

A case of microscopic polyangiitis presenting with acute spinal subdural hemorrhage

Won Yong Suh¹, Eun Kyoung Lee²

¹Division of Nephrology, Department of Internal Medicine, Cheonan Medical Center, Cheonan, Korea

²Division of Nephrology, Department of Internal Medicine, Dankook University Hospital, Dankook University College of Medicine, Cheonan, Korea

This report describes a case of a 62-year-old woman with microscopic polyangiitis (MPA) who developed acute spinal subdural hemorrhage. MPA was confirmed by positive autoantibodies to myeloperoxidase and focal segmental necrotizing and pauci-immune crescentic glomerulonephritis on renal biopsy. She did not recover from paraplegia due to acute spinal subdural hemorrhage, despite decompression operation and aggressive immunosuppression. Although spontaneous spinal hemorrhage in MPA patients is very rare, the prognosis for such patients is poor. Considering the possibility of ongoing vasculitis activity in extra-renal organs, clinicians should be very cautious to attenuate the strength of immunosuppressant drugs, even in patients with chronic or irreversible renal pathology.

Keywords: Microscopic polyangiitis, Spinal, Spinal subdural hematoma

Introduction

Microscopic polyangiitis (MPA) is a type of antineutrophil cytoplasmic antibody-associated vasculitis (AAV). There are three forms of AAV; MPA, granulomatosis with polyangiitis (GPA or formerly Wegener's granulomatosis), and eosinophilic GPA (EGPA or formerly Churg–Strauss vasculitis). MPA is characterized by necrotizing inflammation of small vessels with circulating autoantibodies to myeloperoxidase (MPO). It involves the kidneys, lungs and skin, presenting as renal failure, rapidly progressive

glomerulonephritis, pulmonary hemorrhage, purpuric skin rash, and/or constitutional symptoms such as fever and weight loss [1]. Central nervous system (CNS) involvement is very rare and has previously been limited to cerebral lesions such as intracerebral hemorrhage, subarachnoid hemorrhage, and hypertrophic meningitis [2,3].

Herein we report, along with a review of literature, the first case of MPA with acute spinal subdural hemorrhage in Korea, which occurred in a patient without cerebral lesions and who was not receiving any antithrombotic agent.

Case report

A 62-year-old woman who presented with azotemia and proteinuria was admitted to our hospital for hemodialysis. Eight days before her admission, renal biopsy was performed in the United States. Her doctor in the United States assessed her renal disease as advanced chronic kidney disease, most likely secondary to vasculitis, based on the preliminary biopsy report and presence of anti-

Received March 12, 2018; **Revised** April 19, 2018;

Accepted April 19, 2018

Correspondence: Eun Kyoung Lee

Division of Nephrology, Department of Internal Medicine, Dankook University Hospital, Dankook University College of Medicine, 119 Dandaero, Dongnamgu, Cheonan 31116, Korea. E-mail: nephrologyek@hanmail.net

ORCID: <http://orcid.org/0000-0001-5864-9679>

Copyright © 2018 by The Korean Society of Nephrology

© This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

MPO antibodies. The preliminary biopsy report showed a significant degree of scarring and fibrous crescents with minimal viable tissue. Her anti-MPO antibody level was 48.2 units/mL (normal range, 0–6 units/mL). Her doctor administered 30 mg of prednisone daily. Although she did not bring the confirmative biopsy report, we decided to maintain the dosage of steroid to avoid aggressive immunosuppression, based on the doctor's note, her long history of hypertension, and her long-term use of ibuprofen for arthritis.

On admission, her blood pressure was 177/101 mmHg, and her pulse rate was 79 beats/minute. Her initial laboratory findings were as follows; hemoglobin 10.7 g/dL, blood urea nitrogen 95.9 mg/dL, creatinine 6.46 mg/dL, and urinalysis showing protein (2+) and occult blood (2+). Serologic parameters including immunoglobulin (Ig) G,

IgA, IgM, C3, C4, antinuclear antibodies, and anti-proteinase 3 antibodies were normal, except anti-MPO antibodies, which were positive > 8.0 (normal range, < 1.0 AI [arbitrary index]). She recovered from general weakness and had normotension after the third cycle of hemodialysis. On the sixth day of admission, she complained of sudden back pain with headache over a few hours, which did not subside with pain controllers. Her blood pressure was measured at 186/108 mmHg upon symptom onset, and computed tomography angiography revealed no evidence of aortic dissection. After five hours of initial back pain, motor and sensory loss of both lower extremities developed. We performed a spinal magnetic resonance imaging scan, which showed subdural hemorrhage in the cervical and thoracolumbar spinal canal with cord compression (Fig. 1).



Figure 1. Magnetic resonance images. (A) The sagittal T1-weighted image reveals prominent spinal cord compression at the level of the mid-thoracic spine (from T5 to T9). (B, C) The axial T2- and T1-weighted image shows subdural fluid compressing the cauda equina anteriorly at the level of L4 to L5.

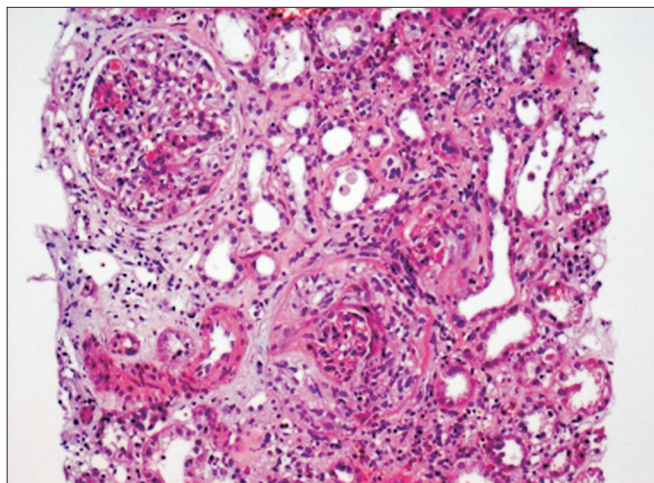


Figure 2. Kidney biopsy finding. Focal segmental necrotizing crescentic glomerulonephritis with moderate tubular atrophy and interstitial fibrosis are shown (H&E stain, $\times 100$).

Contrary to the previous doctor's note, confirmative biopsy results showed focal segmental necrotizing and pauci-immune crescentic glomerulonephritis with moderate tubular atrophy and interstitial fibrosis (Fig. 2). This suggested the occurrence of progressive MPA activity in the kidney. On the ninth day, the patient was treated with three consecutive daily administrations of 500 mg methylprednisolone intravenously and subsequent daily oral administration of 50 mg prednisolone with 50 mg cyclophosphamide.

On the 35th day, we discontinued hemodialysis because the patient's renal function had partially recovered. On the 60th day, the treatment was stopped due to cytomegalovirus stomatitis and pancytopenia. On the 70th day, only prednisolone was resumed. On the 90th hospital day, acute respiratory distress syndrome with massive pulmonary hemorrhage developed. On the 95th hospital day, she died despite plasmapheresis and aggressive immunosuppression. Fig. 3 shows the summary of her clinical course and treatment.

Discussion

To the best of our knowledge, this is the first case of MPA with spinal subdural hemorrhage in Korea.

MPA is a necrotizing vasculitis that primarily affects capillaries, venules, and arterioles, most commonly manifesting as necrotizing glomerulonephritis and/or pulmonary capillaritis. Neurologic involvement may

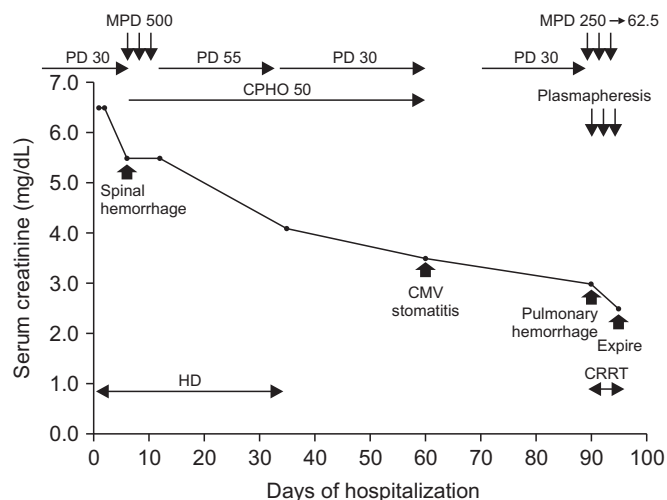


Figure 3. Clinical course and treatment of the patient.

CMV, cytomegalovirus; CPHO, cyclophosphamide (mg/day); CRRT, continuous renal replacement therapy; HD, hemodialysis; MPD, methylprednisolone (mg/day); PD, prednisolone (mg/day).

occur in up to 55–79% of patients with MPA [3]. The peripheral nervous system is more commonly affected than the CNS, with findings such as mononeuritis multiplex or distal symmetric polyneuropathy. CNS involvement is estimated to occur in 10% to 30% of patients with MPA [2]. However, reported cases of MPA with CNS disease were limited to cerebral lesions, such as intracerebral hemorrhage, subarachnoid hemorrhage, and hypertrophic meningitis [2,3]. Decker et al [4] reviewed AAVs with spinal cord involvement that mostly presented as dural mass rather than hemorrhage. They suggested three mechanisms by which the spinal cord may become involved in AAV: (1) necrotizing vasculitis of the spinal vasculature predisposing to hemorrhage or thrombosis; (2) local compression of the spinal cord by inflamed tissues such as the meninges; and (3) formation of primary spinal granulomas in granulomatous vasculitis [4]. The possible pathogenic mechanism of the patient in our case could be the first of these.

Non-traumatic or non-iatrogenic spontaneous hemorrhages in MPA are very rare and hence difficult to diagnose at the time of occurrence. Considering de Beer et al.'s review of 122 cases with spontaneous spinal hematomas [5], the major causes were coagulopathies and vascular malformations. They suggested vasculitis as a rare and new etiologic category. Two cases of MPA [4,6], one case of GPA [7], and three cases of EGPA [8–10] presented with spinal hemorrhage; these two cases of MPA

consisted of one patient with concurrent intracerebral hemorrhage [4] and one autopsy-proven spinal hemorrhage [6].

In this case, vasculitis activity was not accurately assessed because the patient did not bring the confirmative renal biopsy report on admission to our hospital. A Birmingham Vasculitis Activity Score calculated at one point is considered not as disease activity, but only as an outcome parameter in systemic vasculitis [11]. Although Chen et al [12] recently suggested plasma complement factor H as a disease activity index of AAV, it is not yet clinically useful. Spontaneous spinal hemorrhage in MPA patients is very rare; however, prognosis is poor for such patients.

In conclusion, considering the possibility of ongoing vasculitis activity in extra-renal organs, clinicians should be very cautious to attenuate the strength of immunosuppressant drugs, even in patients with chronic or irreversible renal pathology.

Conflicts of interest

All authors have no conflicts of interest to declare.

References

- [1] Jennette JC, Falk RJ, Bacon PA, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 65:1-11, 2013
- [2] Han S, Rehman HU, Jayaratne PS, Carty JE. Microscopic polyangiitis complicated by cerebral haemorrhage. *Rheumatol Int* 26:1057-1060, 2006
- [3] Sassi SB, Ghorbel IB, Mizouni H, Houman MH, Hentati F. Microscopic polyangiitis presenting with peripheral and central neurological manifestations. *Neurol Sci* 32:727-729, 2011
- [4] Decker ML, Emery DJ, Smyth PS, Lu JQ, Lacson A, Yacyshyn E. Microscopic polyangiitis with spinal cord involvement: a case report and review of the literature. *J Stroke Cerebrovasc Dis* 25:1696-1704, 2016
- [5] de Beer MH, Eysink Smeets MM, Koppen H. Spontaneous spinal subdural hematoma. *Neurologist* 22:34-39, 2017
- [6] Baldwin L, Poller D, Ellison D. February 2001: A 74 year old man with a history over 3 months of increasing dyspnea and malaise. *Brain Pathol* 11:389-390; 393, 2001
- [7] Guilfoyle MR, Khan S, Helmy A, et al. Spinal intradural haemorrhage in a patient with Wegener's Granulomatosis. *Clin Neurol Neurosurg* 112:341-343, 2010
- [8] Kukita CC, Gobatto AL, Lobo AZ, Taniguchi LU. Spinal hematoma complicating a Churg-Strauss syndrome patient: a previously unreported association. *Clinics (Sao Paulo)* 67: 855-857, 2012
- [9] Yeo LL, Shanmugam GN, Thamboo TP, Lahiri M, Rathakrishnan R. Spinal cord haematoma due to Churg-Strauss vasculitis. *Rheumatology (Oxford)* 52:1213, 2013
- [10] Diamanti L, Berzero G, Bini P, et al. Spinal hemorrhage in eosinophilic granulomatosis with polyangiitis (Churg-Strauss). *J Neurol* 261:438-440, 2014
- [11] Flossmann O, Berden A, de Groot K, et al. Long-term patient survival in ANCA-associated vasculitis. *Ann Rheum Dis* 70:488-494, 2011
- [12] Chen SF, Wang FM, Li ZY, Yu F, Zhao MH, Chen M. Plasma complement factor H is associated with disease activity of patients with ANCA-associated vasculitis. *Arthritis Res Ther* 17:129, 2015