

Diffuse alveolar hemorrhage as an initial presentation of ANCA-associated vasculitis in an 80-year-old man

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The elderly population is growing, and as life expectancy increases, more elderly patients survive longer with acute and chronic diseases. Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is increasingly recognized in older patients. Due to comorbidities, AAV in an elderly individual may present atypically, with frequent involvement of the kidneys or with vague constitutional symptoms and can thus be difficult to diagnose.

An 80-year-old man with a history of chronic kidney disease, ischemic heart disease, and prostate cancer (treated with flutamide) presented with a 1-week history of anorexia, progressive weakness, and cough with mild hemoptysis. He was not febrile. A physical examination revealed bilateral rales at the lung bases. Laboratory tests showed normocytic anemia (hemoglobin, 7.7 g/dl), mild leukocytosis (white blood cell count, $11.5 \times 10^9/l$), elevated erythrocyte sedimentation rate (51 mm/h), elevated C-reactive protein (107 mg/l), exacerbation of renal impairment (creatinine, 2.94 mg/dl), nephrotic proteinuria (4.55 g/d), and erythrocyturia. Bilateral pulmonary infiltrations were present on chest X-ray (FIGURE 1A). Despite antibiotic therapy (amoxicillin/clavulanic acid with clarithromycin was changed after 4 days to levofloxacin with ceftazidime due to sputum culture positive for *Pseudomonas aeruginosa*) and several blood transfusions, his clinical condition deteriorated through exacerbation of hemoptysis. A physical examination revealed new vasculitic skin rash on the legs (FIGURE 1B). Bronchofiberscopy, chest computed tomography (FIGURE 1C), and lung ultrasonography (FIGURE 1D) confirmed diffuse alveolar hemorrhage (DAH). Serum was strongly positive for cytoplasmic ANCA (1:1280, PR3-ANCA >200 U/ml) and negative for antiglomerular basement membrane antibodies.

On the basis of the above findings, a diagnosis of AAV was established (activity = 27 according to the

Birmingham Vasculitis Activity Score version 3). Methylprednisolone (3×1.0 g IV) and then prednisone (60 mg/d) were started, with the addition of cyclophosphamide in pulses according to the European Vasculitis Study Group guidelines (10 mg/kg dose reduced due to the patient's age and renal failure).^{1,2} Plasmapheresis was considered but was not performed because of the patient's age, comorbidities, and stable kidney function. Immunosuppressive treatment was complicated by disseminated shingles, fungal infection (*Candida albicans*) of the tongue (FIGURE 1E), and lymphopenia. After the fourth infusion of cyclophosphamide (total dose, 2.4 g IV), the patient developed general weakness, anorexia, indifference, and pain located in the cervical and thoracic spine. Chest computed tomography revealed new pulmonary infiltrations (FIGURE 1F). Positive cultures obtained during bronchofiberscopy confirmed bacterial and fungal infection. The results of serum galactomannan antigen test for the diagnosis of aspergillosis were positive. After antibiotic (ceftriaxone, cefepime) and antifungal therapy (voriconazole), partial normalization of inflammation was achieved. During that time, bilateral proximal muscle weakness of the upper limbs occurred. Magnetic resonance imaging revealed the presence of vascular lesions in the brain and spinal cord, besides the metastatic lesions in vertebra C6, Th1, and Th2. Due to ineffectiveness of immunosuppressive therapy (progression of renal failure, new pulmonary infiltrations and nodules, vascular lesions in the central nervous system) in the presence of infectious complications and metastatic cancer, we decided to stop the cyclophosphamide treatment, while treatment with medium-dose steroids was continued. The patient died a month later due to the second cerebral event.

Older age is independently associated with mortality in patients with AAV. Elderly patients

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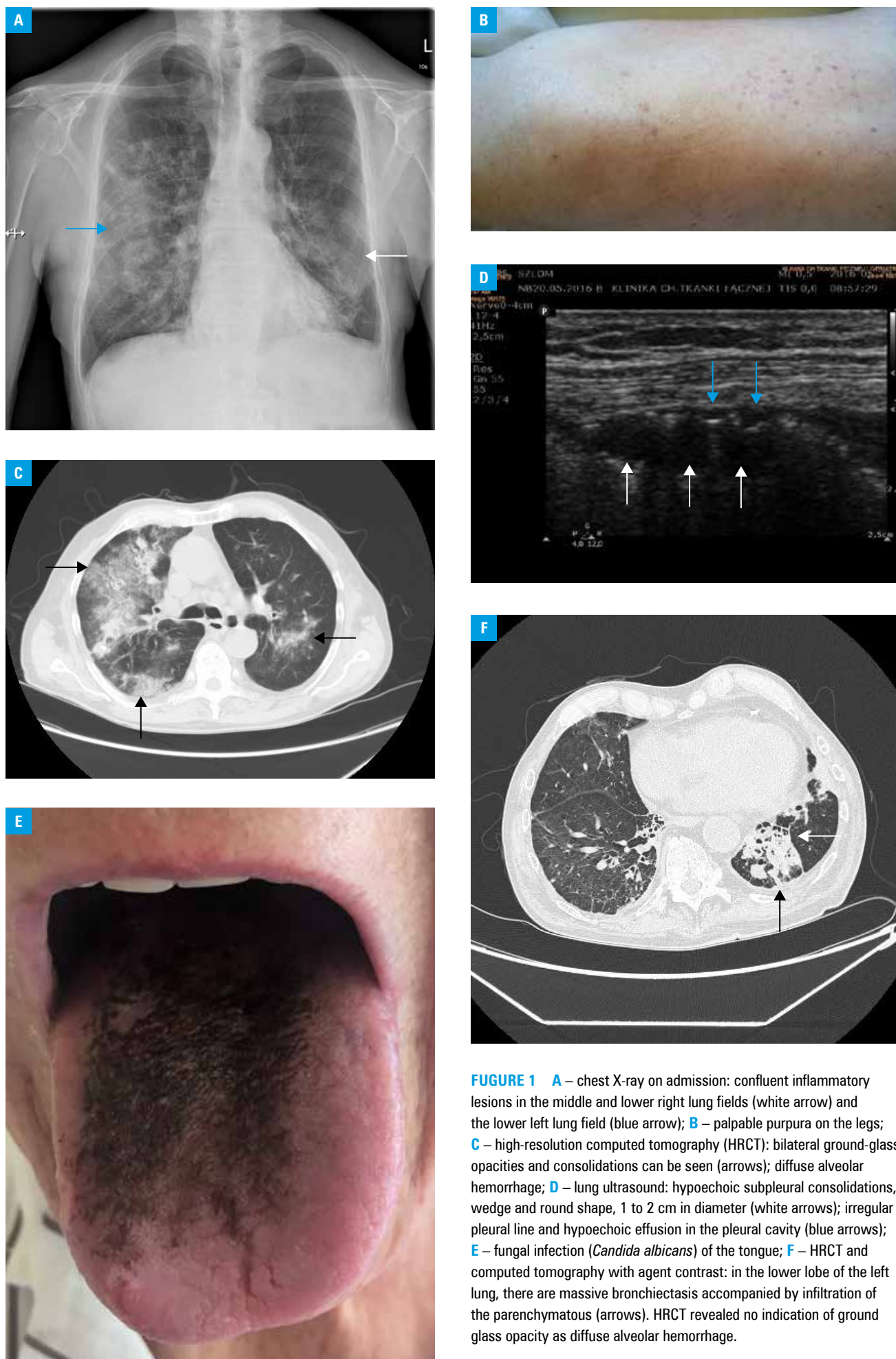


FIGURE 1 **A** – chest X-ray on admission: confluent inflammatory lesions in the middle and lower right lung fields (white arrow) and the lower left lung field (blue arrow); **B** – palpable purpura on the legs; **C** – high-resolution computed tomography (HRCT): bilateral ground-glass opacities and consolidations can be seen (arrows); diffuse alveolar hemorrhage; **D** – lung ultrasound: hypoechoic subpleural consolidations, wedge and round shape, 1 to 2 cm in diameter (white arrows); irregular pleural line and hypoechoic effusion in the pleural cavity (blue arrows); **E** – fungal infection (*Candida albicans*) of the tongue; **F** – HRCT and computed tomography with agent contrast: in the lower lobe of the left lung, there are massive bronchiectasis accompanied by infiltration of the parenchymatous (arrows). HRCT revealed no indication of ground glass opacity as diffuse alveolar hemorrhage.

have usually more severe organ damage, respond less satisfactorily to treatment, are more susceptible to secondary infections, and have a poorer prognosis.³⁻⁵ DAH is well known as a serious AAV symptom associated with high mortality. The guidelines suggest considering the addition of plasma exchange to corticosteroid and cyclophosphamide therapy in patients with advanced kidney dysfunction and severe DAH. Specific questions relating to the type, intensity, and duration of immunosuppression need to be answered in order to optimize the risk-to-benefit ratio.

REFERENCES

- 1 Yates M, Watts RA, Bajema IM, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. *Ann Rheum Dis*. 2016; 75: 1583-1594.
- 2 Sznajd J, Mukhtyar C. How to treat ANCA-associated vasculitis: practical messages from 2016 EULAR/ERA-EDTA recommendations. *Pol Arch Med Wewn*. 2016; 126: 781-788.
- 3 Min Chen, Feng Yu, Ying Zhang, Ming-Hui Zhao. Antineutrophil cytoplasmic autoantibody-associated vasculitis in older patients. *Medicine*. 2008; 87: 203-209.
- 4 Haris A, Polner K, Aranyi J, et al. Clinical outcomes of ANCA-associated vasculitis in elderly patients. *Int Urol Nephrol*. 2014; 46: 1595-1600.
- 5 Weiner M, Goh SM, Mohammad AJ, et al. Outcome and treatment of elderly patients with anca-associated vasculitis. *Clin J Am Soc Nephrol*. 2015; 10: 1128-1135.