Intensive Care Med (1999) 25: 755–757

BRIEF REPORT

U. Da Broi
U. Orefice
C. Cahalin
V. Bonfreschi
L. Cason

ARDS after double extrinsic exposure hypersensitivity pneumonitis

Received: 17 November 1998
Final revision received: 23 March 1999
Accepted: 30 April 1999

U. Da Broi (✉) · U. Orefice · C. Cahalin
Istituto Fisiopatologia Respiratoria,
Ospedale S. Maria Misericordia,
Udine, Italy
e-mail: ugo.dabroi@xnet.it
Fax: + 39-0432-448 37

V. Bonfreschi · L. Cason
Cattedra Anestesia Rianimazione,
Università Udine, Udine, Italy

Abstract Hypersensitivity pneumonitis or extrinsic allergic alveolitis is a lung disease due to T cell and macrophage activation with IgA, IgG or IgE immunocomplex tissue lesions following extrinsic exposure to organic or inorganic agents. We report a case of hypersensitivity pneumonitis (pigeon protein sensitized) with a second nosocomial exposure to *Aspergillus fumigatus* proteins from a contaminated oxygen water humidifier: the second extrinsic exposure induced significant acute respiratory failure with ARDS. A pre-existing COPD syndrome requiring prolonged oxygen therapy (7 days) involved lung disease with delayed clinical diagnosis and therapy. Microbiological and mycological analysis of oxygen water humidifiers should be considered, especially for hypersensitivity pneumonitis patients, when a new inexplicable clinical impairment occurs.

Key words Hypersensitivity pneumonitis · Extrinsic allergic alveolitis · Pigeon proteins · *Aspergillus fumigatus* proteins · Double exposure · ARDS

Introduction

Hypersensitivity pneumonitis or extrinsic allergic alveolitis is an uncommon lung disease due to complex immunopathological mechanisms. Extrinsic prolonged exposure to organic antigens (bacteria, mold, animal proteins) or inorganic antigens (isocyanates) promotes pulmonary CD8 and CD4 T cell sensitization [1, 2, 3]. A final extrinsic antigen challenge activates reactive T cells through macrophage presentation and causes "hypersensitivity pneumonitis fibrosis lesions" with epithelioid and multinucleate giant cells [4, 5]. Antigen challenge induces acute or chronic respiratory syndromes in 50% of exposed patients with pre-existing precipitins. The clinical acute disease generally consists of dyspnea, cough, hyperthermia with chest X-rays demonstrating diffuse alveolar signs. Pulmonary symptoms appear 4–8 h after the final exposure and resolve 12–20 h after this same event [6, 7, 8]. We report a rapid two-stage hypersensitivity pneumonitis (pigeon and *Aspergillus fumigatus* precipitin sensitized) and ARDS in a patient admitted into a medical respiratory intensive care unit (ICU). During a hospitalization of 7 days, the patient was exposed to *A. fumigatus* from oxygen water humidifiers and developed a new hypersensitivity pneumonitis. The pre-existing COPD syndrome with pathological respiratory function augmented his acute respiratory failure and ARDS. This patient required tracheal intubation and prolonged intensive respiratory care treatment.

Case report

A 65-year-old Caucasian male patient, farmer and pigeon breeder with pre-existing COPD disease was admitted to a medical respiratory intensive care department for acute respiratory failure. Respiratory symptoms had appeared 12 h prior to the hospital admission, during his daily chores with the pigeons on his farm. The patient reported severe dyspnea, fever (39 °C), diffuse muscle pain, shivering and a dry cough. Chest X-ray showed diffuse alveolar signs involving both lungs. On hospital admission the blood gas values were: pH = 7.39, arterial oxygen tension (PaO_2) 62 mmHg

(FIO_2 = 0.21), arterial carbon dioxide tension ($PaCO_2$) 51 mmHg, bicarbonate (HCO_3) 24.0 mEq/l, arterial oxygen saturation (SaO_2) 91%. Bacterial or viral lung infection was considered. Treatment included i.v. antibiotic therapy with ceftazidime, aminophylline, crystalloid fluid support and FIO_2 0.4 oxygen mask therapy (Venturi system with a water humidifier warmed to body temperature, 37°C). Blood and lung secretion samples for bacterial and viral laboratory analysis were immediately taken, with negative results. Twenty-four hours after hospital admission, the respiratory symptoms improved. The patient suffered slight dyspnea, the chest X-ray showed a partial reduction of the diffuse alveolar bilateral signs, PaO_2 was 71 mmHg (FIO_2 = 0.4), $PaCO_2$ was 48 mmHg, and his fever disappeared. During the following 6 days the patient's symptoms remained unchanged, while the COPD symptoms clouded the clinical diagnosis**:** persistent slight dyspnea and hypoxemia were wrongly considered as chronic COPD features. The oxygen mask therapy (FIO_2 = 0.3) was maintained for the following 7 days. On day 5, in the light of the patient's clinical history and job (pigeon breeder), new blood and endoscopic bronchoalveolar lavage fluid (BALF) samples were studied for extrinsic allergic alveolitis precipitins: on day 7, the results showed significant levels of blood precipitins of pigeon proteins (ELISA procedure) and an increase of BALF hypersensitivity pneumonitis markers (total cells 68.4×10^6/100 ml, relative lymphocytes 55.2%, CD4 cells 26.8%, CD8 cells 43.2%, CD4/CD8 ratio 0.62, NK cells 6.4%). A skin prick test confirmed the patient's sensitization by pigeon proteins. On the same day the patient suffered significant respiratory symptoms: increased dyspnea, fever (39°C), diffuse muscle pain, shivering and dry cough. A new chest X-ray showed more diffuse alveolar signs involving both lungs. Respiratory dyspnea and blood gas values worsened: pH 7.35, PaO_2 42 mmHg (FIO_2 = 0.4), $PaCO_2$ 72 mmHg, HCO_3 27.0 mEq/l, SaO_2 89%. The patient underwent non-invasive ventilation therapy (NIV nose mask with 5 cmH_2O airway pressure CPAP) for 3 h, followed by emergency tracheal intubation for acute respiratory failure and serious neurological impairment. A severe ARDS resulted with gas exchange, hemodynamic and X-ray signs (Murray Lung Injury Score = 3).

On day 7 new microbacterial and immunological laboratory investigations were performed. The microbacterial and viral blood results were negative for signs of lung infection. Immunological results (on day 9) showed significant levels of blood precipitins of pigeons and *A. fumigatus* (ELISA procedure) and BALF higher hypersensitivity pneumonitis markers (total cells 75.8×10^6/100 ml, relative lymphocytes 60.3%, CD4 cells 23.5%, CD8 cells 45.1%, CD4/CD8 ratio 0.52, NK cells 9.8%). Skin prick tests confirmed the patient's sensitization by pigeon and *A. fumigatus* proteins. A new extrinsic exposure hypersensitivity pneumonitis due to *A. fumigatus* proteins was considered and steroid therapy prednisone (1 mg/kg per day i.v.) started immediately. Water samples were withdrawn from the oxygen water humidifier of the medical respiratory ICU for an *A. fumigatus* laboratory search and mycological investigations confirmed its presence. The ARDS required mechanical ventilation (IPPV-PEEP), inotropic (dobutamine) therapy for 6 days and steroid (prednisone) therapy for 5 days. The patient was extubated and admitted to the medical respiratory unit. Pulmonary function tests (PFT) performed 7 days after tracheal extubation measured carbon monoxide (CO) lung transfer capacity impairment, while a lung biopsy confirmed typical hypersensitivity pneumonitis signs (interstitial and alveolar fibrosis with lymphocyte infiltrates – small granulomas with epithelioid and multinucleated giant cells).

Discussion

Hypersensitivity pneumonitis or extrinsic allergic alveolitis is an uncommon clinical event due to specific immunological mechanisms. Such a clinical syndrome rarely needs intensive care treatment with tracheal intubation and mechanical ventilation; patients often require only the removal of the source of antigen inhalation and systemic long-term steroid therapy [6, 7, 8]. This case is unusual in that there was a double pulmonary exposure to pigeon proteins (from the patient's job on a farm) and *A. fumigatus* proteins (from an oxygen water humidifier in the hospital). The second pathological exposure occurred in a clinical department after inhalation of *A. fumigatus* spores from an oxygen therapy device (Venturi system water humidifier warmed to a body temperature of 37°C). Perhaps a pre-existent COPD syndrome complicated the patient's disease and delayed both the correct clinical diagnosis and therapy. Delayed steroid treatment for the first hypersensitivity pneumonitis occurred because the first blood precipitin check response took place on day 7, when a suspected infective ARDS appeared.

The first hypersensitivity pneumonitis was perhaps not as high as the second: probably the patient's moving from his farm was a sufficient therapeutic procedure without steroid drugs. Seven days of prolonged oxygen therapy provided a long inhalational contact with *A. fumigatus* spores (from the oxygen water humidifier) and a second extrinsic exposure: while a non-existent lung infection was suspected, significant respiratory failure occurred. The first laboratory blood precipitins check was positive for pigeon proteins and negative for *A. fumigatus*, so we suppose that the patient was not sensitized or was only partly sensitized by *A. fumigatus* (perhaps without immunological blood levels) before hospital admission: however we cannot establish whether he had a new *A. fumigatus* sensitization in the ICU. Microbiological and mycological analysis of oxygen water humidifiers should be considered, especially for hypersensitivity pneumonitis patients when a new inexplicable clinical impairment occurs. A new exposure or full sensitization by *A. fumigatus* from oxygen water humidifiers could be excluded or confirmed [9, 10].

References

1. Peratoner A, Struzzo P, Orefice U (1996) A study on immunological activation of BAL fluid in exposed and farmer's lung-affected subjects. Am J Respir Med 153 (4): A546
2. Kunkel SL, Lukak NW (1996) Th1 and Th2 cell responses regulate experimental lung granuloma development. Sarcoidosis Vasc Diffuse Lung Dis 13: 120–128
3. Orefice U, Da Broi U (1998) Immunological mechanisms of granulomatous response in hypersensitivity pneumonitis. Eur Respir J 12 (28): 330
4. Moritaka S, Hisato Y, Kazuko N, Hirotsugu K, Msayuki N (1997) A mechanism accounting for granulomatous responses in hypersensitivity pneumonitis. Sarcoidosis Vasc Diffuse Lung Dis 14: 131–138
5. Richerson HB, Bernstein IL, Fink JN, Hunninghake GW, Novey HS, Reed CE, Salvalaggio JE, Schuyler MR, Schwartz HJ, Stechschulte DJ (1989) Guidelines for the clinical evaluation of hypersensitivity pneumonitis. Report of the subcommittee on hypersensitivity pneumonitis. J Allergy Clin Immunol 84 : 839–844
6. Salvalaggio JE (1997) Extrinsic allergic alveolitis (hypersensitivity pneumonitis): Past, present and future. Clin Exp Allergy 27 (Suppl I): 18–25
7. Kaltreider HB (1993) Hypersensitivity pneumonitis. West J Med 159: 570–578
8. Ando M, Suga M (1997) Hypersensitivity pneumonitis. Curr Opin Pulm Med 3: 391–395
9. Suda T, Sato A, Ida M, Gemma H, Hayakawa H, Chida K (1995) Hypersensitivity pneumonitis associated with home ultrasonic humidifiers. Chest 107: 711–717
10. Williams AJ, Gordon IJ (1987) Extrinsic allergic alveolitis caused by a cold water humidifier. Thorax 42: 399