

## PHOTO QUIZ

## Bloody, tropical fever

D.E. Sampimon<sup>1</sup>, M. Amelink, P.J.E.J. van de Berg<sup>2</sup>, W.K. Lagrand<sup>2</sup>, P.I. Bonta<sup>3</sup>, A.P.J. Vlaar<sup>2</sup>

Department of <sup>1</sup>Internal Medicine, <sup>2</sup>Intensive Care Medicine and <sup>3</sup>Pulmonary Medicine, Academic Medical Center, Amsterdam, the Netherlands

### Correspondence

D.E. Sampimon - d.e.sampimon@amc.nl

### Case

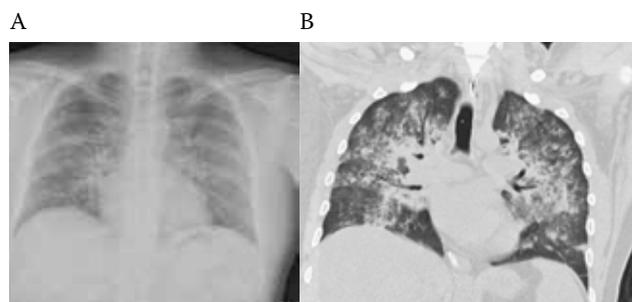
A 41-year-old pilot living in Rome presented at our emergency room after arrival at Schiphol airport with subacute dyspnoea. Since one month he had complaints of arthralgia (knees, ankles) followed by a period of fever. Recently he travelled to South-East Asia and South America where he only visited urban areas. Vital signs indicated tachycardia 110/min and fever 39.1°C. His knees and ankles were not red or swollen. Further physical examination was unremarkable. The leukocyte count was  $10 \times 10^9$  g/l, creatinine was 75  $\mu\text{mol/l}$ . Chest X-ray and computed tomography of the chest (chest CT) showed diffuse bilateral consolidations, and ground glass (*figure 1*). Blood and sputum cultures were taken and afterwards broad-spectrum antibiotics (ceftriaxone, erythromycin and co-trimoxazole) and antiviral therapy (oseltamivir) were given at admission. Due to rapidly progressive respiratory failure, the patient was admitted to the intensive care unit (ICU) and intubated. A bronchoscopy revealed focal areas of vulnerable, ulcerative mucosa and diffuse endobronchial blood compatible with diffuse alveolar haemorrhage (*figure 2*) and a bronchoalveolar lavage (BAL) was performed. Because of his recent visit to tropical areas, an infectious disease was suspected. Diagnostic work-up for infections, including human immunodeficiency virus and examination of the BAL were negative including staining, culture, molecular and immunoassays for micro-organisms including respiratory bacteria and viruses, tuberculosis, leptospirosis and aspergillosis.

*What is your diagnosis?*

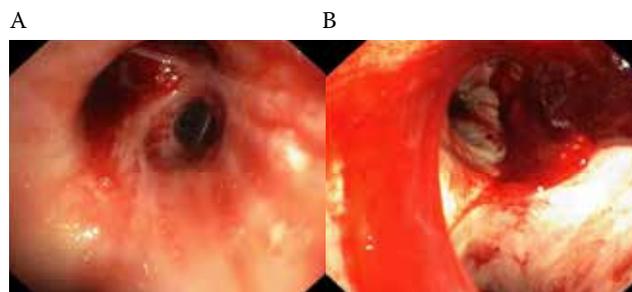
### Answer

You will find the answer on page 77 in this issue.

**Figure 1A.** Chest-X-ray showing bilateral consolidations. **B:** Chest CT with bilateral peribronchovascular consolidations with ground glass



**Figure 2.** Bronchoscopy showing diffuse endobronchial blood with focal areas of ulcerative, vulnerable mucosa compatible with diffuse alveolar haemorrhage. **A:** Endobronchial blood in the ostium of the right upper lobe; **B:** Diffuse endobronchial blood in the left main bronchus (upper ostium left upper lobe, lower ostium left lower lobe)



## ANSWER TO PHOTO QUIZ

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### Diagnosis

The clinical findings, chest CT and bronchoalveolar lavage (BAL) are supportive for diffuse alveolar haemorrhage (DAH), which is caused by a disruption of the alveolar-capillary basement membrane.<sup>[1]</sup> The differential diagnosis of DAH is broad, but can be divided into non-immune mediated (ARDS including infectious aetiology, drug-induced, cardiac failure, coagulopathy) and immune-mediated (vasculitis and connective tissue disease). In *table 1*, we present our differential diagnosis of DAH and bilateral consolidations with ground glass after a visit to South-East Asia and South America. The medical history, physical exam and primary work-up showed no signs of heart or renal disease, coagulopathy or drug abuse. Due to his travelling we considered endemic infectious causes. The joint pain together with the bilateral consolidations and DAH also made us consider immune-mediated cause.

**Table 1.** Differential diagnosis of diffuse alveolar haemorrhage and bilateral pulmonary consolidations with ground glass after a visit to South-East Asia and South America

ARDS	Infectious	Viral respiratory infections including influenza and Hantavirus, bacterial respiratory infection including Leptospirosis, Chlamydia pneumoniae, Rickettsiosis, Brucellosis, Mycoplasma, Melioidosis
	Opportunistic infections	AIDS with tuberculosis/ pneumocystis pneumonia, aspergillosis
Immune mediated	Systemic vasculitis and connective tissue diseases	Granulomatosis with polyangiitis, microscopic polyangiitis
	Rheumatic diseases	Anti-GBM disease/Goodpasture syndrome, isolated pulmonary capillaritis, mixed connective tissue disease, rheumatoid arthritis, systemic lupus erythematosus

Bronchial and nasal biopsies showed non-specific, ulcerative inflammation. Anti-glomerular basement membrane antibodies (anti-GBM) were negative. However, anti-neutrophil cytoplasmic antibody analysis was positive, with high titres of anti-proteinase3 (PR3-ANCA 1152 KIU/l) confirming an immune-mediated cause of DAH, most probably granulomatosis with polyangiitis (GPA). Eighteen hours after presentation to the emergency room and negative work-up for infections, we initiated plasma exchange and high-dose glucocorticoids (1 g/day for 3 days followed by 1 mg/kg/day) were given.

Presentation of a GPA vasculitis with predominant/ single pulmonary involvement is rare. Approximately 40 cases have been reported.<sup>[2]</sup> A retrospective study of biopsy-proven

capillaritis/vasculitis showed that in the majority (21 of the 36 patients) GPA caused DAH.<sup>[3]</sup> A positive PR3-ANCA has a sensitivity of 91% and specificity of 99% for GPA.<sup>[4]</sup> In life-threatening cases of DAH caused by vasculitis, treatment consists of high-dose glucocorticoids combined with cyclophosphamide and plasma exchange.<sup>[5]</sup> Thereafter, maintenance therapy with prednisone in combination with azathioprine or mycophenolate can be prescribed.<sup>[4,6]</sup> In our case cyclophosphamide was postponed till the cultures remained negative and semen preservation was performed.

The patient improved clinically and he could be weaned from mechanical ventilation. Plasma exchange was continued for five days. At day 6 he was discharged from the ICU and at day 15 he was discharged from the hospital. Nine months after his presentation he was completely recovered.

### Conclusion

In conclusion, patients with high suspicion for DAH should be screened for vasculitis, also in the absence of renal failure. Furthermore, infectious diseases should be suspected in DAH especially with a recent travel history to tropical areas.

### Disclosures:

All authors declare no conflict of interest. No funding or financial support was received.

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