study.

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**Conflict of Interest:** The authors have no conflicts of interest to declare.

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