

Correspondence

Amiodarone pneumonitis: three further cases with a review of published reports

SIR,—We read with interest the paper by Dr JI Darmanata and his colleagues (January 1984;39:57) describing three new cases of amiodarone induced pneumonitis and reviewing 32 other reported cases. The authors conclude that proof of an underlying immunological process is lacking.

Even if in the majority of cases the mechanism of the disease appears to be a purely toxic one, it seems possible that an immunological process may be involved in others for the following reasons: (1) In one case¹ deposits of C3 have been found in lung biopsy material as Dr Darmanata and others point out. (2) In six patients bronchoalveolar lavage was performed.¹⁻⁶ In four of these a lymphocytosis of 23-59% was observed in the bronchoalveolar lavage fluid.³⁻⁶ Lymphocytosis is a good sign of extrinsic allergic alveolitis in general and of pneumonitis due to drug hypersensitivity in particular.⁷ (3) An inversion of the ratio of lymphocyte subsets in bronchoalveolar lavage fluid was found in our case of amiodarone lung.³ A similarly inverted ratio has been noted in hypersensitivity pneumonitis after inhalation of organic antigens.⁸ (4) Peripheral blood lymphocytes from our patient when cultured in the presence of the drug were found to secrete a significant amount of a LIF-like lymphokine by comparison with control lymphocytes, suggesting cell mediated hypersensitivity.

These arguments suggest that in some cases at least an immunological mechanism—cell mediated hypersensitivity—is the originator of amiodarone pneumonitis.

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¹ Suarez LD, Poderoso JJ, Elsner B, Bunster AM, Esteva H, Bellotti M. Subacute pneumopathy during amiodarone therapy. *Chest* 1983;83:566-8.

² Acar J, Pernes JM, Grimberg D, Jaillon P. Fibrose pulmonaire lors d'un traitement par l'amiodarone. Un effet secondaire possible. *Presse Me d* 1983;12:47.

³ Akoun G, Gauthier-Rahman S. Le poumon de l'amiodarone: données immunologiques préliminaires. *Presse Me d* 1983;12:1824.

⁴ Brambilla C, Chavez L, Piot M, Rigaud D, Paramelle B. Pneumopathie à l'amiodarone. *Presse Me d* 1983;12:1236.

⁵ Chebat J, Caubarrere I. Pneumopathie grave et amiodarone. *The rapie* 1983;38:111.

⁶ Vergnon JM, Wiesendanger T, Brune J. L'amiodarone, nouvelle étiologie des pneumopathies interstitielles diffuses? A propos d'un cas personnel. *Rev Fr Mal Respir* 1983;11:249-50.

⁷ Akoun GM, Herman DP, Mayaud CM, Perrot JY. Acebutolol-induced hypersensitivity pneumonitis. *Br Med J* 1983;286:266-7.

⁸ Leatherman JW, Michael AF, Kronenberg RS, Schwartz BS, Hoidal JR. Evolution of cell-mediated immunity in the lung by monoclonal antibodies in hypersensitivity pneumonitis and asymptomatic pigeon breeders. *Am Rev Respir Dis* 1983;127:62.

SIR,—The presence of C3 deposits is not the sole determinant of a specific immunological process in the lung. Recently, one of us described the non-specific character of such findings in patients with manifest immunological lung disease.¹

Bronchoalveolar lavage enables one to assess changes in cellular traffic in the alveolar spaces. Although significant alteration of the cellular composition (that is, lymphocytosis) of the bronchoalveolar lavage fluid was demonstrated in four out of six patients with amiodarone pneumonitis,² lymphocytosis per se or an inverted ratio of lymphocyte subsets does not necessarily imply that hypersensitivity is the underlying derangement of the pulmonary reaction or that a pathogenetic mechanism has been elucidated.³ As experience with drug induced pulmonary toxicity accumulates, it becomes clear that the same drug may exhibit a varying pattern of reactions.⁴ Recently one of our patients who had pneumonitis at low doses of amiodarone had an eosinophilic reaction in the bronchoalveolar lavage fluid (20% eosinophils, 3% basophils, 47% polymorphonuclear cells, 16% lymphocytes, and 15% alveolar macrophages). Lymphocytosis itself could also be part of the inflammatory response secondary to the formation of toxic intermediates of amiodarone.

In this context it is worth noting that bronchoalveolar lavage fluid of the patient described by Brambilla *et al*⁵ contained a significant amount of amiodarone and its metabolite, which gradually decreased after withdrawal of the drug, confirming our observation of a significant accumulation of amiodarone and its metabolite in the lung.

We are of the opinion that pulmonary accumulation of amiodarone with the formation of toxic intermediates may form the basis of the observed pulmonary changes and it may be accompanied by a significant reaction of the immunological system.

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¹ Jansen HM, Schutte AJH, Ekma JD, *et al*. Local immune complexes and inflammatory response in patients with chronic interstitial pulmonary disorders associated with cardiovascular disease. *Clin Exp Immunol* (in press).

² Akoun GM, Gautier-Rahman S, Milleron BJ, Perrot JY, Margaud CM. Amiodarone-induced hypersensitivity pneumonitis. *Chest* 1984;85:133-5.

³ Jansen HM, Schutte B, The TH, *et al*. Local immunopathologic studies using BAL in patients with fibrosing alveolitis and connective tissue diseases. *Chest* 1982;82:239.

⁴ Bedrossian CWM. Pathology of drug-induced lung diseases. *Semin Respir Med* 1982;4:98-106.

⁵ Brambilla C, Chavez L, Piot M, Rigaud D, Paramelle B. Pneumopathie à l'amiodarone. *Presse Me d* 1983;12:1236.

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