Tanaffos (2011) 10(2), 75-78

A 46-Year-Old Man with Fever and Numbness of Limbs

Ilad Alavi Darazam [1], Shirin Karimi [2], Mehrdad Bakhshayesh Karam [3], Seyed Davood Mansouri [1,4]

[1] Department of Internal Medicine, Division of Infectious Disease and Clinical Immunology, [2] Mycobacteriology Research Center, [3] Pediatric Respiratory Disease Research Center, [4] Clinical Tuberculosis and Epidemiology Research Center, NRITLD, Shahid Beheshti University of Medical Sciences, Tehran- Iran.

WHAT IS YOUR DIAGNOSIS?

A 46 year-old man was referred to this center with low grade fever and gradual progressive numbness of lower extremities since 4 months ago. He reported loss of superficial sensation of the distal aspect of the left foot started 4 months ago; it then extended to the right side and also both hands. He had no other symptoms or abnormal findings in recent months. Primary evaluations including laboratory analysis and imaging studies were unremarkable. He was a dentist, married, with three children, non-smoker and with no habitual history. His past medical history was insignificant with no history of recent travelling, exposure or transfusion. On admission, he looked well. Physical examination revealed low grade fever, pallor and loss of superficial sensation in feet and hands with no other significant findings. Laboratory analysis showed 11,000/mm3 white blood cells, 10 gr/dl hemoglobin and 300,000/mm3 platelet count, 80 mm/hr erythrocyte sedimentation rate with normal liver function tests, coagulation profile, serum lactate dehydrogenase, urinalysis, blood urea and creatinine concentrations. Angiotensin converting enzyme (ACE), antinuclear antibody (ANA), antineutrophil cytoplasmic antibodies (ANCA), serum protein electrophoresis and cerebrospinal fluid analysis were all normal. Brain and neck magnetic resonance imaging (MRI) were unremarkable. Electromyography and NCV study (EMG-NCV) were repeated because of gradual development of motor dysfunction when grasping and standing during admission and revealed severe motor nerve dysfunction. Chest x-ray showed reticular pattern in upper and lower lobes of the right lung. Chest computed tomography of the patient is shown in Figure 1. Scan of paranasal sinuses showed right maxillary sinusitis. Bronchoscopy was performed to evaluate lung lesions. A nodular endobronchial lesion was seen in right main bronchus. Histopathologic examination was non-specific and non-diagnostic. Following admission, multiple macular reddish lesions appeared on legs. Dermal biopsy showed perivascular infiltration. Finally a diagnostic procedure was performed. ***(Tanaffos 2011; 10(2): 75-78)***

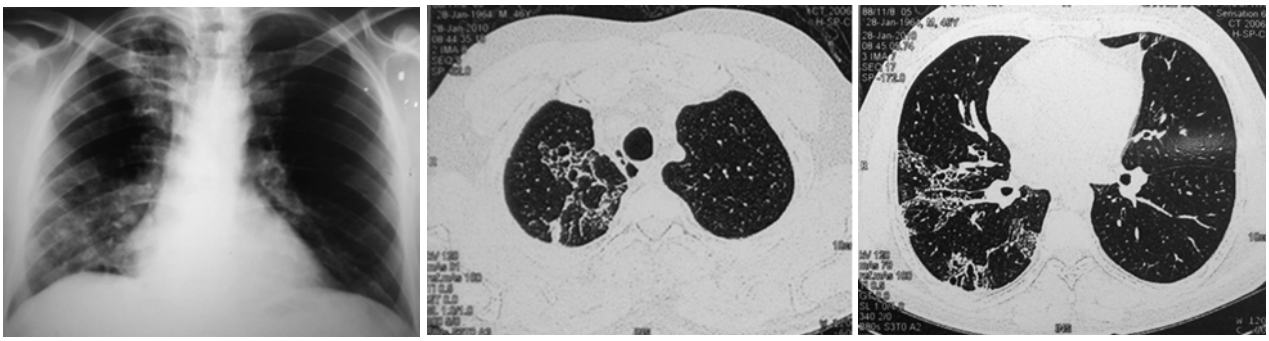

Figure 1. Chest x-ray and high resolusion computed tomography of the chest.

Correspondence to: Mansouri SD
Address: NRITLD, Shaheed Bahonar Ave, Darabad, TEHRAN 19569, P.O:19575/154, IRAN
Email address: dmansouree@yahoo.com

Diagnosis: Microscopic Polyangiitis (Polyarteritis)

Because of neural involvement detected on examination and EMG-NCV, sural nerve biopsy was performed and since the patient was highly suspicious for systemic vasculitis syndrome, serologic tests were repeated. P-ANCA was reported positive with 1:60 titers. Histopathologic examination of sural nerve revealed extensive vasculitis of small perineurial and epineurial arterioles of the vasa nervosum and also capillaries (Figure 2). Finally, based on constitutional symptoms, progressive polyneuropathy, skin rashes, pulmonary infiltrations, sinusitis, positive P-ANCA and compatible histopathologic findings of nerve and skin biopsies, diagnosis of microscopic polyarteritis (MPA) was confirmed.

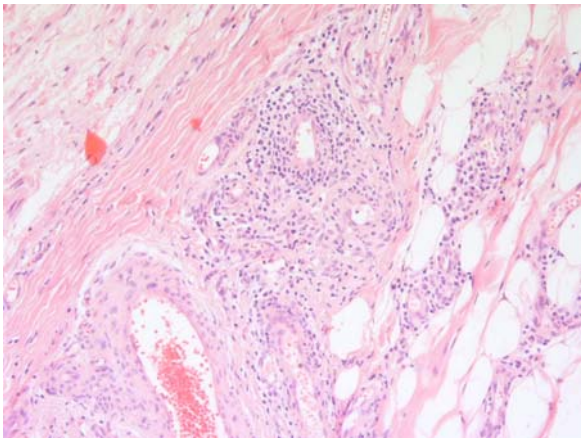

Figure 2. Histopathologic examination of sural nerve, H&E staining

Microscopic polyangiitis was initially considered a "microscopic" form of polyarteritis nodosa and was not definitely distinguished from it until the Chapel Hill nomenclature in 1994 (1,2). MPA is defined as a systemic necrotizing vasculitis that clinically and histologically affects small-sized vessels (i.e. capillaries, venules or arterioles) without granuloma formation (3). Involvement of small and medium-sized arteries may also be present.

Its main clinical symptoms were renal manifestations (78.8%), weight loss (72.9%), skin involvement (62.4%), fever (55.3%), mononeuritis multiplex (57.6%), arthralgia (50.6%), myalgia (48.2%), hypertension (34.1%), pulmonary involvement (24.7%), alveolar hemorrhage (11.8%), and cardiac failure (17.6%) (4).

But in other series, peripheral neuropathy is found in only 14 to 36% of the cases; thus, occurring less frequently than in polyarteritis nodosa (3).

Antineutrophil cytoplasmic antibodies were present in 38 of 51 in a case series (74.5%), of whom 33 had a perinuclear staining pattern (P-ANCA) and 5 had a cytoplasmic pattern (4).

The rarity of abnormal angiogram findings and the high frequency of P-ANCA are characteristic of MPA (3).

In MPA, diffuse alveolar hemorrhage as a result of alveolar capillaritis is the most frequent manifestation of respiratory involvement, and is clinically expressed as hemoptysis, respiratory distress and anemia. However, diffuse alveolar hemorrhage may also be subclinical and should be suspected when a chest radiograph demonstrates new unexplained bilateral alveolar infiltrates in the context of falling hemoglobin levels. Normal and high-resolution CT have a higher sensitivity than chest radiography for demonstrating airway, parenchymal and pleural lesions. However, many of these radiological findings are nonspecific; and therefore, their interpretation must take into account all clinical, laboratory and pathological data (5).

Microscopic polyangiitis, Wegener's granulomatosis (WG), Churg-Strauss syndrome, and pauci-immune necrotizing glomerulonephritis have

common pathogenic, pathological, and clinical features. All of them have limited renal form or systemic multi-organ involvement affecting upper respiratory tract, the lungs, the skin, or a number of other organs in various combinations (6).

Both Wegener's granulomatosis and MPA are associated with ANCA and have similar features on renal histologic examination. Although MPA and WG share many pathogenetic and clinical features, there are a number of differences between these disorders. Histologic examination shows absence of granulomatous inflammation in MPA. WG is primarily associated with PR3-ANCA, while MPA is primarily associated with MPO (myeloperoxidase)-ANCA (7).

The vasculitis in patients with MPA is pathologically indistinguishable from the vasculitis seen in Churg-Strauss syndrome. Asthma and eosinophilia distinguish Churg-Strauss syndrome from MPA (7). However, marked peripheral and tissue eosinophilia may be seen in MPA as an overlap syndrome or a separate disease (8).

ANCA serologies are also particularly useful in distinguishing MPA from classic polyarteritis nodosa. Although nearly three-fourths of patients with MPA are ANCA-positive, classic polyarteritis nodosa is not associated with antibodies to either PR3 or MPO (7). Therapy relies on the combination of corticosteroids and pulse intravenous cyclophosphamide, which can be switched, as soon as remission is achieved, to azathioprine or methotrexate, for a total duration of treatment of at least 18 months (9). Ten-year survival rate now exceeds 80%, but relapses are frequent. The precise place of new biologics, such as rituximab, needs to be further defined (9). The effectiveness of rituximab was demonstrated in a single controlled trial, in which 197 adults with MPA or WG were evaluated (10).

With the use of an alkylating agent, the rate of remission is about 75%, but relapses occur in about 30% of patients who achieve a remission, and in about 17% of patients after renal transplantation. Despite the improved outcome of patients with ANCA vasculitis in the recent decade, their long-term prognosis continues to be primarily determined by a rapid diagnosis, and prompt institution of therapy (6).

Factors influencing remission, relapse, and overall survival include the type of immunosuppressive therapy used, pattern of organ involvement, presence of ANCA, older age and male gender (11).

In this case, methyl-prednisolone pulse therapy was started for progressive neural dysfunction before the histopathology report, and after confirmation, cyclophosphamide was added to the regimen.

Clinical response to therapy was dramatic and gradually the patient was able to stand, walk and grasp.

Delayed positive P-ANCA after the third test, its 4-month duration, presence of polyneuropathy as the primary and dominant manifestation and absence of renal involvement were interesting findings in this case report.

REFERENCES

1. Pagnoux C, Guilpain P, Guillevin L. Microscopic polyangiitis. ***Presse Med*** 2007; 36 (5 Pt 2): 895- 901.
2. Jennette JC, Falk RJ, Andrassy K, Bacon PA, Churg J, Gross WL, et al. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. ***Arthritis Rheum*** 1994; 37 (2): 187- 92.
3. Lhote F, Cohen P, Généreau T, Gayraud M, Guillevin L. Microscopic polyangiitis: clinical aspects and treatment. ***Ann Med Interne (Paris)*** 1996; 147 (3): 165- 77.
4. Guillevin L, Durand-Gasselin B, Cevallos R, Gayraud M, Lhote F, Callard P, et al. Microscopic polyangiitis: clinical and laboratory findings in eighty-five patients. ***Arthritis Rheum*** 1999; 42 (3): 421- 30.

5. Pesci A, Manganelli P. Respiratory system involvement in antineutrophil cytoplasmic-associated systemic vasculitides: clinical, pathological, radiological and therapeutic considerations. ***Drugs R D*** 2007; 8 (1): 25- 42.
6. Falk RJ, Nachman PH, Hogan SL, Jennette JC. ANCA glomerulonephritis and vasculitis: a Chapel Hill perspective. ***Semin Nephrol*** 2000; 20 (3): 233- 43.
7. King T J, Glassock R J, Sheridan A M. Clinical manifestations and diagnosis of Wegener's granulomatosis and microscopic polyangiitis. *UpToDate©*. 2009 October. Available from URL:http://www.uptodate.com.
8. Weninger W, Kain R, Tschachler E, Stingl G. Microscopic polyangiitis with eosinophilia--an overlap syndrome or separate disease entity? A case report and review of the literature. ***Hautarzt*** 1997; 48 (5): 332- 8.
9. Pagnoux C. Wegener's granulomatosis and microscopic polyangiitis. ***Rev Prat*** 2008; 58 (5): 522- 32.
10. Stone JH, Merkel PA, Spiera R, Seo P, Langford CA, Hoffman GS, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. ***N Engl J Med*** 2010; 363 (3): 221- 32.
11. Mukhtyar C, Flossmann O, Hellmich B, Bacon P, Cid M, Cohen-Tervaert JW, et al. Outcomes from studies of antineutrophil cytoplasm antibody associated vasculitis: a systematic review by the European League Against Rheumatism systemic vasculitis task force. ***Ann Rheum Dis*** 2008; 67 (7): 1004- 10.