Scientific papers

Clearance of inhaled particles in ankylosing spondylitis

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SUMMARY Patients with ankylosing spondylitis may uncommonly develop apical fibrobullous lung disease, the cause of which is unknown. It is postulated here that rigidity of the thoracic cage leads to reduced apical clearance of inhaled particles and may thereby predispose to chronic infection. Deposition and clearance of inhaled technetium-99m sulphur colloid particles were studied in eight male patients with ankylosing spondylitis who had chest wall rigidity (mean (SD) chest expansion 1.8 (1.07) cm) but normal chest radiographs. As a reference population eight healthy male volunteers were also studied. Particle deposition showed an increasing gradient from apex to base, with no significant difference between patients and controls. Clearance was assessed by comparing absolute counts, corrected for decay, at 24 hours with the baseline value. No delay in particle clearance in those with ankylosing spondylitis was apparent.

Ankylosing spondylitis is an idiopathic inflammatory disorder of the sacroiliac joints and spine that affects predominantly young men. Involvement of the apophysal and costovertebral joints leads to rigidity of the spine and thoracic cage, with straightening of the lumbar spine and limitation of dorso-lumbar movements and chest expansion. Diaphragmatic movement is, however, intact and partially compensates for any thoracic cage restriction, with the result that in most subjects there is only modest impairment of lung function.¹

Aside from its mechanical effects on the chest wall, 8 to 15% of subjects with ankylosing spondylitis may develop upper lobe fibrobullous disease, the cause of which is unknown. This usually appears several years after the onset of joint symptoms, often when the arthritis is relatively quiescent, and is independent of the other extra-articular manifestations of the disease. Although it may begin unilaterally, both lungs are usually involved. The histological features are non-specific, consisting of inflammatory changes in the early stages, and later on, dense fibrosis accompanied by bronchiectasis and bullae. Cavitation is common, as is colonisation

by *Aspergillus* species, with mycetoma formation. Although the fibrosis may cause further restrictive lung impairment, it is often asymptomatic.

It has been suggested that differences in regional lung ventilation exist between subjects with ankylosing spondylitis and controls. Stewart *et al* showed a reduction in the proportion of inhaled xenon reaching the lung apices, relative to controls without chest restriction, and proposed that this disparity in regional ventilation might be a contributing factor to the upper zone disease.² The deposition of inhaled particles in general is proportional to ventilation.³ It has been suggested that particle clearance is influenced by respiratory movements,⁴ and one might then infer that clearance would be reduced disproportionately to deposition in regions of limited chest wall movement. We postulated then that the mechanical rigidity of the upper thorax in ankylosing spondylitis, and the consequent reduction in respiratory movements therein, may lead to impaired apical alveolar particle clearance, relative to deposition and thereby predispose to chronic inflammation and infection, and eventually fibrosis.

Patients and methods

PATIENTS

Eight subjects with the typical findings of ankylosing

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spondylitis⁵ were studied. Chest expansion was measured by the method of Moll and Wright.⁶ Subjects with apical fibrobullous disease were excluded as any abnormalities in particle deposition and clearance might be attributable to the pulmonary disease itself. All subjects underwent spirometry and measurement of static lung volumes.

VENTILATION AND DEPOSITION/ CLEARANCE STUDIES

Paired studies of regional ventilation with xenon-133 (¹³³Xe) and regional particle deposition with technetium-99m (^{99m}Tc) sulphur colloid were done in all subjects. Ventilation studies were undertaken so that particle deposition could be corrected for lung volume. Scanning was repeated at 24 hours to assess alveolar clearance of the ^{99m}Tc particles. The methodology involved in these studies has been described elsewhere.³

CONTROLS

Comparable data from eight healthy male volunteers were available from another, similar study undertaken in this unit.

DATA ANALYSIS

Scintigraphic information from ventilation and particle deposition studies was displayed in a colour coded fashion, according to the relative concentrations of activity, on a video screen. A composite xenon image consisting of the first 20 frames was used to draw the regions of interest on the screen by dividing the lung horizontally into upper, mid, and lower zones. These regions were then stored for subsequent superimposition onto the ¹³³Xe and ^{99m}Tc images.

A ¹³³Xe image at equilibrium was chosen (usually frame 20 at 100 seconds) for analysis of regional ventilation. The number of counts per region and for the total lung was displayed and recorded. The baseline and 24 hour ^{99m}Tc images were then analysed in the same fashion.

The particle deposition per unit lung volume, for a particular region of interest, *i*, was designated the 'deposition index' (ID_{*i*}) and was calculated as follows:

$$ID_i = \frac{Tc_i / Tc_{lung}}{Xe_i / Xe_{lung}}$$

where Tc_{*i*} and Xe_{*i*} represent the counts over the given region of interest for the technetium and equilibrium xenon scans respectively, and Tc_{lung} and Xe_{lung} represent counts for the entire lung. Differences in mean regional ventilation, deposition index, and particle clearance were analysed for statistical significance with Student's *t* test.

Table 1 Characteristics of subjects and controls. Values are means (SD)

Characteristic	Subjects (n=8)	Controls (n=8)
Age (years)*	42 (7.6)	28.4 (4.3)
Height (cm)	182 (7.4)	175 (9.6)
Weight (kg)	84.1 (15.2)	87.8 (35.8)
Percentage predicted FVC†	86.1 (18.9)	102.9 (4.19)

*p<0.001.

†FVC=forced vital capacity.

Results

CHARACTERISTICS OF PATIENTS AND CONTROLS

All eight subjects had typical clinical findings of ankylosing spondylitis; four had radiographic evidence of sacroiliitis, three others had thoracolumbar spinal abnormalities consistent with the diagnosis, and an additional subject had both types of x ray findings. Table 1 shows the characteristics of subjects and controls. Chest expansion was reduced in all (mean (SD) 1.8 (1.07) cm). Mean (SD) duration of disease was 10.8 (4.1) years. Four subjects were smokers, but only one of these had spirometric evidence of airflow obstruction, which was mild in degree. The control group consisted of eight healthy male volunteers, who were well matched by weight and height but were significantly younger than the subjects and also tended to have a higher percentage predicted forced vital capacity. This last difference, however, was not statistically significant. None of the control subjects smoked.

REGIONAL VENTILATION

In both groups the lung bases were significantly better ventilated than the apices, as would be expected (see Table 2). Region for region, however, there was no difference between subjects and controls.

DEPOSITION INDICES

In both groups the deposition index showed an increasing gradient from apex to base, reflecting differences in regional ventilation (Table 3). Again,

Table 2 Ventilation of upper (B), mid (C), and lower (D) zones relative to the entire lung (A) in subjects and controls. Values are means (SD)

Zone of interest	Subjects	Controls
B/A	0.28 (0.036)	0.27 (0.039)
C/A	0.45 (0.026)	0.45 (0.024)
D/A	0.36 (0.041)	0.35 (0.023)

Table 3 Deposition indices in subjects and controls. Values are means (SD)

Deposition index	Subjects (n=8)	Controls (n=8)
(B'/A')/(B/A)*†	0.82 (0.12)	0.84 (0.04)
(C'/A')/(C/A)	1.01 (0.11)	1.00 (0.07)
(D'/A')/(D/A)	1.12 (0.11)	1.15 (0.10)

*A=entire lung; B, C, D=upper, mid, and lower zones.

†B'=particle count in zone B; A'=particle count in entire lung; B=xenon count in zone B; A=xenon count in entire lung.

Table 4 Mean percentage clearance* of particles at 24 hours from entire lung (A), apex (B), mid-zone (C), and base (D). Values are means (SD)

Region of interest	Subjects	Controls	p Value
A	10.5 (4.8)	2.1 (3.0)	<0.01
B	9.0 (9.4)	-1.1 (10.8)†	>0.05
C	10.8 (4.1)	1.6 (4.1)	<0.01
D	9.5 (5.8)	2.9 (7.4)	>0.05

*Percentage reduction in activity, corrected for decay, at 24 hours.

†Minus sign denotes an increase in activity in this region despite overall decrease of 2.1% of baseline activity in the entire lung.

region for region there was no significant difference between the two groups.

PARTICLE CLEARANCE

Activity in the apex at 24 hours was corrected for decay and length of imaging, and the difference between this and the baseline value was expressed as a proportion of the baseline, yielding an estimate of the percentage clearance (Table 4). Subjects were shown to clear a mean of approximately 9.0% of particles from the upper zone at 24 hours, while controls showed an excess of activity in the same region of 1.1% of the baseline value. This reflected an apparent redistribution of activity despite an overall mean clearance from the control lungs of 2.1%. The difference in upper zone clearance was not significant ($p>0.05$), though patients did show a significantly higher mean rate of clearance of particles from the lung as a whole than controls ($p<0.01$).

Discussion

Although no study has yet attempted to correlate the occurrence of apical fibrobullous disease with the severity of skeletal deformity in ankylosing spondylitis, the available data suggest that such a link may exist. In Davies' series of seven patients with apical fibrobullous disease all had severe

ankylosing spondylitis with marked rigidity of the whole (or nearly whole) spine, and in none of the subjects did lung involvement precede onset of ankylosing spondylitis.⁷ Moreover, interstitial disease had its onset an average of 17 years after the onset of pleuropulmonary involvement could be recorded radiographically the average interval after onset of joint disease was 21 years.⁸ Again, in no case did pulmonary disease precede joint disease. The amount of chest expansion was less than 2.0 cm in 20 of the 21 cases in which this measurement was recorded.

The pathology of the apical lung disease of ankylosing spondylitis lends some credence to our hypothesis about a link between chest wall rigidity, particle clearance, and eventual fibrosis. Early changes are predominantly inflammatory with patchy chronic pneumonia and round cell infiltration. In advanced cases dense fibrosis, bronchiectasis, thin walled bullae, and development of cysts and cavities are characteristic. Additional evidence for chronic infection can be found in Jessamine's series of seven reported cases,⁹ most of whom had a chronic tracheobronchial infection before and after pneumonia well documented. As well, a 1965 study by Brown and Doll reported 2.5 times the expected incidence of pneumonia in these patients.¹⁰

Despite demonstrated chest wall rigidity and smaller forced vital capacity in our group of patients with ankylosing spondylitis we were unable to show any significant difference between subjects and controls in regional ventilation. These findings confirm those of an earlier study, which, using krypton-81m, observed no difference in the upper to lower zone ratio of ventilation per unit lung volume between 24 subjects with ankylosing spondylitis and controls.¹¹ Although particle deposition, similarly, did not differ between our two groups, particle clearance did tend to be more rapid in patients than in controls. Why patients with ankylosing spondylitis should show enhanced particle clearance is not inherently clear. It is possible that cough may have led to a spurious increase in particle clearance in the four of our patients with ankylosing spondylitis who were smokers. Nonetheless, it would appear from these data that if an association exists between the upper zone fibrosis and mechanical rigidity of the chest wall in ankylosing spondylitis, it does not relate to reduced particle clearance. The cause of upper zone fibrosis in this disease thus remains unknown and requires further study.

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