Mucociliary clearance in pulmonary vascular disease

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The mucociliary clearance function was studied by radioaerosol inhalation lung cine-scintigraphy and its quantification in 8 patients with pulmonary vascular diseases; pulmonary embolism, 5 cases, and right pulmonary artery hypoplasia, pulmonary arteriovenous fistulas, aortitis syndrome, 1 case each. The mucociliary clearance function was found to be well maintained in pulmonary vascular diseases unless ventilation was disturbed. There was no difference in the mucociliary clearance function between pulmonary embolism and other pulmonary vascular diseases.

Key words: Radioaerosol inhalation lung cine-scintigraphy, Mucociliary clearance function, Pulmonary vascular diseases, Pulmonary embolism, Aortitis syndrome

INTRODUCTION

With the advent of radioaerosol inhalation lung cine-scintigraphy, the mucociliary clearance status of the lungs can be visually and qualitatively assessed easily in vivo. The quantitative analysis of this potentially important nonrespiratory lung function has also become possible. In airway obstructive lung disease, mucociliary clearance mechanisms have been shown to be generally deranged, but in pulmonary fibrosis or sarcoidosis they are usually not, unless there is the complication of obstructive airways disease. There is, however, no literature to our knowledge that describes how mucociliary clearance mechanisms function or behave in pulmonary vascular diseases.

The purpose of this article is to document the mucociliary clearance status in pulmonary vascular diseases.

MATERIALS AND METHODS

Eight patients, 4 male and 4 female, were studied; pulmonary embolism 5 cases, right pulmonary artery hypoplasia 1 case, pulmonary arteriovenous (A-V) fistulas 1 case, and aortitis syndrome 1 cases. The ages ranged from 15 to 65 years. No patients were current smokers. Cases 4 and 5 were ex-smokers.

All of them were initially studied with perfusion lung imaging with 99mTc-MAA and showed perfusion defects compatible with pulmonary vascular diseases except for the patient with pulmonary A-V fistulas, who showed nearly normal perfusion in the lungs but accumulation of radioactivity in the kidneys, indicating the presence of right to left shunt. Radioaerosol inhalation lung cine-scintigraphy was done by having the patient inhale 99mTc albumin aerosol as described previously within 24 to 48 hours of perfusion imaging. The so-called perfusion and ventilation mismatch was present in all but the patient with pulmonary A-V fistulas.

Qualitative or visual evaluation of radioaerosol inhalation lung cine-scintigraphy was done to see whether inhaled aerosol deposited in the lungs homogeneously or not; whether mucociliary transport was cephalad in direction in steady motion or not; if not, whether the mucus glob showed temporary but frequent stopping and starting in the airways or stasis in the course of lung clearance; whether there was a reversal of mucus flow or regurgitation; whether mucus strayed into the opposite lung or into different parts of the lungs than
where the mucus globs originated; or whether there was a spiral or zigzag transport of radioactivity or not.\(^\text{3,4}\)

The lung retention ratio (LRR), or the amount of radioactivity remaining in the lungs at time \(t\), was calculated quantitatively at each 10 minute interval from the time activity curve. The airway deposition ratio or the amount of radioactivity throughout the ciliated airways relative to the total radioactivity initially deposited in the lungs, the airway retention ratio or the ratio indicating what percentage of radioactivity initially deposited on the ciliated airways still remains there at time \(t\), and the airway clearance efficiency which indicates what percentage of the radioactivity deposited on the ciliated airways has already been cleared by time \(t\), were calculated by using the respective LRR and the alveolar deposition ratio (ALDR) which was equivalent to the LRR at 24 hours.\(^\text{3,4}\) The ALDR was calculated by the following formula: \(\text{ALDR} = -48.08 + 0.47 \times \text{FEV 1.0\%} + 0.59 \times \text{LRR 60}\), where FEV 1.0\% was forced expiratory volume in one second divided by forced vital capacity in percent and LRR 60, the LRR at 60 minutes.\(^\text{9}\)

Pulmonary function tests were done on the same day or within 1 or 2 days of radioaerosol inhalation lung cine-scintigraphy.

The patients were treated correspondingly when their perfusion defects were first noted. Multiple follow-up perfusion studies were done to confirm the effect of therapy. Definitive diagnoses were made by serial perfusion lung imaging in pulmonary embolism which generally showed with time a gradual return of regional perfusion. In one patient with pulmonary embolism (Case 1), however, pulmonary angiography was necessary because no perfusion recovery was noted during the therapy. Pulmonary angiography was done in the remaining 3 cases with unilateral pulmonary artery hypoplasia, pulmonary A-V fistulas, and aortitis syndrome, respectively.

RESULTS

1. Deposition patterns of inhaled radioaerosol

In all patients, inhaled radioaerosol deposited in lung regions where perfusion was absent, indicating the presence of ventilation in nonperfused lung regions, as shown in Table 1. Furthermore, inhaled radioaerosol deposition was homogeneous in distribution in all but one (Case 5) in whom the left posterior base showed a decreased and nonhomogeneous deposition where perfusion was also nearly absent. Pulmonary function tests were within normal limits without any evidence of obstructive airways disease in all patients.

2. Radioaerosol inhalation lung cine-scintigraphy and mucociliary clearance function

In all patients, mucociliary clearance function was well within normal limits; no evidence of regurgitation, stry, stasis or spiral motion of radioactive globs on the airway (4) were noted. Quantitative analysis indicated that the LRR, the ALDR (Fig. 1a), the airway deposition ratio, the airway retention ratio and the airway clearance efficiency (Fig. 1b) were within normal limits.

CASE REPORT

Case 1. A 26-year-old woman had left chest pain, arrhythmia and shortness of breath of 7 days' duration and was hospitalized at another hospital. She had no history of thrombophlebitis or pelvic infections. Pneumonia was suspected, despite the absence of definite consolidations on chest X-rays, and treated as such. Shortness of breath continued. No

<table>
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<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Laterality</th>
<th>Aerosol deposition</th>
<th>FVC (%)</th>
<th>FEV 1.0% (%)</th>
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<td>Bilat.</td>
<td>Homogeneous</td>
<td>95</td>
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</table>

FVC: Forced vital capacity in % of predicted (15); FEV 1.0\%: Forced expiratory volume in one sec divided by FVC; F: Female; M: Male; PE: Pulmonary embolism; RPAH: Right pulmonary artery hypoplasia; PAVF: Pulmonary arteriovenous fistulas; AS: Aortitis syndrome; Bilat.: Bilateral lungs; Right: Right lung; Left: Left lung
LUNG RETENTION RATIO

Airway Clearance Efficiency

Fig. 1 a and b Lung retention ratio (a) and airway clearance efficiency (b) in right and left lungs. Mean ± SE of 8 patients is shown. Stippled bands indicate 95% confidence intervals of normal values of each index (16). No statistical difference is present in either index between patients and normal subjects. Lung retention ratio at 24 hrs is equal to alveolar deposition ratio which is also within normal range.

Anticoagulants were used. She was transferred to us 2 months later for further examination.

Perfusion lung scan indicated multiple perfusion defects in the right and left lungs (Fig. 2a) where aerosol inhalation lung images showed homogeneous deposition of inhaled aerosol, indicating the presence of normal ventilation in nonperfused lung regions (Fig. 2b). She was placed on heparin followed by warfarin sodium but subsequent studies did not show any return of perfusion to the regions of perfusion defect. Pulmonary angiography confirmed multiple pulmonary emboli which were probably organized. Radioaerosol inhalation lung cine-scintigraphy and quantitative analysis were within normal limits. She was followed up subsequently for 2 years without recurrence.

Case 5. A 65-year-old man was transferred from another hospital for dyspnea and chest pain of 3 days' duration. His chest X-rays were within normal limits. His perfusion scan showed multiple defects involving both the right and left lungs, while aerosol inhalation scan showed a good filling of the nonperfused areas with inhaled aerosol, except in the left posterior base where both perfusion and aerosol deposition decreased. Aerosol deposition was nonhomogeneous, especially in the left lung. He was placed on heparin for 14 days followed by warfarin sodium.

His repeat perfusion scans showed a gradual and steady return of perfusion except to the left base. After discharge he was closely followed up and given warfarin sodium for the subsequent 7 months.

Twelve months later he returned with a complaint of dyspnea on exertion. Perfusion scan indicated defects in the right lower lobe and lateral and posterior basal segments of the left lower lobe (Fig. 3a). Aerosol studies also indicated a good filling in the nonperfused lung regions except in the left posterior base (Fig. 3b). Mucus transport patterns and quantitative data were within normal limits.

Case 6. A 41-year-old woman complained of a mild temperature elevation and bloody sputum. Her chest X-rays showed a small area of consolidation in the right midlung field. Perfusion imaging revealed absent perfusion in the right lung, while aerosol inhalation imaging showed a nearly normal deposition of inhaled aerosol (Fig. 4a, b). Radioaerosol inhalation lung cine-scintigraphy and quantitative indexes for evaluating mucociliary clearance function were all within normal limits. Closer examination of her chest X-rays indicated a rather hyperlucent, less vascular right lung.

Pulmonary angiography showed a hypoplastic or rudimentary right pulmonary artery, while bronchial arteriography indicated well developed bronchial
arteries. Bronchography showed a supernumerary branch or a short tracheal bronchus in addition to the normal bronchial trees in the right lung. Bronchoscopy revealed normal airway mucosa. She has been followed up for the subsequent 4 years. Her course has been uneventful without any particular complications.

Case 7. A 15-year-old boy was found to have abnormal round densities on chest X-rays and polycythemia (RBC 6.48 million/cmm) at the annual mass survey at his school. The round densities were less than 2 cm in diameter. He was referred to us for further examinations. Perfusion scans were essentially normal (Fig. 5a) except that the kidneys were also visualized (Fig. 5b). This raised the possibility of the presence of right-to-left shunts. Pulmonary A-V malformation was most likely and was proved by pulmonary angiography. Close examination of previous school survey films also indicated the presence of smaller lesions bilaterally which evidently had grown in size over the years.

Radioaerosol inhalation lung cine-scintigraphy indicated normal aerosol distribution (Fig. 5c) and mucociliary clearance bilaterally.

Case 8. A 29-year-old woman was known to have aortitis syndrome after being examined for hypertension 4 years previously. She was found to have a coin lesion in the right upper lateral lung field at
the annual chest mass survey and was transferred to our hospital.

Bronchoscopy, brushing and sputum cytology and repeated cultures for acid fast bacilli were negative. Perfusion scan showed multiple defects, while aerosol inhalation showed normal deposition of inhaled aerosol except at the site of the coin lesion, which proved to be a tuberculoma (Fig. 6 a, b). Pulmonary angiography indicated multiple narrowing of the right and left pulmonary arteries roughly coinciding with perfusion defects.

**DISCUSSION**

As ventilation can be normal in nonperfused lung regions, mucociliary clearance function has also

**Fig. 4 a and b** Perfusion (a) and radioaerosol inhalation (b) lung images of 41-year-old woman (Case 6) with hypoplastic right pulmonary artery. Note complete absence of perfusion in left lung where inhaled radioaerosol deposits are near normal.

**Fig. 5 a, b and c** Perfusion lung image (a), kidneys (b, posterior view) and radioaerosol inhalation lung image (c) of 15-year-old man (Case 7) with pulmonary A-V fistulas. Lung images, both anterior in projection, are within normal limits.
Otherwise, perfusion follows the changes in ventilation and shows less perfusion in the areas with less ventilation. This is considered to be due to hypoxic vasoconstriction.11-13 Vice versa, however, is not always true. Ventilation can be present normally in the ischemic lung regions only if bronchial patency is preserved. This may be the very reason why ventilation can be unaltered in the ischemic lung regions. In pulmonary vascular diseases, the mucociliary clearance function seems to be well preserved as long as ventilation is well maintained, and there does not seem to be any difference in the clearance function between pulmonary embolism and other pulmonary vascular diseases in which perfusion is either absent or decreased distal to the embolic or stenotic pulmonary arterial trees.

Mucociliary clearance is effected by the interplay of the mucus and the ciliary motion.14 No increase in mucus production or ciliary function changes are described for pulmonary embolism or other vascular diseases. In the present series of patients, the effect of smoking on the mucociliary clearance function required little consideration because there were no current smokers. Even in normal subjects, the airway deposition ratios are significantly larger in smokers than in nonsmokers, but the airway clearance efficiency does not differ.3

From the present study we might be able to conclude that the mucociliary clearance function is not affected in pulmonary vascular diseases unless there are associated ventilatory disturbances.

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