LETTERS TO THE EDITOR

ANCA-associated vasculitis after Pfizer-BioNTech COVID-19 vaccination: two case reports

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Dear Editor,

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a necrotising small vessel vasculitis. The annual global incidence of AAV has been stable since the early 2000s, but recent clusters of new cases have been reported[1]. Herein, we report two cases of AAV after COVID-19 vaccination.

A 26-year-old woman presented to the emergency department with a one-week history of cough, chest pain, and fever. The patient was initially diagnosed with community-acquired pneumonia and treated with azithromycin. However, due to worsening respiratory complaints and the onset of haemoptysis, the patient was later admitted. She had a history of sinusitis and active smoking and denied any regular medication or recreational drug use. Two weeks before the onset of symptoms, the patient had been administered the first dose of the Pfizer-BioNTech COVID-19 vaccine. At the admission, the patient had an erythrocyte sedimentation rate (ESR) of 102mm/h, C-reactive protein (CRP) 21.0mg/dL, 18400 white blood cells (WBC)/µL, 51% neutrophils (9400/µL) and 38% eosinophils (7000/µL), and serum creatinine 1.4mg/dL. The urine sample showed microscopic haematuria and granular cylinders. A chest CT scan showed parenchymal consolidations and mediastinal adenopathies (Figure 1A/C). Blood and urine cultures and viral and bacterial serologies (including COVID-19 polymerase chain reaction and IGRA) were negative. Despite intravenous piperacillin/tazobactam treatment, the patient had a worsening fever. After one severe haemoptysis episode, the patient was admitted to the intensive care unit for transfusional support and non-invasive ventilation. A chest CT scan revealed worsening condensations (Figure 1 B/D). Intravenous methylprednisolone (1000mg/day for three days) was started, followed by oral prednisolone 1mg/Kg/day. Blood workups were positive for ANCA-anti-proteinase-3 antibodies (PR3, 1610UI/mL) and negative for antinuclear antibodies (ANA) and ANCA-anti-myeloperoxidase (MPO). Bronchoscopy and bronchoalveolar lavage were compatible with alveolar haemorrhage. Rituximab 1000mg was initiated but switched to intravenous cyclophosphamide 15 mg/kg/dose due to adverse events. The patient is currently asymptomatic, with normalised renal function, and remarkable chest CT improvement (figure 1E/F), under treatment with methotrexate (15mg/week) and prednisolone (5mg/day).

A 47-year-old man presented to his general practitioner (GP) with a three-month history of increasing fatigue, anorexia and abdominal pain. He had a history of active smoking and denied any regular medication or recreational drug use. The symptom onset coincided with the administration of the second dose of the Pfizer-BioNTech COVID-19 vaccine. A blood workup revealed serum creatinine 4.0mg/dL and elevated prostate-specific antigen. The patient was treated with oral cefuroxime for a month due to suspected prostatitis, but serum creatinine levels rose to 8.0mg/dL, so he was admitted. The patient had an ESR of 65mm/h, CRP 5.81mg/dL, 11600 WBC/µL, 73% neutrophils (8400/µL). The urine sample showed proteinuria (6g/24h) and haematuria with dysmorphic erythrocytes. The renal biopsy showed pauci-immune necrotising crescentic glomerulonephritis. Blood workups were positive for ANCA-MPO (>134 UI/mL) and negative for ANA and ANCA-PR3. Blood and urine cultures and viral and bacterial serologies were negative. The patient underwent six plasmapheresis sessions, three infusions of intravenous cyclophosphamide (800-1000mg) and methylprednisolone (500mg/day for three days), followed by oral prednisolone 1mg/Kg/day. There was an initial decrease of serum creatinine to as low as 5.2mg/dL, but about three months later, the patient became uremic and started haemodialysis and rituximab, which was later suspended due to inefficacy. The patient is currently under regular haemodialysis

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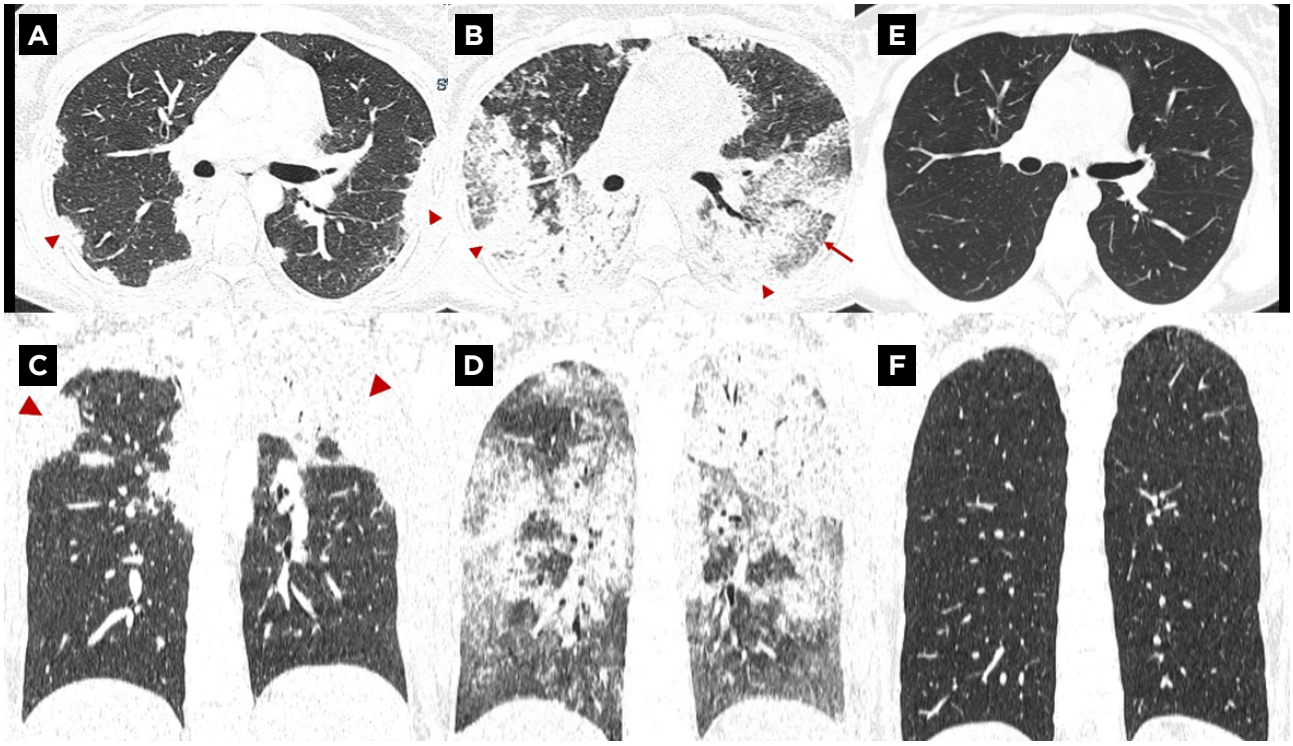

Figure 1. High-resolution thoracic CT scan images. A) Axial image of the first CT scan at the level of the inferior lung lobes demonstrates bilateral and peripheral consolidations. B) Axial image of the second CT scan at the same level shows significant worsening of the parenchymal lung findings. There are more extensive bilateral and diffuse lung consolidations (arrowheads) and new areas of ground-glass opacities with superimposed smooth intralobular and interlobular septal thickening, producing the crazy-paving pattern (arrow). These findings are compatible with acute/subacute diffuse alveolar hemorrhage in this clinical scenario. C and D) Coronal image reconstructions show the extensive craniocaudal involvement of both lungs, again demonstrating the worsening of lung damage from the first CT scan to the second. E and F) Axial and coronal images of the posttreatment CT scan demonstrates a remarkable response to treatment, with complete resolution of the parenchymal lung findings.

and treated with prednisolone 10mg/day.

mRNA vaccines activate CD8+ and CD4+ T cells and may promote immune-mediated diseases in predisposed individuals[2]. Cellular immunity is central in AAV pathogenesis, as CD4+ T cells promote ANCA production and CD4+ and CD8+ T cells recognise ANCA antigens deposited in peripheral tissues[3]. De novo AAV has been reported after COVID-19 infection[4,5] and vaccination[5–10]. In these two cases, temporal coincidence suggests an onset of AAV induced by vaccination, although casual association cannot be excluded. Despite this, both cases further support the increasing evidence in the literature documenting the occurrence of AAV after COVID-19 vaccination. Research into the immune responses following mRNA vaccination may improve the knowledge of AAV pathophysiology.

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