Antineutrophil Cytoplasmic Antibodies Negative Microscopic Polyangiitis With Initial Pulmonary Manifestation

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Microscopic polyangiitis (MPA) is a small vessel vasculitides mostly associated with anti-neutrophil cytoplasmic antibodies (ANCA). The kidney is the most commonly affected organ in MPA. We report the case of a 9-year-old girl with ANCA-negative MPA who initially presented with respiratory symptoms, including cough, sputum, and dyspnea. Based on her symptoms, atypical pneumonia was suspected. Also, childhood interstitial lung disease was considered based on findings seen on chest CT. Despite initial improvement of symptoms with oral corticosteroid therapy, dyspnea with initiation of corticosteroid tapering was noted. A final diagnosis of MPA was made after lung biopsy. ANCA was negative in both the initial and repeat blood tests. Oral cyclophosphamide and prednisolone treatments led to full remission. Since then, the patient has been treated with low dose prednisolone and azathioprine for maintenance. A good treatment response was achieved and her clinical symptoms, pulmonary functions, and radiologic findings have since improved. Thus, early and precise diagnosis of MPA is crucial for remission induction and prevention of symptom relapse. (J Rheum Dis 2020;27:203-208)

Key Words. Microscopic polyangiitis, Interstitial lung diseases, Antineutrophil cytoplasmic antibodies, Child

INTRODUCTION

According to the revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides (CHCC) in 2012, microscopic polyangiitis (MPA) is a non-granulomatous necrotizing vasculitis with few or no immune deposits, predominantly affecting small vessels [1]. The incidence of MPA is estimated to be from 2.7 to 11.6 per million in Europe [2]. The mean age of onset is between 50 and 60 years. However, the mean age of onset in children is 12 years. Child-onset MPA shows clinical features similar to adult-onset MPA; however, unlike adult-onset MPA with no gender predilection, there is a female predominance (about 80%) in children [3,4]. In pediatric patients, renal system involvement is the most common in MPA (75% ~ 100%), followed by systemic, musculoskeletal, cutaneous, and lower respiratory involvement (79%, 57%, 44%, and 37%, respectively) [3,5,6].

Although the confirmation of MPA is based on pathologic findings, it is generally associated with anti-neutrophil cytoplasmic antibodies (ANCAs) and, thus, it is classified as ANCA-associated vasculitis (AAV). A recent systematic review reported that ANCA are detected in more than 90% of cases [3]. However, a single-center study reported that 26% of 48 children with MPA were ANCA negative [7]. Thus, a negative ANCA test cannot exclude MPA.

There are no reports on the clinical characteristics of child-onset ANCA-negative MPA in Korea. So far, only two cases of ANCA-positive MPA with renal involvement in the pediatric population have been reported in Korea [8,9]. We present a rare case of ANCA-negative MPA in a 9-year-old girl with initial pulmonary manifestations.
CASE REPORT

A 9-year-old girl presented to the hospital with dyspnea, cough, productive of sputum, and rhinorrhea which she has had for 16 days. A few days after symptoms onset, she continued to experience worsening dyspnea and chest discomfort despite treatment with oral mucolytics and short-term prednisolone at a primary clinic. At the initial presentation to our hospital, she was noted to have coarse breathing sounds with crackles on auscultation. Her initial chest X-ray (CXR) showed peribronchial infiltration in both lungs (Figure 1A). There were no cutaneous lesions, lymph node enlargement, mucosal ulceration, arthralgia, or ophthalmological symptoms. Also, her growth and development were normal (height 50~75 percentile, weight 10~25 percentile, and body mass index 10~25 percentile).

Despite a 5-day treatment course with roxithromycin in our hospital, no improvements in dyspnea and CXR findings were seen; she was thus admitted. On hospital day 1 (HD#1), her blood pressure was 98/49 mmHg, respiratory rate was 32 breaths/min, heart rate was 102 beats/min, and body temperature was 37.1°C. Her percutaneous oxygen saturation (SPO2) was 92% at room air, necessitating supplemental oxygen via nasal cannula. Her initial white blood cell count was 16,850/mm³ with 83.6% segmented neutrophils. Her initial serum chemistry was within normal limits, except for mild elevation of C-reactive protein (1.89 mg/dL). Immunoglobulin M anti-mycoplasma antibody and multiplex real-time polymerase chain reaction (PCR) for respiratory viruses were negative. Urinalysis was significant for 1+ urine albumin and microscopic hematuria. Chest computed tomography (CT) showed diffuse bronchocentric ground-glass opacity and consolidations in the lungs (Figure 1A). On HD#3, the patient was noted to have a fever and her SPO2 dropped to 88% on room air. Diagnostic bronchoscopy with bronchoscopic alveolar lavage (BAL) and fluid analysis showed 42% macrophages, 49% neutrophils, and 9% lymphocytes. No microorganism, including respiratory syncytial virus, adenovirus, influenza virus, parainfluenza virus, Epstein-Barr virus, cytomegalovirus, mycoplasma, chlamydia, legionella, fungi, and acid-fast bacilli were detected from BAL fluid following PCR or cultures. On HD#5, intravenous piperacillin/tazobactam and immunoglobulin were initiated. Although her fever sub-

Figure 1. Chest X-ray & chest computed tomography (CT) before lung biopsy. (A) Initial chest X-ray and CT scan: Initial chest X-ray (09/11/2016) showed peribronchial hazy infiltrations in both lower lung zones. Chest CT scan showed diffuse bronchocentric ground glass opacity and consolidations in bilateral lungs suspected to atypical pneumonia. (B) Follow-up chest X-ray and CT scan in the period of symptom worsening: Chest X-ray showed an interval improved aeration but residual streaky and granular infiltrations. Chest CT scan showed a resolution of previously noted ground glass opacities in both lungs, leaving diffuse fibro-streaky changes and some consolidations.