Anthracofibrosis attributed to mixed mineral dust exposure: report of three cases

J-M Naccache,[1,2] I Monnet,[3] H Nunes,[1,2] M-A Billon-Galland,[4] J-C Pairon,[3] F Guillon,[1,2] D Valeyre[1,2]

[1] Université Paris 13, EA2363, Hôpital Universitaire Avicenne, Assistance Publique–Hôpitaux de Paris, Bobigny, France; [2] Service Pneumologie, Hôpital Universitaire Avicenne, Assistance Publique–Hôpitaux de Paris, Bobigny, France; [3] Service de Pneumologie et de Pathologie Professionnelle, Centre Hospitalier Intercommunal de Créteil, Créteil, France; [4] Laboratoire d'Etude des Particules Inhalées, Paris, France

Correspondence to: Dr J-M Naccache, Service de Pneumologie, Hôpital Avicenne, 125 rue de Stalingrad, 93009 Bobigny Cedex, France; jean-marc.naccache@avc.ap-hop-paris.fr

Received 14 August 2006
Accepted 16 October 2006

ABSTRACT

Anthracofibrosis, defined as bronchial luminal narrowing with black pigmentation of the overlying mucosa, has been attributed to tuberculosis. Three patients with anthracofibrosis without mycobacterial infection are described who had previous occupational exposure to mixed dusts. CT scans showed calcified hilar lymph nodes in two patients. Surgical biopsy in one patient and autopsy in another revealed fibrotic lymph nodes with black pigmentation. Mineralogical analysis by transmission electron microscopy of pulmonary, hilar and/or bronchial samples found high levels of particle retention, raised percentages of free crystalline silica and mica in two patients, and free crystalline silica, kaolin and other silicates in the third. No evidence of any other contributory factor was found, suggesting that mixed mineral dust was the most probable cause. These observations suggest that exposure to mixed mineral dust should be added to the aetiology of anthracofibrosis.

Anthracofibrosis is defined as narrowing or obliteration of the bronchial lumen associated with black pigmentation (anthracosis) of the overlying mucosa.[1 2] The main characteristics are atelectasis with bronchial stenosis surrounded by calcified or non-calcified lymph nodes on CT scans, frequent active tuberculous infection and absence of pneumoconiosis. Silica dust-induced lung disease mainly involves the parenchyma and small airways rather than the large bronchi.[3] We describe three cases with features consistent with a diagnosis of anthracofibrosis as defined above. Clinical investigations excluded tuberculosis. Based on mineralogical analyses, a diagnosis of anthracofibrosis attributed to mixed mineral dusts containing free crystalline silica and other silicates is proposed.

CASE REPORTS

Patient 1

A 66-year-old man was evaluated in February 2002 for recurrent episodes of pneumonitis. He had stopped smoking 15 years earlier (30 pack-years). He worked principally as a forklift driver in a foundry and as a solderer in a metallurgy firm. He was exposed mostly to silica and aluminium. His medical history was noteworthy for type 2 diabetes.

He complained of a chronic cough with dyspnoea. Chest auscultation detected ronchi and inspiratory wheezing in the right upper lung area. A CT scan revealed bilateral calcified hilar adenopathies, bronchial stenoses and subsegmental collapse in the right upper lobe (fig 1A). Fibreoptic bronchoscopy showed anthracosis and stenoses of all the bronchi predominantly in the right upper lobe (fig 1B). Histological examination of bronchial biopsy specimens revealed fibrosis of the lamina propria without granulomas. Sputum and bronchial aspirates were smear- and culture-negative for *Mycobacterium tuberculosis*. Pulmonary function tests and blood gas analyses revealed severe airway obstruction (forced expiratory volume in 1 s/forced vital capacity (FEV_1/FVC) 46%) and moderate arterial hypoxaemia (Pa_{O_2} 9.3 kPa (70 mm Hg)). Echocardiography showed pulmonary hypertension which was confirmed by catheter examination (mean pulmonary arterial pressure 32 mm Hg; mean pulmonary capillary wedge pressure 7 mm Hg). Angiography revealed stenoses of the lower right and lower left pulmonary arteries (fig 1C). The patient died in September 2003 after acute pneumonitis.

The autopsy showed hilar fibrosis with anthracosis, bronchial and vascular stenoses, but no granuloma. Mineralogical analyses by transmission electron microscopy (TEM) of lung and hilum samples showed high mineral particle counts (lung: 41×10^7 p/g (normal value mean (SD) 9 (8)$\times10^7$ p/g); hilum: 2296×10^7 p/g) and raised percentages of free crystalline silica (lung: 34% (normal value mean (SD) 14.5 (9)%); hilum: 44%) and mica particles (lung: 28% (normal value mean (SD) 18.7 (10.8)%), hilum: 46%). Normal values are based on studies of non-exposed individuals from our own laboratory. A diagnosis of hilar fibrosis with anthracofibrosis and vascular compression was made and attributed to mixed mineral dust exposure.

Patient 2

A 63-year-old man was investigated in February 2000 for a left lung nodule on his chest radiograph. He had never smoked. He had worked principally as a bricklayer in Morocco, where he was exposed to silica and asphalt, and in a supermarket in France. His medical history was noteworthy for hypertension.

He was in his usual state of good health. A CT scan of the thorax detected a 2.5×4 cm nodule in the left upper lobe, with mediastinal and hilar adenopathies and subsegmental atelectasis in the right middle lobe. Bronchoscopic examination showed diffuse inflammatory mucosa with mucosal anthracosis and stenosis of the left upper lobe bronchus. Bronchial biopsies were non-informative. Mediastinoscopy revealed hard nodes with sclerohyaline formation, calcifications and anthracosis. Wedge resection of a scleronecrotic nodule by thoracotomy found no granulomatosis or malignancy. All the samples (sputum, bronchial aspirates, lung specimens) were smear- and culture-negative

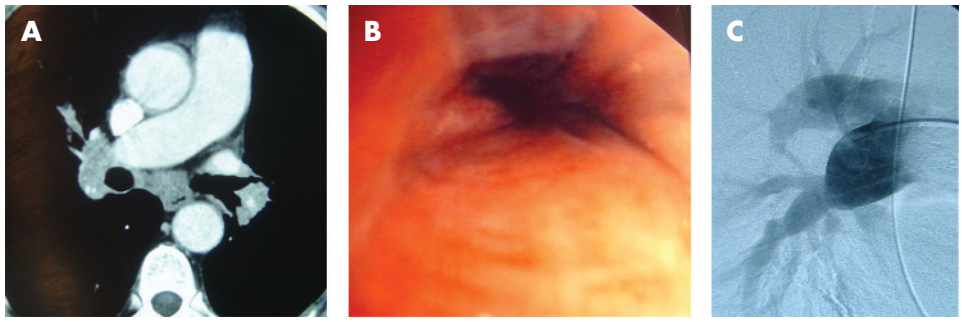

Figure 1 Patient 1: (A) CT scan showing bilateral mildly enlarged calcified lymph nodes with anterior segmental right upper atelectasis. (B) Bronchoscopy showing black pigmentation (anthracosis) at a stenosis in the right upper lobe bronchus. (C) Angiogram showing stenosis of the lower right pulmonary artery.

for *M tuberculosis*. TEM mineralogical analyses of lung tissue found high mineral particle counts ($>10^{10}$ p/g) with raised percentages of free crystalline silica (30%), kaolin (32% (normal mean (SD) 13.3 (5)%)) and other silicates (10% (normal mean (SD) 2.1 (2.1)%)). The outcome was marked by recurrent bronchitis and mild airway obstruction. The last bronchoscopic examination showed persistent anthracosis with stenoses of the left upper lobe bronchus and of the right middle lobe. Anthracofibrosis secondary to mixed mineral dust exposure was diagnosed.

Patient 3

A 73-year-old man underwent evaluation in February 2006 after an episode of pneumonia. He had stopped smoking 1 year earlier (40 pack-years). He had worked principally as a mason and was probably exposed to silica. His medical history was noteworthy for type 2 diabetes.

The patient complained of a chronic cough with dyspnoea. Chest auscultation found inspiratory wheezing in the left upper lung area. A CT scan showed mediastinal and hilar calcified adenopathies with bronchial narrowing. Bronchoscopic examination showed diffuse anthracosis with stenoses of all the bronchi predominantly in the left upper lobe. Histological examination of bronchial biopsy specimens noted fibrosis of the lamina propria and inflammatory mucous membranes. Sputum and bronchial aspirates were smear- and culture-negative for *M tuberculosis*. Pulmonary function tests revealed moderate airway obstruction. TEM mineralogical analyses of bronchoalveolar lavage fluid showed an increased percentage of mica particles (28% (normal mean (SD) 11.3 (9.4)%)). Mineralogical analyses of bronchial anthracosis specimens confirmed a high percentage of free crystalline silica and mica particles (36% each). Anthracofibrosis secondary to mixed mineral dust exposure was diagnosed.

DISCUSSION

Eighty-four cases of anthracofibrosis have been reported previously.[1 2 4] The authors have suggested that it might be a unique disease entity with distinctive clinical features and that tuberculosis is its most likely cause.[1] However, 30 of the 84 cases apparently did not have tuberculosis, and their aetiological diagnoses are unclear. On the other hand, similar findings—not categorised as anthracofibrosis—have been described in patients chronically exposed to indoor biomass or wood smoke.[5] None of our three cases had signs of tuberculosis or had been exposed to biomass or wood smoke.

Malignancies should always be kept in mind in cases of bronchial stenosis, but bronchial biopsies of visible endobronchial lesions usually provide a definitive diagnosis. Non-malignant bronchial stenosis can result from infiltration of the bronchial wall (ie, granulomatous diseases) or extrinsic compression. The presence of compressive hilar lymph nodes and bronchial wall infiltration in our patients supports a mechanism of extrinsic compression and bronchial wall invasion by hilar tissue. The causes of benign extrinsic bronchial compression are usually either enlarged lymph nodes (tuberculosis, sarcoidosis) or mediastinal fibrosis (tuberculosis, histoplasmosis, drugs or idiopathic). However, anthracosis is not a classical feature of these diseases but rather a hallmark of exposure to elemental carbon and/or mineral dusts.[6]

Although TEM does not detect carbonaceous material, no history of coal exposure and the detection of free crystalline silica and silicates during mineralogical analyses suggested silica dust-induced lung disease. This entity[3] is a parenchymatous disease with predominant nodules which is commonly associated with adenopathies. It can lead to obstructive pulmonary disease, usually chronic obstructive pulmonary disease or centrilobular or paracicatricial emphysema.[3] Proximal bronchial lesions are rarely described and blackened airways and external compression of bronchi are not common features. Diagnostic criteria are based on exposure history, radiological findings, pathological specimens and mineralogical analyses. The atypical radiological and bronchoscopic findings in our patients are not typical of simple silicosis.

However, silica exposure was suspected because of atypical manifestations involving the hilum and/or proximal bronchi, with or without signs of silicosis: predominant bilateral hilar lympadenopathy,[7] airway obstruction by broncholitiasis formation[8] or vascular compression by silicotic hilar lymph nodes.[9] Features of anthracofibrosis were also reported.[10–12] Occupational exposure was not conclusive in some previously reported patients whose domestic or environmental exposures were considered. The most illustrative cases,[10] similar to ours, were three patients with proximal bronchial obstruction with mucosal anthracosis without other frank silicosis lesions in two. The three autopsies found calcified and pigmented fibrotic processes surrounding the hilum and provoked stenoses of lobar or segmental bronchi and the pulmonary artery. Mineralogical analyses showed predominant free silica in one patient and equal proportions of free silica and aluminum/potassium silicates in the others.

The mechanism of anthracofibrosis remains obscure. In patient 1, the high percentage of crystalline silica and mica particles in the hilum compared with the lung parenchyma[13] is striking. It raises the possibility that mineral particles preferentially concentrate within hilar and mediastinal lymph nodes as a result of the passage of particle-laden macrophages into local lymphatic vessels which leads to fibrosis. Moreover, lymph nodes may invade the adjacent bronchi, generating fibrotic responses such as healing. The factors precipitating such excessive fibrotic responses are unknown. Non-fibrous silicate

minerals are known to modify the fibrogenic effects of crystalline silica.[14] Our finding of exposure to mixed mineral dust (eg, free crystalline silica and non-fibrous silicates such as mica and kaolin) and mineralogical analysis findings similar to those of Kampalath *et al*[10] and Mulliez *et al*[12] tend to support their aetiological contribution.

In conclusion, mixed mineral dust toxicity should be considered in the aetiological diagnosis of anthracofibrosis. Repeated bronchial biopsies, sputum and bronchial fluid analyses for acid-fast bacilli enable exclusion of cancer and tuberculosis. Detailed history taking of potential exposure and/or mineralogical analyses can identify causative mineral dusts.

Competing interests: None.

REFERENCES

1. **Chung MP,** Lee KS, Han J, *et al*. Bronchial stenosis due to anthracofibrosis. *Chest* 1998;**113**:344–50.
2. **Kim HY,** Im JG, Goo JM, *et al*. Bronchial anthracofibrosis (inflammatory bronchial stenosis with anthracotic pigmentation): CT findings. *AJR Am J Roentgenol* 2000;**174**:523–7.
3. **Cohen R,** Velho V. Update on respiratory disease from coal mine and silica dust. *Clin Chest Med* 2002;**23**:811–26.
4. **Long R,** Wong E, Barrie J. Bronchial anthracofibrosis and tuberculosis: CT features before and after treatment. *AJR Am J Roentgenol* 2005;**184**(Suppl 3):S33–6.
5. **Amoli K.** Bronchopulmonary disease in Iranian housewives chronically exposed to indoor smoke. *Eur Respir J* 1998;**11**:659–63.
6. **Newman JK,** Vatter AE, Reiss OK. Chemical and electron microscopic studies of the black pigment of the human lung. *Arch Environ Health* 1967;**15**:420–9.
7. **Baldwin DR,** Lambert L, Pantin CF, *et al*. Silicosis presenting as bilateral hilar lymphadenopathy. *Thorax* 1996;**51**:1165–7.
8. **Cahill BC,** Harmon KR, Shumway SJ, *et al*. Tracheobronchial obstruction due to silicosis. *Am Rev Respir Dis* 1992;**145**:719–21.
9. **Mahnken AH,** Breuer C, Haage P. Silicosis-induced pulmonary artery stenosis: demonstration by MR angiography and perfusion MRI. *Br J Radiol* 2001;**74**:859–61.
10. **Kampalath BN,** McMahon JT, Cohen A, *et al*. Obliterative central bronchitis due to mineral dust in patients with pneumoconiosis. *Arch Pathol Lab Med* 1998;**122**:56–62.
11. **Meysman M,** Monsieur I, Noppen M, *et al*. Localised obliterative bronchitis due to non-occupational mineral dust inhalation. *Acta Clin Belg* 2000;**55**:341–3.
12. **Mulliez P,** Billon-Galland MA, Dansin E, *et al*. [Bronchial anthracosis and pulmonary mica overload]. *Rev Mal Respir* 2003;**20**:267–71.
13. **Dumortier P,** De Vuyst P, Yernault JC. Comparative analysis of inhaled particles contained in human bronchoalveolar lavage fluids, lung parenchyma and lymph nodes. *Environ Health Perspect* 1994;**102**(Suppl 5):257–9.
14. **Craighead J,** Kleinerman J. Diseases associated with exposure to silica and nonfibrous silicate minerals. *Arch Pathol Lab Med* 1988;**112**:673–720.

Lung alert

OSA and survival after stroke

Sleep apnoea has been associated with increased mortality following stroke, but not independently of potential confounding factors. This is the first study to distinguish between obstructive and centrally mediated sleep apnoea following a stroke and to investigate the influence of each on mortality.

One hundred and fifty-one patients admitted to an in-hospital stroke rehabilitation unit at the Umea University Hospital in Sweden were invited to enrol in the study. Of these, 138 consented and underwent overnight sleep studies. At study inclusion, 15 patients had had a haemorrhagic stroke and 49 patients had experienced two or more strokes; 23 patients (17.4%) had obstructive sleep apnoea and 28 (21.2%) had central sleep apnoea. The remaining 79 patients served as controls. The primary outcome measure was all-cause mortality.

Obstructive sleep apnoea was associated with increased mortality after adjustment for age, sex, body mass index, current smoking, hypertension, diabetes mellitus, atrial fibrillation, Mini-Mental State Examination score and Barthel index of activities of daily living. These findings were not replicated in the group with central sleep apnoea.

The authors conclude that it may be beneficial to perform sleep studies on patients following a stroke and to offer continuous positive airway pressure to those with obstructive sleep apnoea, although low compliance with treatment is expected. This study highlights an avenue for improving the long-term outcome after stroke and may come to hold yet more relevance in the future if better tolerated treatments for obstructive sleep apnoea are developed. One limitation of this study was that patients with minor strokes and transient ischaemic attacks were not included as they would not have undergone in-hospital stroke rehabilitation. This group may also benefit from investigation.

► Sahlin C, Sandberg O, Gustafson Y, *et al*. Obstructive sleep apnea is a risk factor for death in patients with stroke: a 10-year follow-up. *Arch Intern Med* 2008;**168**:297–301.

J Mann

Correspondence to: J Mann, Foundation Year 2 Doctor/Senior House Officer, Royal Free Hospital, London, UK; Jack.mann@gmail.com