CASE REPORT

Diffuse alveolar haemorrhage in ANCA-associated vasculitis following cocaine use

J. Blom1,2, F.W. Visser2, B.P. Grady1

1Department of Intensive Care, 2Department of Internal Medicine, Hospital Group Twente, Almelo, the Netherlands

Correspondence
J. Blom - j.blom@zgt.nl

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Case presentation

A 32-year-old man presented to the emergency department with haemoptysis and cough developing over a few days. His medical history included MPO-ANCA-associated vasculitis (AAV), since 2014, which had resulted in end-stage kidney disease requiring haemodialysis. His AAV was believed to be exacerbated by the use of cocaine resulting in several relapses in previous years. The patient had been clean for several months and denied cocaine use.

Physical examination revealed an oxygen saturation of 100% with ambient air, a heart rate of 70 beats/min and a blood pressure of 139/94 mmHg. The remainder of the physical examination was unremarkable, in particular no purpura or other skin alterations were seen that could be associated with a relapse of his known vasculitis.

Laboratory studies showed a normocytic anaemia of 6.5 mmol/l with a normal platelet count, low inflammation markers, serum creatinine was 567 μmol /l and urea 8.9 mmol/l. Clotting times were not determined. A chest X-ray showed subtle bilateral consolidations (figure 1, panel A). A CT scan demonstrated opacification of the right lower lobe suggestive of alveolar haemorrhage.

Based upon clinical recognition, the patient’s history and recently measured high ANCA-MPO levels in the weeks prior to admission (>221.9 kU/l), a relapse of AAV was assumed and treatment was initiated with high-dose prednisolone (60 mg a day). Bronchoalveolar lavage (BAL) was performed and aliquots with fresh blood from both lungs were retrieved. Unfortunately, sequential BAL could not be finished because the patient experienced major distress. Cultures and molecular diagnostics of BAL fluid came back negative for infectious agents. Diffuse alveolar haemorrhage was diagnosed based on the combination of the radiological pattern, clinical presentation, high ANCA-MPO level, the findings during BAL and with an infectious or cardiogenic aetiology being unlikely. His clinical situation slowly deteriorated, with progressive dyspnoea, hypoxia and ongoing haemoptysis, despite the start of rituximab at day 5 and high-dose methylprednisolone (1000 mg a day, three days) at day 13.

Acute coronary syndrome as a cause of the clinical deterioration was excluded by ECG and stable troponin levels during follow-up. Dialysis was intensified to avoid any fluid overload. Haemodynamic instability was not observed during dialysis. An echocardiogram was not performed.

On day 17 he was admitted to the ICU requiring respiratory support with high-flow oxygen therapy. The chest X-ray displayed extensive bilateral alveolar consolidation (figure 1, panel C).

With ongoing clinical deterioration leading to respiratory failure, four days after intensifying immunosuppressant therapy with methylprednisolone, plasmapheresis was initiated with the aim of avoiding the need for invasive ventilation and progression of both the life-threatening pulmonary bleeding and pulmonary manifestation of AAV. After initiation of plasmapheresis, clinical improvement occurred rapidly in accordance with major improvement of the radiological findings. Analysis of the patient’s hair confirmed recent use of cocaine.

Discussion

Diffuse alveolar haemorrhage is most commonly due to pulmonary capillaritis and is considered an imminent life-threatening clinical syndrome, requiring fast diagnosis and treatment. The main symptoms include haemoptysis, anaemia,
hypoxia and dyspnoea. Typical findings on plain radiograph are diffuse bilateral infiltrative opacification patterns, sometimes with a predilection towards the mid zones, with apical or subpleural sparing. The differential diagnosis should include cardiogenic oedema and pulmonary infections. If diffuse alveolar haemorrhage is suspected, bronchoscopy with BAL is the preferred method to confirm its presence. Sequential BAL is performed by sequentially injecting and retrieving three aliquots of 50 ml saline from the bronchopulmonary segments where opacification of the lung was seen on imaging. Receiving progressively more haemorrhagic aliquots from the same location is diagnostic for diffuse alveolar haemorrhage. Pulmonary capillaritis has several potential causes, including AAV, infections, medications, but also to vasculitis secondary to drugs of abuse, in particular cocaine.

Cocaine is frequently cut with cheap chemical agents such as levamisole to lower production costs and to enhance the adrenergic effect of cocaine. Levamisole is an anti-helminth drug and levamisole-related vasculitis, among other serious side effects, has been reported. Both cocaine itself and levamisole have been associated with immune responses potentially provoking AAV. Isolated pulmonary manifestation of drug-induced AAV is uncommon, but has been described to cause diffuse alveolar haemorrhage due to a direct toxic effect following cocaine use as well as by provoking relapse of pre-existing AAV, with catastrophic consequences. The exact mechanism of the immune stimulatory properties of cocaine and levamisole is still under investigation. In the USA an estimated 71% of samples are contaminated with levamisole. However, in the Netherlands the percentage of levamisole found in cocaine samples has decreased from 74% in 2014 to 35% in 2018. Unfortunately in this case, we had insufficient serum to test for the presence of levamisole.

Our patient experienced cocaine-induced relapse of AAV and developed severe diffuse alveolar haemorrhage resulting in progressive respiratory failure, despite prednisone, rituximab and methylprednisolone. Initiation of plasmapheresis was of major importance for our patient. Diffuse alveolar haemorrhage should be considered in patients with known cocaine use, pulmonary infiltrates and anaemia, as fast recognition and treatment is crucial. Furthermore we want to emphasise that cocaine-induced relapse of AAV can be therapy resistant despite aggressive immunosuppressive therapy and that plasmapheresis can be lifesaving.

Disclosures
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Informed consent was obtained from the patient for the publication of this case report

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