

Bronchoalveolar lavage in pulmonary mycotoxicosis (organic dust toxic syndrome)

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ABSTRACT Two cases of pulmonary mycotoxicosis (organic dust toxic syndrome) are described in which bronchoalveolar lavage was undertaken during the acute phase and after recovery. Both cases occurred after exposure to mould dust in a silo in the course of removing the top mouldy layer of silage or oats at the start of unloading. The workers suffered an acute febrile illness accompanied by cough and dyspnoea. One patient had impaired ventilatory function and both had arterial desaturation in the acute phase. There was mild impairment of diffusing capacity (transfer factor). Bronchoscopy showed inflammation of the bronchial mucosa in one patient. Fungal spores were cultured from the lavage fluid in both patients. In both patients there was an increase in the percentage of neutrophils in the lavage fluid without increase in lymphocytes. The immunoglobulin concentration in the lavage fluid was normal. At the follow up lavage the neutrophils had returned to normal while a mild lymphocytosis of the lavage fluid was seen in both patients.

An acute bronchopulmonary response to a massive inhalation of fungal spores has previously been described and termed pulmonary mycotoxicosis.¹ The condition is also known as organic dust toxic syndrome. Typically acute pulmonary mycotoxicosis presents as a febrile illness with dry cough, dyspnoea, and inspiratory crackles beginning a few hours after exposure to a large quantity of spores. Silo unloading is the principal occupational setting. The chest radiograph shows either normal appearances or minimal interstitial infiltration.¹ Symptoms usually resolve spontaneously after withdrawal from exposure and the disease leaves no sequelae. APM must be distinguished from acute extrinsic allergic alveolitis. A recent presentation of 30 cases by May *et al* suggests that the incidence of APM is grossly underestimated.² To our knowledge no data on bronchoalveolar lavage fluid in acute pulmonary mycotoxicosis have been published. We report two cases of APM and present the cellular biochemical aspects of bronchoalveolar lavage fluid both at diagnosis and at follow up.

Case reports

CASE 1

Three hours after decapping a corn silo, a 26 year old non-smoking dairy farmer developed a dry cough, dyspnoea, chills, and a frontal headache. The silo had been filled nine months previously. Twelve hours after his exposure to extremely moldy silage he had a fever of 39°C, but no wheezes or crackles. The chest radiograph was normal. Peripheral blood analysis showed a white blood cell count of $17.5 \times 10^9/l$ with 95% neutrophils. The forced vital capacity (FVC) and FEV₁ were decreased to 67% and 51% of predicted values with an FEV₁/FVC ratio of 0.63; there was no improvement after bronchodilator inhalation (salbutamol 200 µg). The total lung capacity (TLC) was 87% of the predicted value and the carbon monoxide transfer factor (TLCO) steady state 69% of predicted normal. The arterial oxygen tension (PaO₂) was 62 mm Hg (8.3 kPa) and the carbon dioxide tension (PaCO₂) 33 mm Hg (4.4 kPa). Bronchoalveolar lavage was carried out by fiberoptic bronchoscopy. The bronchial mucosa appeared to be inflamed; little secretion was evident. Lavage fluid was processed as previously described³; the results showed appreciable neutrophilic alveolitis (table). Direct microbiological analysis of the bronchial aspirates disclosed no bac-

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Analysis of bronchoalveolar fluid in two patients with pulmonary mycotoxicosis

	Time (days)*	Fluid recovered (% of infused)**	Total number of cells ($\times 10^6/ml$)	Macrophages† (%)	Lymphocytes† (%)	Neutrophils† (%)	IgG/alb‡	IgA/alb	IgM/alb
Case 1	1	66	175	31.5	7.5	61	0.02	0.04	ND
	40	60	18	67	31.5	1.5	0.17	0.11	ND
	211	48	7	75	21	3	0.22	0.17	ND
Case 2	3	49	85	48.5	7.5	43.5	0.55	0.07	0.02
	32	41	39	73.5	24	2.5	0.24	0.13	ND
Volunteers: median (range)§	—	69.7 (82.7–4.5)	5.6 (1.8–14.4)	90.7 (60.0–98.7)	6.3 (1.0–39.8)	1.5 (0–4.6)	0.21 (0.10–0.40)	0.08 (0–0.16)	0 (0–0.04)

*Time elapsed after exposure to fungi.

**Fluid recovery was always greater than 40% of infused volume.

†Cell differential counts were obtained from both Wright-Giemsa and non-specific esterase stained cytocentrifuged preparations. A few eosinophils were occasionally seen.

‡Immunoglobulin to albumin ratio in lavage fluid.

§Forty two healthy, non-smokers (immunoglobulin results from only 15 of these).

ND—not detectable.

teria, but cultures showed *Aspergillus fumigatus* and *A nidulans*. Serum precipitating antibodies were positive for *Aspergillus* (with the serum concentrated twofold) and negative for *Micropolyspora faeni*, *Thermoactinomyces vulgaris* (fourfold concentration).

No treatment was given and one week after his admission to hospital all symptoms had disappeared. One month later the patient was symptom free. Bronchoalveolar lavage was repeated and the results showed that a moderate lymphocytic alveolitis persisted. The chest radiographic appearance was normal. The serological reactions were negative. A third bronchoalveolar lavage was carried out six months later; the lymphocyte count was still slightly increased (table).

CASE 2

A 29 year old non-smoking dairy farmer developed a dry cough with headache, chills, and dyspnoea immediately after the removal of mouldy material from the top of an oat filled silo that had been filled a year before. After the acute reaction his cough increased and he sought medical help three days later. On admission to hospital he had a temperature of 38.6°C and normal chest radiographic appearances. Peripheral blood analysis showed a white blood cell count of $10.3 \times 10^9/l$ with 77% neutrophils. The FVC was 94% of the predicted value, the FEV₁ 87%, and the FEV₁/FVC ratio 0.74. The maximal mid expiratory flow rate was decreased to 68% of predicted normal, increasing to 99% after inhalation of 200 µg of salbutamol. TLC was 104% of predicted normal and TLC₀ (single breath) 82%. Arterial blood gas analysis showed a PaO₂ of 55 mm Hg (7.5 kPa) and PaCO₂ of 39 mm Hg (5.2 kPa). Serum precipitins to mould antigens were negative. Cultures of the bronchial fluid showed *A fumigatus*, *A nidulans*, and *Penicillium* sp. Within two days his temperature returned to normal and the cough gradually disappeared over three

weeks. One month after the acute illness the chest radiograph was normal; results of pulmonary function tests were normal, and there was a positive serological reaction to *faeni* (with the serum concentration twofold). Initially the lavage fluid showed a considerable neutrophilic response; this had disappeared a month later, when a slight increase of lymphocytes was present (table).

Discussion

We believe that our cases are examples of acute pulmonary mycotoxicosis as previously described,^{1,2} and that they demonstrate the differences between this clinical entity and the better known respiratory ailments extrinsic allergic alveolitis and silo filler's disease. The timing between silo filling and contact, the absence of a brownish smoke, and the absence of patchy alveolar infiltrates on the chest radiographs we believe eliminate silo filler's disease in our cases.⁵ Differentiation of acute pulmonary mycotoxicosis from extrinsic allergic alveolitis is more difficult. Like pulmonary mycotoxicosis, extrinsic allergic alveolitis occurs after exposure to mouldy organic matter and presents with fever and audible crackles but rarely with a normal chest radiograph.^{6,7} Transfer factor is considerably decreased in extrinsic allergic alveolitis but remains near normal in acute pulmonary mycotoxicosis. A restrictive pattern of lung disease is usually found whereas TLC is usually normal in acute pulmonary mycotoxicosis.^{2,8} Serum precipitins are usually present in high titres in extrinsic allergic alveolitis⁹; they were absent or barely detectable in both of our patients. The acute inflammation of the bronchial mucosa is also different from extrinsic allergic alveolitis, where bronchoscopy usually shows a normal looking bronchial tree. In the alveolitis fungus spores are rarely found, whereas these were present in both our cases.

Our bronchoalveolar lavage findings are of interest. In the acute phase our patients had an increase in polymorphonuclear cells in the lavage fluid and a normal percentage of lymphocytes (table). An increase of polymorphonuclear cells may occur in acute extrinsic allergic alveolitis, but it is usually less pronounced and invariably associated with appreciable alveolar lymphocytosis.^{3 10} In previous studies we reported data from 22 cases of acute farmer's lung disease.¹¹ Those patients had a median of 47.8% lymphocytes in their lavage fluid (range 18.7–84.5) and 6.0% neutrophils (range 0–45). In absolute numbers the patients with acute pulmonary mycotoxicosis had 13.1×10^4 and 6.4×10^4 lymphocytes/ml of lavage fluid while patients with acute farmer's lung had a median lymphocyte count of 30.6×10^4 (range 12.6–71.0)/ml. Differences in neutrophils were even more striking: our two patients with acute pulmonary mycotoxicosis had 106.7×10^4 and 37×10^4 cells/ml while patients with farmer's lung had a median of 2.5×10^4 (range 0–18.9)/ml. In our two cases sequential lavage samples showed a relative alveolar lymphocytosis ($<10 \times 10^4$ cells/ml) and normal neutrophil ($<1.0 \times 10^4$ cells/ml) counts; in healthy volunteers the counts were: lymphocytes, median 0.36×10^4 (range 0.02–3.58) cells/ml; neutrophils, 0.07 (0–0.04) cells/ml (table). In this later phase an erroneous diagnosis of extrinsic allergic alveolitis could be made; the lymphocyte count was, however, lower than that found in acute and chronic extrinsic allergic alveolitis.^{10–12} Lavage fluid immunoglobulin concentration may also be useful with differential diagnosis between extrinsic allergic alveolitis and acute pulmonary mycotoxicosis. We and others^{3 13} have previously found that immunoglobulins in lavage fluid are increased in extrinsic allergic alveolitis. In our two cases results were within the normal range.

Our finding of an increased number of neutrophils in lavage fluid is similar to the findings in the animal model for acute pulmonary mycotoxicosis of Marx *et al.*,¹⁴ and supports the histopathological findings of Emanuel *et al.*¹ The suggested mechanism responsible for this clinical entity is the inhalation of a large amount of toxin produced by the fungi, with a resulting inflammatory reaction of the respiratory mucosa. Our two cases had heavy exposure and we did identify fungi in their lavage fluid. Edwards *et al.*¹⁵ have shown that organic dusts can activate the alternative pathway of complement, and have suggested this mechanism to explain the inflammatory response seen in such patients. These workers did not believe, however, that acute pulmonary mycotoxicosis represents an entity distinct from farmer's lung.

Bronchoalveolar lavage may be a useful tool to help differentiate acute pulmonary mycotoxicosis from other bronchopulmonary diseases, especially

extrinsic allergic alveolitis. Other studies, with larger numbers of cases, will be needed to confirm the findings.

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