Microscopic Polyangiitis Presenting With A Pure Sensory Peripheral Symmetric Polyneuropathy

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Microscopic Polyangiitis Presenting With A Pure Sensory Peripheral Symmetric Polyneuropathy

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Background

- Microscopic polyangiitis (MPA) is a systemic small-vessel necrotizing vasculitis with a strong association with anti-myeloperoxidase anti-neutrophilic cytoplasmic antibodies (MPO-ANCA). MPA has little or no immune deposit and is not associated with granulomatous inflammation.[1]
- In most cases MPA presents with rapidly progressive necrotizing glomerulonephritis and occasionally with pulmonary hemorrhage.[2] Over 70% of patients have constitutional symptoms at diagnosis and disease manifestations may involve any organ system.[3] MPA may also present without renal or pulmonary involvement.[2,4]
- Peripheral neuropathy has frequently been reported as a symptom of ANCA-associated vasculitis and is commonly present at disease onset. It may also be an initial manifestation of the disease state, but there is limited evidence comparing the incidence of neuropathy with the other manifestations of systemic vasculitides.[1,4,5]
- Studies have shown that a majority of those with ANCA-associated vasculitis report peripheral neuropathy at some point in the disease process, but less than 25% report it at initial presentation. Among the ANCA-associated vasculitides, MPA appears to have the lowest incidence of reported peripheral neuropathy; sensory or motor.[1,5]
- A recent case report of MPA presents a patient with lower extremity polyneuropathy preceding renal manifestations.[6]
- MPA is treated in two phases: Induction phase is acute treatment with systemic corticosteroids and immunosuppressive agents such as cyclophosphamide or rituximab. Maintenance phase begins 1-2 months after resolution of inflammation and typically involves azathioprine.[7,8] Patients may also be treated with plasma exchange during induction phase.[2,8]

First Admission		Second Admission
11.1 / 33	Hemoglobin / Hematocrit	6.2 / 18.1
1.47	Serum Creatinine	5.89
100	ESR	125
2.2	CRP	10.3
780	Rheumatoid Factor	584
	CCP Antibody	Negative
Negative	ANA Panel with Reflex	Negative
Negative	Lyme Titer	
6.3%	HgbA1c	5.9%
	ASO Titer	27 (Ref. <240)
	Hepatitis/HIV Screen	Negative
	ACE Level	29 (Ref. <20)
	PR3-ANCA (c-ANCA)	6.2 (Ref. <20)
	MPO-ANCA (p-ANCA)	148 (Ref. <20)
	Anti-GBM	Negative
	Cryoglobulins	Negative
Chronic Inflammatory Stress Response	SPEP Interpretation	Polyclonal hypergammaglobulinemia

Table 1. Selected laboratory values from two hospital admissions. Hemoglobin/Hematocrit and serum creatinine are from initial presentations.

Case Presentation

A 58 year old woman without significant past medical history presented with the chief complaints of weakness and loss of balance. She described a weakness and heaviness of her bilateral lower extremities and felt off-balance with difficulty ambulating. She also described a clumsiness and inability to correctly use her left hand.

This occurred in the context of a one year history of "pins and needles" sensation in her bilateral feet.

Physical exam revealed a stocking-glove distribution of decreased pinprick sensation, decreased vibration sense in the bilateral toes, ataxic gait, and a positive Romberg sign. The patient underwent extensive imaging revealing the following results:

- CT Head: no acute abnormality
- MRA Head/Neck: 50% stenosis of proximal right ICA, 75% stenosis of left ICA, both felt to be artifactual
- MRI Brain: scattered foci of non-specific supratentorial white matter signal abnormality, but no acute abnormality
- Chest XR: interstitial prominence laterally at both lung bases most likely represents chronic interstitial disease
- 2D ECHO: aneurysmal interatrial septum without evidence of shunt, EF 60%
- CT Chest: interstitial lung disease, mild mediastinal and hilar adenopathy, mild honeycombing at bilateral bases
- CT Abd/Pelvis: 6cm cystic right pelvis mass, representing likely ovarian cyst

Laboratory studies revealed an elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), positive rheumatoid factor (RF), and elevated serum creatinine. Patient was ultimately discharged home with a diagnosis of peripheral neuropathy likely secondary to thiamine deficiency.

Three months after discharge the patient presented with the acute onset of substernal chest pain exacerbated by inspiration and associated with shortness of breath.

Initial laboratory examination revealed marked acute oligoanuric renal failure, proteinuria, anemia, and new diffuse bilateral perihilar infiltrates on chest x-ray and CT. Bronchoscopy revealed acute alveolar hemorrhage. Further laboratory studies demonstrated elevated anti-myeloperoxidase anti-neutrophilic cytoplasmic antibodies (MPO-ANCA). The patient then underwent renal biopsy which revealed acute and chronic pauci-immune necrotizing, sclerosing, and crescentic glomerulonephritis associated with focal necrotizing vasculitis; typical of changes seen with MPO-ANCA seropositivity, leading to a diagnosis of microscopic polyangiitis.

The patient was initiated on hemodialysis due to her rapidly progressive glomerulonephritis. She was treated with pulse dose methylprednisolone followed by stress dose prednisone, as well as therapeutic plasma exchange and oral cyclophosphamide. Her maintenance phase included azathioprine and prednisone. Her peripheral neuropathy persists despite treatment. She remains dialysis dependent despite two weaning attempts and is currently undergoing transplant evaluation.

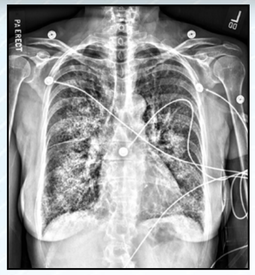

Figure 1. Chest x-ray from second admission showing new diffuse bilateral perihilar opacities.

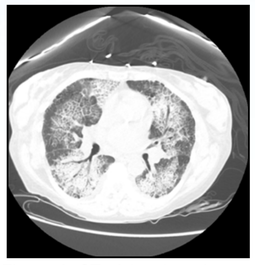

Figure 2. CT of the chest from second admission demonstrating alveolar groundglass opacities and air bronchograms.

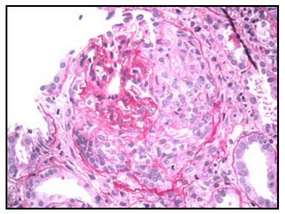

Figure 3. Light microscopy of renal biopsy demonstrating crescentic glomerulonephritis.

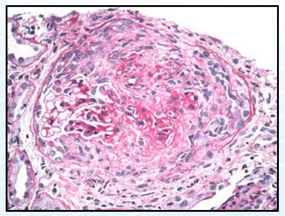

Figure 4. Light microscopy of kidney biopsy again demonstrating compression of the glomerulus by a cellular crescent.

Discussion

Our case is a rare presentation of microscopic polyangiitis (MPA) with concurrent diffuse alveolar hemorrhage and dialysis dependent rapidly progressive glomerulonephritis in the setting of long-standing bilateral stocking-glove distribution pure sensory symmetric peripheral neuropathy.

Previous literature has demonstrated that a majority of those with ANCA-associated vasculitis report peripheral neuropathy at some point in the disease process, but few had active vasculitic neuropathy at baseline.

Patients with vasculitic nephropathy at baseline have a higher median number of organ systems involved when compared with those without neuropathy, and also reported higher Birmingham Vasculitis Activity Scores, which is a clinical checklist of items organized by organ system used to determine disease activity.

The European Vasculitis Study Group trials showed that a pure sensory neuropathy, which our patient developed early in her disease course, was not reported in any patients with MPA. However, our patient did not undergo electrophysiologic confirmation of her neuropathy.

Studies demonstrate that non-specific symptoms may be present for months to years prior to diagnosis of MPA. This case demonstrates the difficulty of recognizing MPA when only a single organ system is involved and that ANCA-associated vasculitis should be included on the differential diagnosis of peripheral neuropathy with unclear etiology. It also exemplifies the need for further research on peripheral neuropathy in systemic vasculitides, specifically in MPA where these early presenting signs have previously shown to be less prevalent.

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