Int J Clin Exp Med 2015;8(9):16850-16853
www.ijcem.com /ISSN:1940-5901/IJCEM0011411

Case Report

Pulmonary arterial hypertension associated with rare cause of ANCA-associated vasculitis misdiagnosed as idiopathic one

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Received June 14, 2015; Accepted September 6, 2015; Epub September 15, 2015; Published September 30, 2015

Abstract: Pulmonary arterial hypertension (PAH) and ANCA-associated vasculitis (AAV) are both rare and complex diseases with poor prognosis especially when misdiagnosis. We report a rare case of a young woman presented with idiopathic pulmonary arterial hypertension (IPAH), but who was later found to have PAH associated with AAV. This case reminds us the very importance of differential diagnosis to PAH patients and the identification of rare cause likes ANCA-associated vasculitis. To our knowledge, this patient represents the first published case of misdiagnosis of PAH secondary to ANCA-associated vasculitis.

Keywords: Pulmonary arterial hypertension, ANCA-associated vasculitis

Introduction

Pulmonary arterial hypertension (PAH) and ANCA-associated vasculitis (AAV) are both rare and complex diseases with poor prognosis especially when misdiagnosis. We report a rare case of a young woman initially diagnosed with idiopathic pulmonary arterial hypertension (IPAH), but who was later found to have PAH associated with AAV. In this case, we discuss the identification of AAV, the rare cause of secondary PAH, and the importance of the differential diagnosis in PAH patient.

A 21-year-old female had cough, sputum, and dyspnea on exertion (NYHA class III) which could be aggravated (NYHA class IV) by common cold since a child. She was firstly misdiagnosed as IPAH and had bosentan with no effect for one month in the local hospital. Echocardiogram revealed pulmonary artery pressure about 38 mmHg (1 mmHg=0.133 kPa) (**Figure 1**). Heart catheterization established the diagnosis of moderate PAH with mean pulmonary arterial pressure of 47mmHg. High-resolution CT (HRCT) scan of chest (**Figure 2**) showed diffuse ground-glass opacity, air-space opacities and inflammatory nodules in lungs. P-ANCA was detected positive and the serum level of MPO-ANCA was up to 2. Distance walked in 6 min was about 320 meters. A diagnosis of AAV was established by the positive of p-ANCA and elevated serum level of MPO-ANCA, as well as the signs presented in High-resolution CT. The patient was administered methylprednisolone and cytoxan to treat primary disease. After three-month treatment, her dyspnea was relieved obviously and exercise tolerance was improved with NYHA I. Distance walked in 6 minutes was increased to 650 meters and echocardiography examination suggested relieved of pulmonary arterial pressure to 27 mmHg. The detection of ANCA also turned into negative.

A case of PAH secondary to ANCA-associated vasculitis which was initially misdiagnosed as IPAH and ultimately effectively treated when aiming at primary disease was presented. Because therapeutic options closely follow the diagnostic categories, classifying pulmonary arterial hypertensive disorders based on clinical criteria is very important. Therefore, we firstly ruled out PAH owing to left heart disease, chronic thromboembolic pulmonary hypertension, portopulmonary hypertension and high-

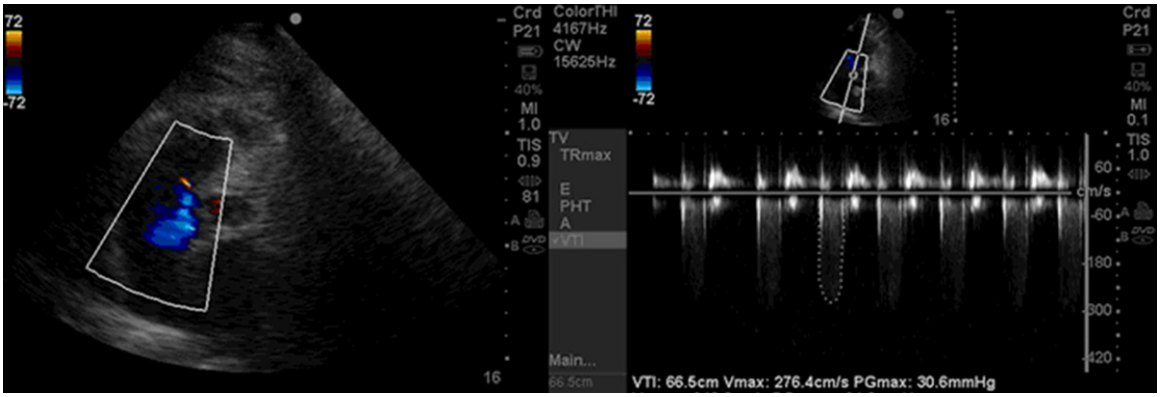

Figure 1. Echocardiogram (on admission) revealed mild enlargement in root of pulmonary artery and tricuspid regurgitation with pulmonary artery pressure about 38 mmHg.

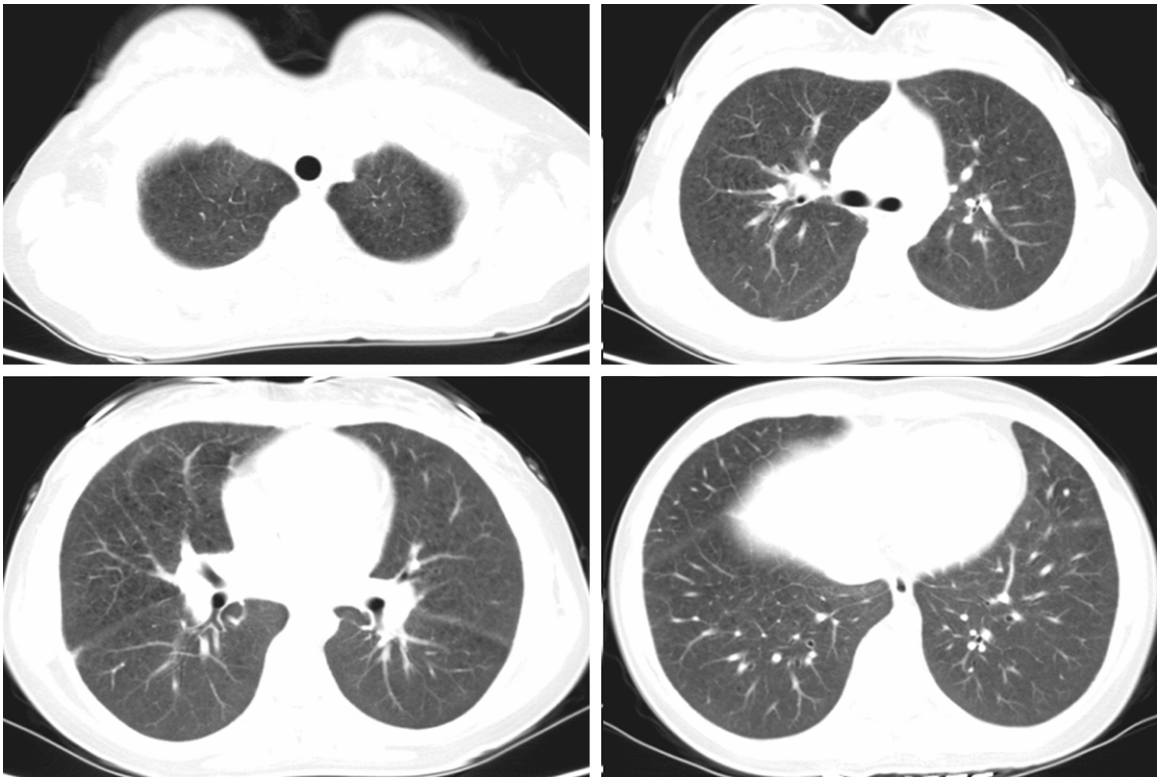

Figure 2. High-resolution chest CT scan (on admission) showed diffuse ground-glass opacity, air-space opacities and inflammatory nodules in lungs.

altitude pulmonary hypertension successively due to the lack of related signs and symptoms, and variety examinations.

The diagnosis of IPAH is exclusive, which could easily result in the misdiagnosis once physicians neglect rare causes. ANCA-associated vasculitis could exactly be such a rare cause. It is a systemic autoimmune disease of which diagnosis is among the most demanding challenges because its signs and symptoms are nonspecific and overlap with those of infections, connective tissue diseases, and malignancies. To this patient, her main complaint and her other signs and symptoms are all nonspecific for ANCA-associated disease. The radiographic lung features of vasculitis are extremely variable and still not that specific. However, the radiologic manifestations of diffuse ground-glass opacity, air-space opacities,

and nodules represented in high resolution chest CT of this patient are proved more typical for small-vessel vasculitis [1].

Early diagnosis is important for commencing therapy instantly so as to reduce the risk of poor prognosis. Although the early symptoms and radiology images of this disease lack specificity, ANCA (Anti-neutrophil cytoplasmic antibodies) are already detectable in the sera in most cases in these early stages [2]. Its positivity is common in ANCA-associated vasculitis but not universal; thus, ANCA negativity does not completely rule out these diseases. A meta-analysis calculated an overall sensitivity of 82% and an overall specificity of 99% for the use of the combined IIF and ELISA assays for cANCA/PR3 and pANCA/MPO in the diagnosis of vasculitis [3]. Of the greatest clinical importance is the association of PR3-ANCA with Wegener's granulomatosis and MPO-ANCA with microscopic polyangiitis (MPA) [4]. For this patient, it was the detection of p-ANCA, confirmed by positive MPO that definite the diagnosis of ANCA-associated vasculitis and further indicated the underlying diagnosis of MPA. Furthermore, the correlation of ANCA titers with clinical disease activity was confirmed by many studies [5]. The detection of ANCA of this patient turning into negative and the obviously relieved symptoms after three-month treatment also verified the diagnosis of ANCA-associated vasculitis. In providing extremely long-term survival data, many studies confirmed that PAH is indeed a deadly condition with 5-year case-fatality rates of between 40% and 75% [6]. However, PAH carries heterogeneous prognosis due to heterogeneous mechanisms; REVEAL (Registry to Evaluate Early and Long-Term PAH Disease Management) suggests that current median survival is 7 years for patients with PAH compared with 2.8 years for patients with IPAH in the U.S. National Institutes of Health (NIH) Registry [7]. ANCA-associated vasculitis, in particular MPA, though has a very poor prognosis of 93% within 2 years if left untreated [8]. However, the immunosuppressive therapy with glucocorticoids and cyclophosphamide, which are just the same with drugs used in this patient, has transformed 5-year survival rates now approaching 80% [9]. This treatment has dramatically improved 5-year survival rates now approaching 80% for AAV and 81% for MPA [10]. Therefore, differential diagnosis, being closely related to treatment and prognosis, is particularly important to PAH patients.

This case is special in the diagnosis of PAH secondary to the rare cause of ANCA-associated vasculitis, the patient achieved dramatically relief after the treatment with corticosteroid and cytoxan. It reminds us the very importance of differential diagnosis to PAH patients and the identification of rare cause likes ANCA-associated vasculitis. To our knowledge, this patient represents the first published case of misdiagnosis of PAH secondary to ANCA-associated vasculitis.

Disclosure of conflict of interest

None.

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