RESTRICTION OF LUNG VOLUMES BUT NORMAL PULMONARY TISSUE FUNCTION IN PATIENTS WITH MULIBREY NANISM

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BACKGROUND

- Mulibrey nanism (MUL) is a rare growth restriction disorder with multiple organ manifestations.
- It is caused by genetic defects affecting TRIM37 protein.
- Perimyocardial heart disease is the most serious manifestation.
- Patients are short (adult height less than 3 SD below the population median), the thorax is small, and the extremities are slender.
- MUL patients often suffer from exercise-induced dyspnea, which can only partly be explained by the heart disease.
- Many MUL patients are treated with asthma medicines.
- Aim: to characterize the pulmonary pathophysiology of MUL.

Figure 1.
Bell-shaped thorax with thin ribs in a 15-year old MUL patient

METHODS

- 33 Finnish MUL patients
- Lung function tests
 - flow-volume spirometry with bronchodilatation test
 - single-breath diffusing capacity for carbon monoxide
 - single-breath lung volume measurements with helium dilution
 - thoracic gas volume, airway resistance and specific conductance measurements with a body plethysmograph
- All variables were compared with predicted values and correlated with blood BNP

RESULTS

- Lung volumes (VC, FVC, TLCHe, TLCb) were markedly reduced (45.1-53.6 % of predicted, p mostly <0.001).
- Reduced forced expiratory volume in the first second (FEV1, p<0.001, 47-57%).
- No signs of airway obstruction (normal FEV1/FVC, specific airway conductance SGaw and residual volume RV/TLC).
- Diffusing capacity (DLCO) was decreased (p<0.001, 60-67%), but when related to alveolar volume (DLCO/VA), it was increased (p<0.001, 130-148%).
- Bronchodilatation suggesting asthma (dFEV1 >12% and >200 ml) was found only in one patient.
- BNP correlated negatively with lung volumes.

References:

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CONCLUSIONS

- MUL patients typically have volume restriction of the lungs.
- Function of the pulmonary tissue remains intact.
- Airflow limitation is not typical.
- Asthma is a rare finding.
- The results suggest that in MUL, functionally normal lungs are stuffed into an abnormally small thoracic cage.

Figure 2. Individual lung values

a lung volume values VC, FVC, TLCHe and TLCb

b FEV1/FVC and RV/TLC

c Specific conductance (sGaw) and airway resistance (Raw)

d Diffusion capacity (DLCOc) and specific diffusion capacity (DLCOc/VA)

Characteristics of 33 Finnish MUL patients

	male	female
N (%)	17 (52)	16 (49)
age, years	25.05 (15.93-38.77)	29.03 (15.21-49.96)
weight, kg	46.0 (23.0-57.9)	39.9 (30.0-54.1)
measured height, cm	152.5 (137.0-162.4)	137.7 (130.0-152.0)
estimated height ^a , cm	161.5 (142.3-169.2, n=15)	144.0 (134.0-161.3, n=15)
BMI, kg/m ²	19.8 (12.3-23.6)	21.1 (16.8-28.2)
Steroid medication, n (%)	0 (0)	4 (25)
Current smoker, n (%)	3 (18)	2 (13)
Diastolic dysfunction in ECG, n (%)	7 (41)	4 (25)
Pericardiectomy performed earlier, n (%)	9 (53)	4 (25)
BNP, ng/L ^b	9.3 (4.0-90.0)	23.0 (9.1-71.0)

Values are in median (range) unless else specified

^aestimated total height derived from sitting height

^bnormal value <18.7 ng/L

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