Case Report / *Olgu Sunumu*

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Microscopic Polyangiitis Histopathologically Confirmed By Lung Biopsy and Rheumatoid Arthritis: A Case Report

Akciğer Biopsisi ile Histopatolojik Olarak Doğrulanan Mikroskobik Polianjiitis ve Romatoid Artrit, Bir Olgu Sunumu

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Summary

Microscopic polyangiitis (MPA) is a systemic necrotizing vasculitis affecting small vessels. MPA is associated with renal dysfunction in most cases and occasionally with pulmonary hemorrhage. However, inflammatory polyarthritis is a rare manifestation. Here, we report the case of a 26-year-old man with MPA who developed rheumatoid arthritis. The patient presented with fever, general fatigue, weight loss, hemoptysis, polyarthritis, and macular rash. Clinical examination showed pulmonary capillaritis. Pathological findings revealed vasculitis of small vessels, including cutaneous leukocytoclastic vasculitis by the skin biopsy. MPA was diagnosed based on clinical symptoms, elevated perinuclear antineutrophil cytoplasmic (p-ANCA) antibody testing and the histopathological findings of lung biopsy specimens. The patient also had rheumatoid arthritis with positive anti-CCP antibody. He had no renal involvement and a negative antiglomerular basal membrane. We aimed to draw attention to the differential diagnosis of joint involvement with a case presenting MPA and RA coincidence. *Turk J Phys Med Rehab 2013;59:151-3.*

Key Words: Microscopic polyangiitis, rheumatoid arthritis

Özet

Mikroskobik Polianjiitis (MPA) küçük damarları etkileyen sistemik nekrotizan bir vaskülittir. MPA çoğu olguda renal disfonksiyonla ve bazı olgularda pulmoner hemoraji ile ilişkilidir. Ancak inflamatuvar poliartrit sık olmayan bir bulgudur. Makalemizde MPA tanısı olan ve romatoid artrit gelişen 26 yaşında bir olgu sunulmuştur. Olgumuz ateş, genel yorgunluk, kilo kaybı, hemoptizi, poliartrit ve maküler döküntü ile başvurmuş, klinik değerlendirmeler akciğerde kapillaritis ortaya koymuştur. Cilt biopsisinde patolojik bulgular küçük damarlarda lökositoklastik vasküliti göstermiştir. Klinik semptomlar, yüksek perinükleer antinötrofil sitoplazmik antikor (p-ANCA) düzeyleri ve akciğer biopsisindeki histopatolojik bulgular dikkate alındığında olguda MPA tanısı düşünülmüştür. Olguda aynı zamanda pozitif anti-CCP antikoru ile birlikte romatoid artrit de gelişmiştir. Antiglomeruler bazal membran antikoru negatif olan olguda renal tutulum tespit edilmemiştir. MPA ve RA koinsidansı olan bir olgu ile eklem tutulum ayırıcı tanısına dikkat çekmeyi amaçladık. *Türk Fiz Tıp Rehab Derg 2013;59:151-3*.

Anahtar Kelimeler: Mikroskobik polianjitis, romatoid artrit

Introduction

Microscopic polyangiitis (MPA) is described as a necrotizing vasculitis affecting small vessels (i.e., capillaries, venules, or arterioles) with few or no immune deposits (1,2). A patient with perinuclear anticytoplasmic antibody (p-ANCA) and a pulmonary renal vasculitic syndrome almost always has MPA rather than Wegener's granulomatosis (WG) (1,2).

Its typical clinical manifestations are rapidly progressive glomerulonephritis and alveolar hemorrhage. Lung involvement and alveolar hemorrhage have been reported in 12-29% of patients (3-5). The disease is also associated with general symptoms, arthritis, artralgia, mononeuritis multiplex and other manifestations (3). Clinical signs and symptoms depend on the size, type and organ of the involved vessels (6).

Besides typical renal and pulmonary involvement, it was also reported that joint manifestations including arthralgia and arthritis may be expected to be relatively common in MPA (7). However, rheumatoid arthritis (RA) and MPA coexistence has been reported in a few previous case reports (7-10).

Here, we report a patient who had a previous MPA diagnosis with pulmonary capillaritis, no renal involvement and positive p-ANCA testing and new developing coexistence of RA with

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this vasculitis. We reviewed previously reported cases of MPA associated with RA and discussed the relationship between MPA and RA.

Case Report

A 26-year-old man was referred to our department with the complaints of fever, fatigue and urticarial skin rash on his back lasting seven years. Due to worsening in these complaints, he was hospitalized at another medical center two years ago and depending on the clinical and histopatological findings, a diagnosis of vasculitis was considered. In spite of 60 mg daily corticosteroid treatment, hemoptysis, dyspnea and malena were added to his clinical symptoms. Due to bronchoscopic alveolar hemorrhage, a lung biopsy was performed and the results of histological examination were consistent with pulmonary capillaritis. Biopsy from the skin revealed cutaneous leukocytoclastic vasculitis. Serum p-ANCA was mildly elevated at 20 EU/mL (negative: ≤5.0 EU/mL; positive: 5.1-400.0 EU/mL) and c-ANCA, anti-ds DNA, ANA, anti-GBM were found to be negative. Based on the clinical symptoms, elevated serum p-ANCA level and histopathological findings of skin and lung biopsy specimens, MPA was diagnosed and an oral treatment with prednison (64 mg/day) and cyclophosphamide (2 mg/kg/day) were started two years ago. During the next 6 months, the patient improved gradually with the exception of macular rash and his drug doses were decreased because of the clinical remission. Due to relapsing of hemoptysis and dsypnea, iv pulse cyclophosphamide for six months and prednison were administered continuously.

In his systemic evaluation, he had oral aphthous stomatitis, urticaria on his neck, trunk and lower extremities, and hepatosplenomegaly. There was no peripheral edema and no neurological abnormalities in the extremities. In the locomotor system examination, besides tenderness in peripheral joints including metacarpophalangeal (MCP), proximal interphalangeal (PIP), metatarsophalangeal (MTP) joints and the ankle, swelling in 4. and 5. MCP joints and swan neck deformities were found bilaterally in second fingers of the hands (Figure 1). In addition, he described morning stiffness lasting more than one hour in his hands and feet. Laboratory investigations revealed white blood cell (WBC) count $4.4x10^3$, hemoglobin 13.3 g/dl, hematocrit 40.2%, platelets 410x104, erythrocyte sedimentation rate (ESR) 60 mm/h. Renal and liver function tests were normal. The patient's urine was positive for protein 15 mg/dl. Urine analysis showed no microscopic hematuria and red blood cell casts in the urinary sediment. A fecal sample was negative for occult blood. Serological examinations showed rheumatoid factor (RF) positivity and high anti-CCP antibody with 20 U/mL (negative:<5/mL), elevated C-reactive protein 5,57 mg/dl (<0.5 mg/dl considered as normal) and negative results for antinuclear antibody. HLA-DRB 07 and HLA-DRB C5 were positive.

Based on these findings, including symmetrical polyarthritis in hands and feet, morning stiffness, RF and anti-CCP positivity, the patient was diagnosed as having MPA coexisting with RA.

Abdominal ultrasound showed a mild hepatosplenomegaly and thorax computerized tomography detected bilateral pleural nodules. Skin biopsy revealed a vasculitis of small vessels. Serum p-ANCA was mildly elevated, although anti-glomerular basement membrane and c-ANCA were negative.

Based on the clinical symptoms, elevated p-ANCA level and the histopathological findings from skin and lung biopsy, MPA had been diagnosed in our patient when he was 19 years old. RA was also added to his existing MPA diagnosis with polyarthritis clinic and positive RF and anti-CCP antibody 7 years after the first diagnosis. The patient was initially treated with cyclophosphamide (2 mg/kg/day), prednison (1 mg/kg/day) and MTX (10 mg/ week). He responded well to these drugs with the clinical remission in fever, fatigue, urticaria, and arthritis.

Discussion

MPA is a small vessel vasculitis according to the Chapel-Hill Consensus Conference on the nomenclature of systemic vasculitis establishing the names and definitions of many vasculities that affect the kidneys (1). MPA was defined as follows: necrotising vasculitis with few or no immune deposits, affecting small vessels i.e., capillaries, venules or arterioles. Necrotizing arteritis involving small and medium sized arteries may be present. Necrotizing glomerulonephritis is very common. Pulmonary capillaritis often occurs. Based on definitions agreed by the Consensus Conference, we confirmed the diagnosis of MPA in our patient with clinical symptoms, elevated p-ANCA testing and histopathological findings of skin and lung biopsy. The presence of ANCA can be very helpful for the diagnosis of MPA, because ANCA is known to be frequently found in MPA, WG and Churg-Strauss Syndrome (11-13). Anti-MPO ANCA pathogenicity has been established in animal models and a recent report describes transplacental transfer of these antibodies in humans resulting in pulmonary hemorrhage and renal involvement in neonates (13). However, the conference report also commented that direct demonstration of certain pathologic processes noted in the definitions was not necessarily required in order to make a diagnosis.

Figure 1. Swan neck deformity.

According to the revised Japanese criteria for the diagnosis of MPA put forward by the National Study Group of Angiitis, the diagnosis of 'definite MPA' is made in the existence of one of the two following conditions: MPO-ANCA is detected in patients presenting with both rapidly progressive glomerulonephritis (RPGN) and pulmonary hemorrhage or histological evidence is demonstrated in patients presenting with more than any two of the following three symptoms: (I) RPGN, (II) pulmonary hemorrhage and (III) other symptoms, such as purpura, subcutaneous hemorrhage, gastrointestinal bleeding and mononeuritis multiplex (1,11,12). Our patient satisfied the second criteria for definite MPA. It has been suggested that the presence of ANCA has a high sensitivity and specificity for so-called pauciimmune necrotizing and crescentic glomerulonephritis (12,14).

Due to the systemic characteristics of MPA, patients with MPA can present with several different symptoms. More than 70% of patients have constitutional symptoms, such as fever or weight loss (15). Renal involvement is the major clinical feature of MPA and pulmonary involvement including hemoptysis and alveolar hemorrhage, infiltrations, pleural effusion, pulmonary edema, pleuritis, and interstitial fibrosis can be seen in about half of the patients. Several skin lesions, such as palpable purpura, livedo reticularis, nodules, urticaria, and necrotic skin ulcers can be found in 30% to 60% of patients (15). Besides, gastrointestinal symptoms and neurologic involvement may be seen in MPA. As a systemic disorder, joint involvement may also be present. Although it was reported that joint manifestations including arthralgia and arthritis may be expected to be relatively common in MPA (15-65 % and 6-17%, respectively), there are few articles reporting RA and MPA coexistence (7-11).

Our patient had also clinical signs of arthralgia and arthritis seven years after the first diagnosis. The findings supported a newly developing RA with symmetrical polyarthritis, morning stiffness, positive RF and anti-CCP that has a high sensitivity and specificity for the diagnosis and prognosis of RA. Our patient was considered as a rare case of MPA associated with anti-CCP positive RA.

As expected for an illness that affects multiple systems, patients with MPA can have also arthritis. In addition, as in our case and previous cases in the literature, RA may be present coincidentally in patients with vasculitis. Because it is known that ANCA may be present in patients with several rheumatic diseases such as RA or systemic lupus erythematosus, it is important to determine the specificity of the ANCA since presence of p-ANCA with antimyeloperoxidase specificity in a patient with polyarthritis is highly suggestive of systemic vasculitis. Since the approaches will be different, to clear the diagnosis is mandatory in spite of the difficulties with differential diagnosis in some cases.

Conflict of Interest
Authors reported no conflicts of interest.

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