



## Case report

# Infective endocarditis presenting as diffuse alveolar hemorrhage: A case report

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## ABSTRACT

An 80-year-old man was admitted to the hospital because of fever, bloody sputum and exertional dyspnea of 3 days. Laboratory tests showed anemia and increase of the C-reactive protein level. A chest computed tomography scan revealed diffuse bilateral ground-glass opacities. Bronchoalveolar lavage confirmed the clinical diagnosis of diffuse alveolar hemorrhage (DAH). After methylprednisolone pulse therapy, *Enterococcus faecalis* was detected in the blood cultures. A diagnosis of infective endocarditis was made according to the Modified Duke's criteria. The causes of DAH are certainly diverse; however, we should consider infective endocarditis as one of the etiologies of DAH.

## 1. Introduction

Diffuse alveolar hemorrhage (DAH) is diagnosed by diffuse radiographic pulmonary infiltrates and progressively bloody aliquots in sequential bronchoalveolar lavage (BAL) samples. Since DAH is a life-threatening disorder that results from a variety of conditions, immediate diagnosis and treatment are essential [1]. The most common underlying causes of DAH are immune related diseases, and treatment with steroids and immunosuppressants is often prescribed [2]. However, here we report a case of DAH associated with infective endocarditis (IE) cured by antibiotic therapy.

## 2. Case report

An 80-year-old man was admitted to our hospital because of fever, bloody sputum and exertional dyspnea of 3 days. He was a non-smoker, and his medical history included benign prostatic hyperplasia, dyslipidemia, and aortic regurgitation.

Five months before, he had complained of urinary retention and prostate cancer was suspected. He underwent prostate biopsy 70 days before hospitalization to confirm this diagnosis, and received hormonal therapy: a subcutaneous injection of goserelin acetate 23 days before hospitalization.

Besides the above, he was taking silydosine, distigmine bromide, and pravastatin sodium without any other additional medicine or supplements.

On admission, his temperature was 38.5 °C, heart rate 75 beats per minute, blood pressure 147/73 mmHg, respiratory rate 24 breaths per minute, and oxygen saturation was 86% when breathing in room air. Chest auscultation revealed no adventitious breath sounds. The cardiac auscultation disclosed a diastolic murmur, best heard over the left border of the third intercostal sternum. The remainder of the physical examination was normal. We could not find either the Osler node or Janeway spot. The Roth spots were also not found. Laboratory tests revealed a white blood cell count of 10,480/mm<sup>3</sup>, a C-reactive protein level of 16.26 mg/dl, and a haemoglobin level of 7.5 g/dl. Serum Krebs von den Lungen-6 (KL-6) and surfactant protein D (SP-D) levels were 98U/mL (normal: <500 U/mL) and 71.0ng/mL (normal: <110 ng/mL), respectively. Rheumatoid factor (RF) level was 22U/mL (normal: <15U/mL). Arterial blood gas analysis while breathing room air revealed hypoxia (PaO<sub>2</sub> 50.2 Torr) with PaCO<sub>2</sub> of 31.5 Torr and A-aDO<sub>2</sub> of 60.2 Torr. A peripheral blood lymphocyte stimulation test against goserelin proved negative (Table 1).

The electrocardiogram showed a complete right bundle branch block. Chest radiography revealed diffuse bilateral infiltrative shadows (Fig. 1). High-resolution computed tomography (CT) of the chest showed diffuse ground-glass opacities with a crazy-paving appearance (Fig. 2). A bronchoscopic examination demonstrated progressively hemorrhagic BAL in serial samples. This confirmed the clinical diagnosis of DAH. BAL fluids showed 6.4 × 10<sup>5</sup> cells per mL with 63.5% macrophage, 21.5% neutrophils, 13.5% lymphocytes, and 1.5% eosinophils. In cytology, hemosiderin phagocytosis of macrophage was observed by

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Berlin blue staining (Fig. 3). The BAL cultures were free of pathogens. Considering the possibility of autoimmune diseases, methylprednisolone (1000mg × three days) was administered intravenously after bronchoscopy. However, *Enterococcus faecalis* was detected from 2/2 sets of blood cultures obtained at the time of admission. *E. faecalis* was detected in all of the 4 separate blood cultures, including additional blood cultures thereafter collected. It was found to be a strain susceptible to ampicillin (ABPC), benzylpenicillin, gentamicin (GM), teicoplanin, vancomycin, linezolid, and levofloxacin. It was a non-high-level aminoglycoside-resistant strain. It was determined to be erythromycin intermediate and resistant to clindamycin, minocycline, and sulfamethoxazole-trimethoprim.

Urine culture did not detect *E. faecalis*. In addition, chest and abdomen contrast CT did not reveal any source of infection. We therefore considered the possibility of IE, and performed both transthoracic echocardiography and transesophageal echocardiography, but vegetations were not observed. Echocardiography revealed aortic valve calcification and hyperplasia degeneration with moderate regurgitation (pressure half time of AR jet: 383 ms).

Brain MRI revealed hyperintensity in the right frontal lobe on an axial diffusion-weighted image and this was considered to be evidence of an acute vascular embolism (Fig. 4).

We finally made a diagnosis of IE according to the Modified Duke's criteria [3]; 1 important criterion was satisfied (microorganisms consistent with IE from persistently positive 4 separate blood cultures) and more than 3 minor criteria (predisposing heart condition, temperature >38 °C, elevated RF, major arterial emboli (Fig. 4)). The patient completed a 6-week course of intravenous ABPC, 2 g every 4 hours, and ceftriaxone (CTRX), 2 g every 12 hours (Fig. 5). Blood cultures were negative one week after start of treatment, heart failure did not occur during treatment, and valve destruction was not observed 6 weeks after treatment completion. An outpatient follow-up visit a year after discharge revealed complete remission.

### 3. Discussion

The pathological findings of DAH are as follows: (1) Pulmonary capillaritis pattern, which mainly indicates the infiltration of neutrophils into the alveolar septum and the capillary atrium, and from there bleeds into the alveolar space (2) Bland pulmonary hemorrhage pattern in which the alveolar septal walls are not at all destroyed and only bleeding into the alveoli is recognized (3) Diffuse alveolar damage pattern accompanied by edema of the alveolar septal wall and bleeding into the alveolar space to form a hyaline membrane [4,5].

Capillaritis caused by autoimmune diseases such as systemic lupus erythematosus and anti-neutrophil cytoplasmic antibody associated vasculitis are the most common pathological findings of DAH. A review of 34 cases of histopathologically confirmed DAH indicate capillaritis occurred in 88% of occasions [6]. In such instances, treatment typically

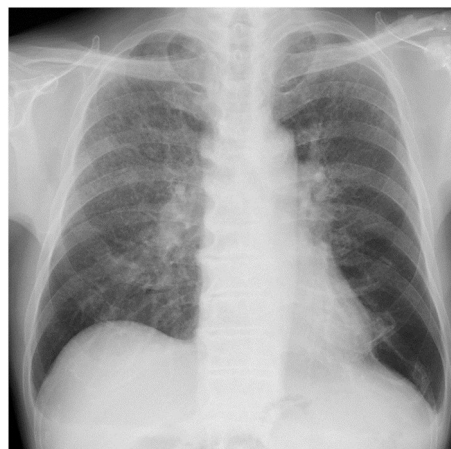


Fig. 1. Chest radiography showed diffuse bilateral infiltrative shadows.

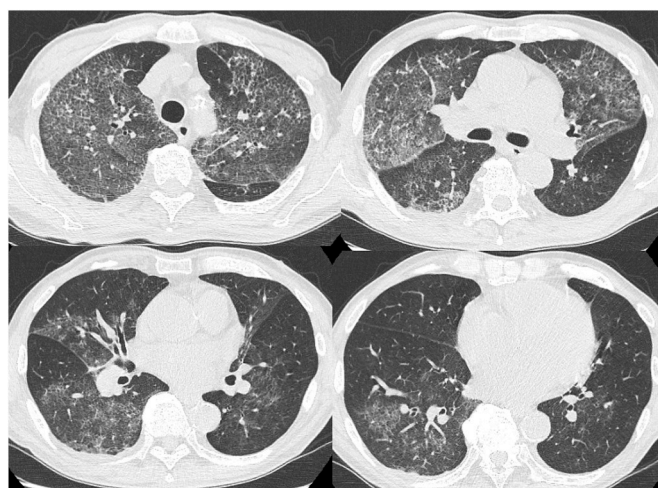


Fig. 2. High-resolution computed tomography of the chest showed diffuse ground-glass opacities with a crazy-paving appearance.

includes corticosteroids, immunosuppressive agents and occasionally plasmapheresis.

Therefore, there is a danger that since DAH is likely to be associated with autoimmune diseases, erroneous treatment selection may occur. It must be remembered that DAH is due to various disorders and, although rare, infectious diseases may also cause DAH [4]. For example, in immunocompromised patients, the main infectious diseases that cause DAH are cytomegalovirus, adenovirus, invasive aspergillosis,

Table 1  
Laboratory findings on admission.

●Arterial blood gas (room air)		●Biochemistry		●Immunology				
pH	7.505	TP	6.80	g/dL	KL-6	98	U/ml	
PaCO2	31.5	Torr	Alb	2.78	g/dL	SP-D	71.0	ng/ml
PaO2	50.2	Torr	AST	29	IU/L	Rheumatoid factor	22.0	IU/ml
HCO3-	24.3	mmol/L	ALT	19	IU/L	anti-CCP antibody	<0.2	U/ml
●Hematology		LDH	244	IU/L	anti-nuclear antibody	40.0		
WBC	10480	/μL	BUN	22	mg/dL	anti-ds-DNA-IgG antibody	4.0	IU/ml
RBC	265 × 104	/μL	Cr	0.85	mg/dL	anti-Sm antibody	<1.0	U/ml
Hb	7.5	g/dL	Na	139	mEq/L	anti-SS-A antibody	432.0	U/ml
Ht	23.1	%	K	3.6	mEq/L	anti-SS-B antibody	1.1	U/ml
Plt	25.6 × 104	/μL	Cl	106.0	mEq/L	MPO-ANCA	<1.0	U/ml
●Coagulation		BNP	95.9	pg/mL	PR3-ANCA	<1.0	U/ml	
PT-INR	1.13		CRP	16.2	mg/dL	anti-GBM antibody	<2.0	U/ml
APTT	25.7	sec	PCT	0.4	ng/mL	LST (SI)	135.0	%
D-dimer	1.3	μg/ml						

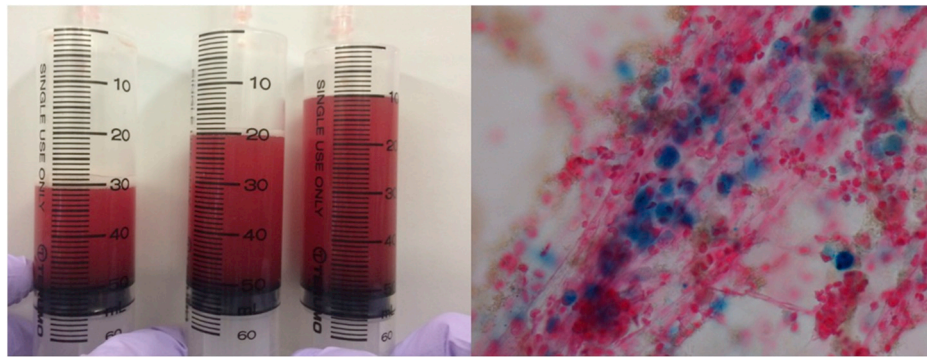


Fig. 3. Bronchoalveolar lavage fluid and Berlin blue staining, 40x.

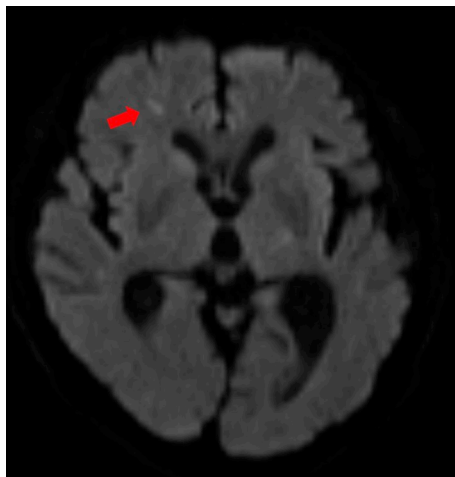


Fig. 4. Hyperintensity in the right frontal lobe on an axial diffusion-weighted image (DWI).

*Mycoplasma*, *Legionella*, and *Strongyloides* [7] In immunocompetent patients, the infectious diseases that most frequently are the reason behind DAH are influenza A (H1N1), dengue, leptospirosis, malaria, and *Staphylococcus aureus* infection [7]. According to our research, there has been few case reports of IE presenting as DAH [8]. It is presumed that small vasculitis occurs in the alveolar capillary, similar to an Osler nodule being formed in the fingertip with small vasculitis established by the immunological mechanism. This case underlines the importance of suspecting infectious diseases such as IE as an etiology of DAH. For treatment of IE by *E. faecalis*, ABPC and GM is recommended in the guidelines. However, this case involved an elderly patient who was concerned about the side effects of GM and was healed by intravenous treatment of ABPC and CTRX for 6 weeks [9,10].

In conclusion, we have here reported a case of DAH associated with IE. IE should be considered in the diagnosis of DAH cases since IE can prove to be lethal if diagnosis is delayed. If accompanied by signs of infection such as fever, it is important to obtain blood cultures for diagnosis.

**Conflicts of interest**

The authors state that they have no Conflict of Interest (COI).

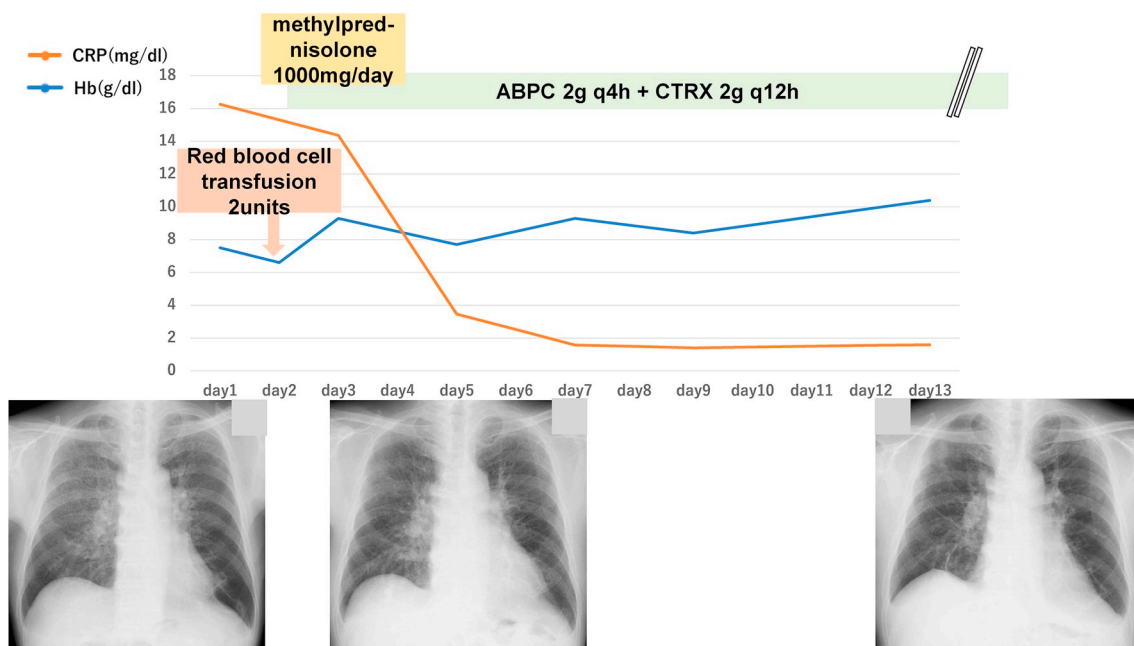


Fig. 5. Clinical course after hospitalization.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmcr.2019.100931>.

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