

Dyspnoea in a girl with short stature and learning difficulties – a case report

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Case

A 12-year-old girl presented with a one-year history of dyspnea and dry cough, with no chest infections or wheeze; trials of antibiotics and inhalers had no effect. The girl had short stature, learning difficulties and previous closure of atrial septal defect. Previous microarray analysis had detected a homozygous deletion at Xp22.33, explaining the short stature. The parents are first cousins.

On examination, small stature was again noted. Chest auscultation was normal, there was no digital clubbing. Lung function showed a restrictive picture with poor technique.

The chest x-rays were highly abnormal, a computed tomography of the chest showed crazy paving pattern.

A lung biopsy showed diffuse filling of alveolar spaces by acellular proteinaceous material and scattered cholesterol clefts, staining strongly for glycogen, typical of pulmonary alveolar proteinosis (PAP).

A bronchoscopy showed only slightly turbid lavage fluid, the laboratory findings were consistent with PAP with abundant proteinaceous debris staining strongly positive for glycogen, scattered macrophages and occasional degenerative neutrophils.

Next generation sequencing detected homozygous deletion of the colony stimulating factor 2 receptor alpha subunit (CSF2RA) gene, located within the deleted region on the X chromosome.

Given the poor yield of proteinaceous material, and the stable state of the child, large volume lavage was not performed.

Conclusion

PAP can be caused by mutations in surfactant protein genes and also genes encoding the α - and β -GM-CSF receptor (receptor for granulocyte macrophage colony stimulating factor). Our patient’s Xp22.33 deletion affected 8 genes, including CSF2RA, leading to hereditary PAP. This is a novel association of PAP. We present this case to highlight that childhood interstitial lung diseases (ChILD) may be collateral damage from a chromosomal deletion, and speculate that this possibility should be considered in patients with other chromosomal deletions near ChILD genes.

(290 words)