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Diffuse alveolar hemorrhage

ABSTRACT

Diffuse alveolar hemorrhage can accompany many diseases, including systemic vasculitis and other connective tissue diseases. Rapid diagnostics and immediate implementation of adequate treatment are extremely important. In this paper is presented a 63-year-old patient with fever, dyspnoea and massive haemoptysis, admitted as part of the emergency department

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KEY WORDS: diffuse alveolar hemorrhage; haemoptysis; vasculitis; plasmapheresis; immunosuppressive treatment

INTRODUCTION

Diffuse alveolar hemorrhage (DAH) is defined as the presence of blood in the alveolar lumen, which originates from the pulmonary capillaries. DAH is a medical emergency in rheumatology, which is manifested most commonly by cough, dyspnoea and haemoptysis of varying severity. There is often the development of type I (hypoxaemic) respiratory failure (PaO_2 <60 mm Hg, $PaCO_2$ < 45 mm Hg) with falsely normal or high DLCO (diffusing lung capacity for carbon monoxide) values, as a result of carbon monoxide (CO) binding to haemoglobin extravasated into the alveoli [1].

Imaging examinations are essential in the diagnosis of DAH. High-resolution computed tomography (HRCT) shows characteristic presence of groundglass areas and alveolar consolidations that show evidence of filling of the alveoli [2]. Bronchofiberoscopy and bronchoalveolar lavage (BAL) are also helpful. The presence of > 20% hemosiderin-laden macrophages (siderophages) in the BAL is suggestive of alveolar hemorrhage (AH) [3].

The causes of AH are varied. The most common causes include vasculitis including granulomatosis with polyangiitis, microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis, anti-glomerular basement membrane antibody — associated vasculitis, cryoglobulinemic vasculitis, IgA vasculitis, as well as systemic connective tissue diseases such as systemic lupus erythematosus, mixed connective tissue disease, rheumatoid arthritis, antiphospholipid syndrome. DAH can also occur in the course of pulmonary hypertension, haemorrhagic diathesis, mitral stenosis, after the use of anticoagulants, cytostatics, and after the use of inhaled cocaine (crack) [4].

Treatment of patients should take place in specialist wards. The treatment of DAH is mainly based on the use of immunosuppressants (e.g. glucocorticosteroids, cyclophosphamide) and often requires plasmapheresis or mechanical ventilation in the intensive care unit (ICU) setting.

CASE STUDY

A 63-year-old patient was transferred from the hospital emergency department to the Department of Internal Medicine, Rheumatology and Clinical Immunology as part of the internal medicine emergency service due to dyspnoea, fever, cough and the presence of blood in the sputum (haemoptysis). The patient had no previous chronic treatment.

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History of atherosclerosis, status post cataract surgery of the left and right eye, episode of depression (2021) — the patient was taking antidepressants until December 2021. Physical examination on admission: conscious patient with severe general health status, needed passive oxygen therapy using an oxygen mask with reservoir bag (O_2 saturation at 10 L/min.: 94%), in auscultation there were noticeable crackles at the base of the lungs and wheezing R > L plus vesicular murmur, regular heart rate 122/min., quiet and normally accentuated heart sounds without pathological murmurs.

Blood pressure 150/110 mm Hg, abdomen soft and non-painful without peritoneal signs, peristalsis audible, slight swelling of lower legs, joints without signs of inflammation. After urinary catheterisation, there was a trace of urine in a drainage bag.

Due to high fever and increased dyspnoea, the patient underwent an antigen test and polymerase chain reaction for SARS-CoV-2 infection: the results were negative.

Laboratory tests revealed anaemia: hemoglobin — 7.7 g/dl, white blood cell count — 8.5 G/L, platelets — 402 G/L; slight hyperkalaemia: serum potassium levels of 5.9 mmol/L, impaired renal function: serum creatinine levels of 6.6 mg/dL, increased values of acute phase inflammatory parameters such as C-reactive protein 107 mg/L and elevated serum procalcitonin levels of 2.54 ng/mL.

Numerous leukocytes and erythrocytes, both isomorphic and dysmorphic, and hyaline casts were present in the urine sediment. The patient was consulted by an ENT doctor: the medical examiner found a streak of blood content on the upper trachea, and a swab was taken from the epiglottis for *Pneumocystis jiroveci* infection — the result was negative. Blood was also taken for mycobacterial infection — after 7 days (Quantiferon test) the result was negative.

Diagnostics was extended to include imaging examinations. Chest HRCT revealed the presence of fluid in both pleural cavities, gravitationally aligned on the right side up to 50 mm, on the left side up to 43 mm, with fluid infiltrating the interlobar fissures. Primarily, however, groundglass areas, "cobblestone" areas and small parenchymal consolidations occupying approximately 90% of the lungs were seen in all lobes of both lungs — DAH to be differentiated from the increased inflammatory changes; the lesions described overlap the low-grade centrilobular emphysema. Moreover, thickening of the interlobular septa and fibrotic changes in the lung apices were described (Fig. 1, 2 and 3).

As a matter of urgency, the patient was transfused with 3 units of packed red blood cells and 2 units of fresh frozen plasma; the patient's water-electrolyte abnormalities were balanced and an intravenous infusion of furosemide was administered. Due to the possibility of the overlap of inflammatory changes with the haemorrhage, empirical broad-spectrum antibiotic therapy was applied and passive oxygen therapy (oxygen mask) was continued.

The patient was consulted by a nephrologist and a pulmonologist. Bronchofiberoscopy and BAL were performed, obtaining a high percentage of siderophages in bronchial washings. Due to high serum titres of p-antineutrophil cytoplasmic antibodies (p-ANCA), intravenous methylprednisolone 1 × 1.0 g was implemented for treatment. The infusions were scheduled for 3 consecutive days.

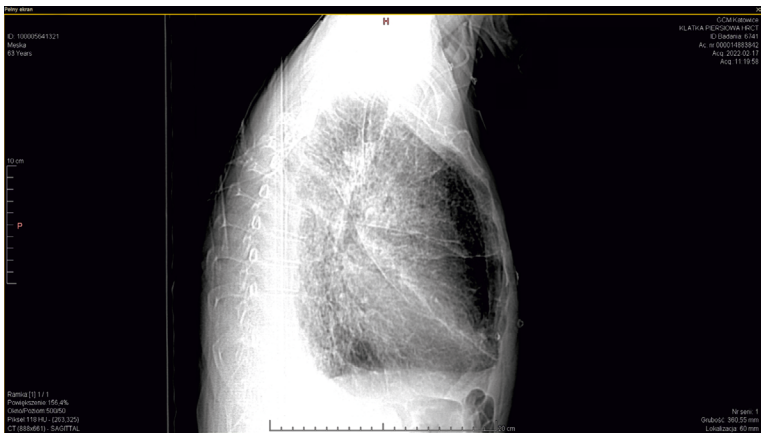

Figure 1. High-resolution computed tomography lesions of the chest, in the course of diffuse alveolar hemorrhage

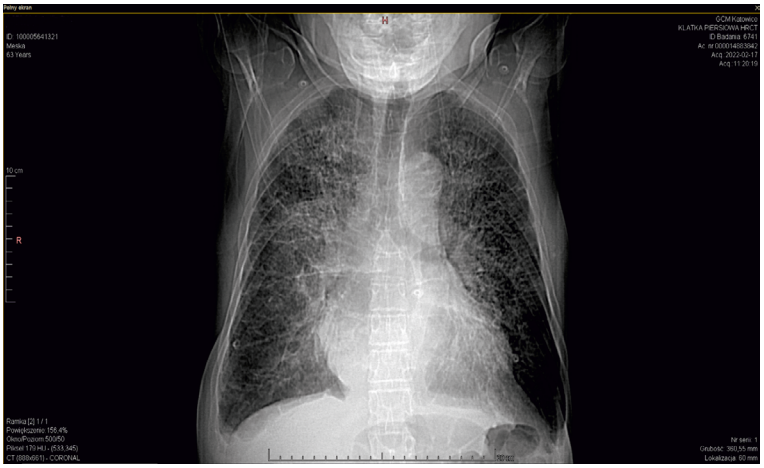

Figure 2. High-resolution computed tomography lesions of the chest, in the course of diffuse alveolar hemorrhage

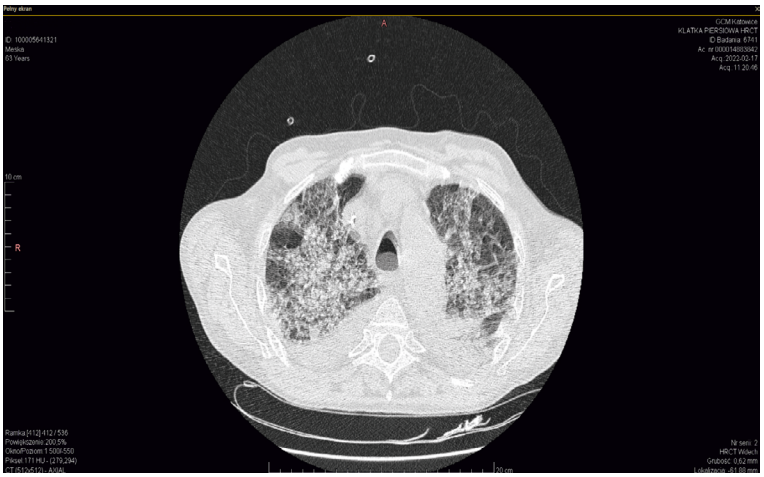

Figure 3. High-resolution computed tomography lesions of the chest, in the course of diffuse alveolar hemorrhage

Due to continued massive haemoptysis, progressive respiratory failure and renal failure, the patient was transferred to the Medical ICU for cycles of plasmapheresis. Passive oxygen therapy (mask with reservoir bag) continued to be used in the Medical ICU. Three cycles of plasmapheresis were performed, intravenous infusions of methylprednisolone 2 × 1.0 g were continued, and continuous veno-venous haemodiafiltration together with citrate anticoagulation was initiated. The patient was finally consulted by a nephrologist regarding his qualification for dialysis therapy.

After 3 days of treatment, the patient, who was cardiovascularly stable and on moderate, passive oxygen therapy (nasal cannula), was transferred back to the Clinic of Internal Medicine, Rheumatology and Clinical Immunology for further treatment. Oral steroid therapy was continued: prednisone 1 mg/kg b.w./d (80 mg/d), antibiotic therapy, and dialysis therapy. Intravenous cyclophosphamide treatment at a dose of 1 g was implemented and a request was made to start treatment with rituximab.

Due to acute steroid psychosis (direct coercion required, intensive drug treatment), which occurred in the patient after several days of steroid therapy, there was a need to reduce the dose of prednisone to 40 mg/d.

After two days, there was a sudden deterioration of the condition of the patient, recurrence of symptoms such as dyspnea, haemoptysis, circulatory and respiratory failure and atrial fibrillation *de novo.* Angio-CT ruled out pulmonary embolism.

The patient was immediately transferred back to the ICU. The patient was qualified for the second cycle of plasmapheresis (3 treatments for 3 consecutive days were performed). Then, haemodialysis and passive oxygen therapy were continued, fluid electro-

lyte and acid-base disorders were monitored and blood cells were replenished. Intravenous broad-spectrum antibiotic therapy was continued.

In the following days of the therapy, due to increasing respiratory failure, the patient was intubated and mechanical ventilation was initiated using multiple ventilation techniques.

A follow-up HRCT of the chest showed a combination of various disorders: initially, DAH in the course of vasculitis, and also inflammatory changes typical of viral infections (COVID-19) and oedema. The antigen test and the polymerase chain reaction for SARS--CoV-2 infection were positive. Remdesivir was introduced to the treatment. Continuous veno-venous haemodiafiltration was restarted with citrate anticoagulation.

In the morning, on the 15th day after a positive test for SARS-CoV-2 infection, the patient was extubated and passive oxygen therapy was initiated (the antigen test for SARS--CoV-2 infection was negative twice).

In the afternoon, due to increasing respiratory failure, the patient required intubation again.

In the following days, a massive amount of pus was removed from the tracheostomy tube, the material was sent for microbiological examination (*S. aureus* MRSA was cultured).

Imaging studies showed severe bacterial pneumonia.

Over the following days of treatment, increasing values of inflammatory parameters and a greater level of procalcitonin in serum were observed, despite the use of targeted antibiotic therapy.

Despite the intensive treatment, the patient developed multiple organ failure (septic shock).

On the 76th day of treatment, sudden circulatory arrest and death of the patient occurred.

DISCUSSION

Diffuse alveolar hemorrhage is a medical emergency associated with many different medical conditions.

The causes of DAH can be divided into two main groups: immunological and non--immunological. In any case, appropriate treatment should be initiated as soon as possible. Usually, the treatment is a two-way one. It is primarily based on stabilising the haemodynamic state of the patient (compensating the deficiency in morphotic elements of blood — transfusion of blood products), oxygen therapy — often passive (oxygen nasal cannula, mask with a reservoir) or the use of advanced mechanical ventilation techniques [4].

The second course of action in the case of bleeding associated with autoimmune diseases is the control of inflammatory activity through the use of immunosuppressive drugs. High doses of glucocorticosteroids are recommended, mainly methylprednisolone, initially intravenously for 3–5 consecutive days, cyclophosphamide mainly intravenously, and in the case of vasculitis with ANCA — the use of rituximab, which is highly effective and gives promising results in long-term observations [5].

In the event of diffuse alveolar hemorrhage associated with vasculitis with the presence of ANCA and anti-glomerular basement membrane antibodies, as well as in patients with systemic lupus erythematosus, plasmapheresis is recommended as an adjuvant treatment [6].

It is also often necessary to ensure rapid local haemostasis.

In many cases, the clinical condition of a patient requires the use of additional antibacterial, antiviral or antifungal drugs. It is necessary to cooperate with a pulmonologist (bronchofiberoscopy, bronchoalveolar lavage) [7] but also with a nephrologist (qualification for dialysis therapy) or a psychiatrist as there are psychiatric complications due to the application of high doses of corticosteroids.

Continuous close observation of the patient is extremely important. A patient with DAH can become hemodynamically unstable at any time, despite ongoing treatment. Moreover, the aggressive immunosuppressive treatment causes viral, bacterial or fungal infections, which can significantly worsen the prognosis and reduce the patient's chance of survival. Furthermore, it should be remembered that there are also infections that can be a causative factor of DAH [8].

CONCLUSIONS

Even minor haemoptysis can be a sign of massive bleeding. The treatment should always take place at the hospital with the possibility of invasive mechanical ventilation, urgent bronchoscopy and intensive, specialised immunosuppressive treatment, depending on the cause of the bleeding.

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