Microscopic Polyangiitis with Spinal Cord Involvement: A Case Report and Review of the Literature

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Background: Microscopic polyangiitis (MPA) is an ANCA-associated vasculitis (AAV; ANCA denotes antineutrophil cytoplasmic antibody) that causes necrotizing inflammation of small blood vessels. Renal and pulmonary manifestations are common whereas central nervous system (CNS) involvement, and in particular spinal disease, is rare. *Methods:* We reviewed a case of MPA presenting with spinal intradural hemorrhage and intracerebral hemorrhage. We also summarized all reported cases of AAV with spinal cord involvement in the literature (database search included MEDLINE, Embase, Scopus, and Proquest with no date or language restriction). *Results:* We reviewed 20 cases of AAV with spinal cord involvement (12 granulomatosis with polyangiitis [GPA], 4 eosinophilic granulomatosis with polyangiitis, 2 MPA, and 2 cases diagnosed as AAV only) and reported demographic information, clinical features, methods of diagnosis, treatment, and patient outcome. Although CNS involvement has been associated with a poor prognosis, 14 of 18 cases that reported outcome data achieved remission during follow-up. Death occurred in 3 patients diagnosed with GPA and in 1 patient with MPA. Our patient with MPA deteriorated rapidly despite use of prednisone and died. *Conclusions:* AAV can present with brain and spinal cord involvement, even in the absence of systemic disease. CNS disease may be responsive to immunosuppressive therapy (e.g., steroids and cyclophosphamide) in several of the cases reviewed. **Key Words:** Microscopic polyangiitis—antineutrophil cytoplasmic antibody-associated vasculitis—spinal cord—myelopathy—central nervous system.

Introduction

Microscopic polyangiitis (MPA) is a systemic necrotizing vasculitis with weak to absent immune deposition (pauci-immune). MPA is an ANCA-associated vasculitis (AAV; ANCA denotes antineutrophil cytoplasmic antibody). There are 3 distinct forms of AAV, all of which primarily affect small vessels, including MPA, granulomatosis with polyangiitis (GPA or formerly Wegener's granulomatosis), and eosinophilic granulomatosis with polyangiitis (EGPA or formerly Churg–Strauss vasculitis).[1] On immunofluorescence, ANCA may cause a cytoplasmic (cANCA) pattern or a perinuclear (pANCA) pattern. The antigenic targets causing cANCA and pANCA are usually proteinase 3 (PR3-ANCA) and myeloperoxidase (MPO-ANCA), respectively. MPO-ANCA and PR3-ANCA can occur in any of the 3 forms of AAV, meaning that these diseases cannot be distinguished on the basis of ANCA specificity alone. Between 80% and 95% of

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ANCA-positive GPA, patients exhibit cANCA or PR3-ANCA whereas 40%-80% of ANCA-positive MPA patients show pANCA or MPO-ANCA positivity. Both MPO-ANCA and PR3-ANCA have been observed in EGPA patients with variable frequency.[2]

MPA is a multisystem disease that often presents with renal, pulmonary, and dermatologic involvement. Findings may include renal failure, rapidly progressive glomerulonephritis, pulmonary hemorrhage, purpuric skin rash, and/or constitutional symptoms such as fever and weight loss.[3] Neurologic involvement may occur in up to 55%-79% of MPA cases.[4] The peripheral nervous system is more commonly affected than the central nervous system (CNS) with findings such as mononeuritis multiplex or distal symmetric polyneuropathy.[4] CNS involvement is less common and is estimated to occur in 10%-30% of MPA patients.[5]

Published data of MPA with CNS disease are limited to case reports involving cerebral lesions such as stroke, intraparenchymal hemorrhage, subarachnoid hemorrhage (SAH), and hypertrophic pachymeningitis.[4] Spinal cord involvement in MPA is rare. We report a case of MPA presenting with spontaneous spinal SAH and intracerebral hemorrhage. We also reviewed the literature and reported a summary of published cases of AAV with spinal cord involvement.

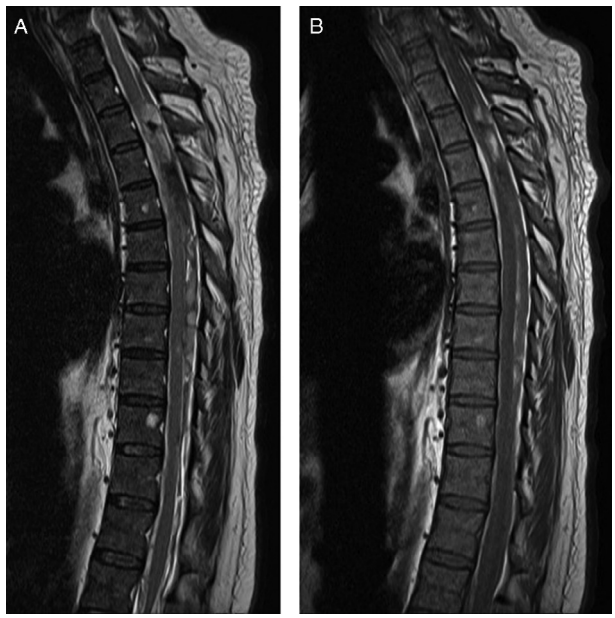

Figure 1. *A T2-weighted MRI (A, left) and T1-weighted MRI (B, right) of the thoracic spine with extensive acute intradural hemorrhage extending from T2 to T12. A small hemorrhage is seen within the spinal cord at T3.*

Case Report

A previously healthy 53-year-old man presented to hospital with acute onset mid-thoracic back pain radiating to the legs, progressive bilateral leg weakness, and urinary retention over a 7-day period. On examination, there were bilateral leg weakness, diminished sensation to the right lower extremity, bilateral upgoing plantar reflex, and saddle anesthesia.

Spinal magnetic resonance imaging (MRI) revealed an intradural extramedullary hemorrhage extending from the level of T2 to T12 associated with a small intramedullary lesion within the cord at T3 (Fig 1, A,B). Computed tomography angiography of the spine showed no apparent cause of the hemorrhage. An urgent T2-T5 laminectomy with intradural evacuation of hematoma and resection of the mass lesion was performed. Microscopic examination of the resected lesion revealed hemorrhagic tissue containing a few blood vessels that were focally necrotizing with transmural inflammatory cell infiltrates (Fig 2). Eosinophils and granulomas were not found. There was no evidence of neoplasm or infection.

The postoperative period was complicated at 5 days by acute testicular pain (ultrasound showing multiple hemorrhages bilaterally). The patient recovered in hospital and was clinically well for discharge home. However, at 14 days postadmission, he became acutely confused. A computed tomography (CT) scan of the head showed 2 separate areas of acute parenchymal hemorrhage within the right and left frontal lobes, accompanied by rupture into the ventricular system and subfalcine herniation (Fig 3). A right frontal craniectomy with evacuation of intraparenchymal hematoma was performed. Histological examination of the evacuated hematoma confirmed necrotizing vasculitis with associated intraparenchymal hemorrhage (Fig 4). Eosinophils and granulomatous formation were not present.

During subsequent workup, the patient was positive for p-ANCA with anti-MPO level of 658 mean fluorescence units. Inflammatory markers were elevated on admission (ESR 73 mm/h and CRP 40.7 mg/L) and peaked at the time of intracerebral hemorrhage with ESR 85 mm/h and CRP 96.2 mg/L. All other immunologic markers tested (including ANA, anti-dsDNA, RF, ENA, anti-SSA, anti-SSB, and anti-RNP) were negative. Complement levels showed an elevation of C4 (.68 g/L) and normal C3 (1.10 g/L). CSF and serum ACE levels, anti-GBM, and cryoglobulin screen were negative. Blood and CSF cultures were negative. Viral testing (HBV, HCV, HIV, CMV, EBV, PV-B19) was also negative. At the time of intracerebral hemorrhage, a lumbar puncture revealed xanthochromia with total white blood cell count 100×10^6/L (93% polymorph, 1% lymphocytes), red blood cell count $11{,}400 \times 10^6$/L, elevated glucose 5.2 mmol/L, and elevated protein 2.16 g/L. The patient's family also reported a history of chronic sinus infections, epistaxis, and hearing loss to the left ear, along with increasing fatigue and weight loss over the preceding year.