Sudden and rapid progression of lung affection but stability in kidney function: a case report of anti-neutrophil cytoplasmic antibody-associated vasculitis

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Abstract: We report the case of a patient with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) who exhibited sudden progression of lung infiltration while maintaining stable kidney function. The 69-year-old man was diagnosed with AAV and renal insufficiency 4 years ago. Pulmonic affectionation was detected in the right lower lobe of lung by a computed tomography (CT) scan. After beginning cyclophosphamide pulse therapy and sequential therapy with low-dose prednisone, he underwent a 4-year follow-up to detect changes in hemoglobin levels and serum creatinine levels, and had chest CT examinations. The CT scan and creatinine assay showed stable pulmonic fibrosis and kidney function. Although there was no increase of creatinine and detectable perinuclear ANCA, the patient suffered a pulmonary hemorrhage and levels of hemoglobin became progressive lower; the lung infiltration was found to be enlarged compared to the last examination the previous year. After immunosuppressive therapy for one week, the lung fibrosis was progressive, increased pulmonary hemorrhage occurred, and the patient died due to respiratory failure but not end-stage renal failure.

Keywords: vasculitis, ANCA, lung fibrosis, pulmonary hemorrhage, renal insufficiency

Introduction

The anti-neutrophil cytoplasmic autoantibodies (ANCA)-associated vasculitides (AAVs) comprise a group of diseases characterized by necrotizing vasculitis of small vessels, frequently with involvement of kidneys and lung. Genetic and environmental factors are involved in their etiopathogenesis, with a possible role for silica exposure in AAVs and Staphylococcus aureus infection in granulomatosis with polyangiitis. In the clinic, alveolar hemorrhage (AH) is a major cause of early death in AAV; severe AH is strongly correlated with renal vasculitis. AAV patients with renal involvement who need renal replacement therapy have the worst survival prognosis. We report a case of AAV that remained stable over 4 years and then showed sudden activity as lung infiltration instead of end-stage renal failure (ESRF).

Case report

A 69-year-old male patient presented as an outpatient with increased creatinine levels (281 µmol/L) associated with proteinuria (2.5 g/24 h) and hematuria (110 g/L). His history was not unusual and he denied any abuse of alcohol, drugs, or over-the-counter stimulants. Review of his history was negative for any recent fever, rash, contact with sick persons, or acute illness involving the respiratory or gastrointestinal tract.
The examination of ANCA and a chest radiograph were unusual. He was diagnosed with ANCA-associated vasculitis after findings of a perinuclear ANCA (p-ANCA) positive reaction (495 U/mL), urine examination, renal insufficiency by creatinine assay, and lung infiltration by CT scan. After starting treatment with cyclophosphamide pulse therapy, sequential therapy with low-dose prednisone (10 mg qid [every other day]), he underwent a 4-year follow-up. During this time, the level of serum creatinine was stable (Figure 1), and both proteinuria and hematuria improved (Figure 2). A chest CT scan was performed, which showed that the lung fibrosis remained unchanged (Figure 3).

However, after the 4-year follow-up, the patient experienced a sudden and rapid deterioration in lung infiltration and exhibited pulmonary hemorrhage (PH) along with a progressively lower hemoglobin (Figure 3). Interestingly, there was not only no increase in creatinine levels (Figure 1), but also a negative conversion of p-ANCA. The galactomannan assay and Mycobacterium tuberculosis antigen-specific interferon (IFN)-gamma release assays (T-SPOT® -TB test; Oxford Immunotec Ltd, Oxford, UK) were both negative. After immunosuppressive therapy (methylprednisolone and cyclophosphamide pulse therapy for 1 week), and empirical widened coverage of anti-infective therapy, progressive

![Figure 1](image1.png) The patient's serum creatinine (Cr) level over a 4-year period.

![Figure 2](image2.png) The patient's hemoglobin level over a 4-year period.
肺纤维化发生，PH恶化，并死于呼吸衰竭。

讨论

导致肉芽肿性疾病的血管炎以ANCA型抗体为特征。在大多数情况下，这些抗体是针对蛋白酶3-ANCA的。这些效应可能对ANCA相关的小血管炎及全身血管炎造成一种促进炎性环境。5,6

肾损伤在AAV中经常存在，并是ESRF的重要原因。据报道，当AAV患者进展到ESRF时，他们不太可能经历疾病的复发。7。此外，AAV也是一种常见原因的弥漫性肺纤维化和致命性疾病。8,9

虽然严重的PH可以在ESRD患者中发生，但AAV的疾病活动和复发应被监测，甚至在患者疾病进展到PH之前。在这种情况下，我们遇到了一名患有AAV的患者，表现为致命的肺部损伤，但其肾功能稳定。根据患者逐渐降低的血红蛋白和CT结果，AH可能参与了肺部损伤。有建议认为出血可能是一种有用的生物标志物，用于评估AAV的临床状态。

诱导治疗用口服环磷酰胺一直是严重肾衰竭患者的治疗标准。10

最近获得的关于AAVs的发病机制的见解已经导致了对这些致命性疾病的更针对性的治疗。此外，侵袭性肺部曲霉菌病被报道为免疫功能低下患者的严重机会性感染。11,12

患者接受免疫抑制治疗时，更容易发生侵袭性肺部曲霉菌病，但仅在少数病例中报告。在这种情况下，血清甘露聚糖检测未发现侵袭性真菌感染，而经验性抗真菌治疗未能逆转他的预后。因此，机会性感染未被发现或未参与急性加重的AAV在该患者。

ANCA相关的血管炎和间质性肺疾病是不常见的状况。两种疾病的共存越来越多被认识。正如Arulkumaran等13所报告，间质性肺病在2.7%的AAV患者中被观察到。已认识到一部分患者特发性肺纤维化会在疾病进程中突然和快速恶化，不能用感染、心力衰竭或血栓形成疾病来解释。14,15

这些事件通常是致命的，并已被称作是基础疾病的急性加重。虽然它们在特发性肺纤维化患者中被最常描述，但也有其他间质性肺疾病的报道。14,15

ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

Figure 3 The patient’s chest CTs over a 4-year period. The CT scan shows a progressive pulmonary affection during the last 2 months. Abbreviation: CT, computed tomography.
lung disease. Further investigation into similarities and common pathways in acute exacerbations of various fibrotic lung diseases (including pulmonary vasculitides) may yield additional insight into this recently recognized syndrome.

Diagnosis of AAV can be made according to clinical symptoms, laboratory test results, and image data; however, the gold standard remains the histological proof of a necrotizing, pauci-immune small vessel vasculitis. We report the case of a patient with AAV suffering fatal pulmonary affection but presenting with almost normal kidney function, indicating that the lungs are possibly the only target organs in acute exacerbations of AAV. It is important to consider the progression of lung fibrosis as a possible complication in AAV patients who have an underlying abnormality of the lung. Even though the optimal strategies for AAV remain unclear, in the future, it might be possible to tailor the treatment modalities according to the risk factors. It is therefore necessary to establish an early diagnosis based on the symptoms. And thanks to new treatments, and despite AAVs being potentially serious diseases, their prognosis has considerably improved in recent years.

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Disclosure
The authors report no conflict of interest in this study.

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