Pulmonary involvement in Niemann-Pick type B disease

Poster No.: C-1758
Congress: ECR 2013
Type: Educational Exhibit
Authors: G. Brondani, S. Meduri; Udine/IT
Keywords: Metabolic disorders, Genetic defects, Diagnostic procedure, CT, Conventional radiography, Respiratory system, Lung, Pathology
DOI: 10.1594/ecr2013/C-1758

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method ist strictly prohibited.
You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.
Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.
www.myESR.org
Learning objectives

To illustrate the spectrum of chest radiography and lung high-resolution CT findings in 4 patients affected by different levels of Niemann-Pick type B disease.

Background

Niemann-Pick disease is a recessive, autosomal hereditary lysosomal storage disease in which deficient activity of acid sphingomyelinase (ASM) causes build-up in several tissues. Depending on which organs are affected, there are various clinical subdivisions of Niemann-Pick disease. The most severe of the six disease subtypes is type A, which has an acute neuronopathic phenotype tending to cause death in early childhood. Type B is a heterogeneous disorder that presents as systemic disease with pulmonary, liver and spleen involvement. A specific diagnosis of type B Niemann-Pick disease can be made with the demonstration of reduced ASM activity in isolated leukocytes and/or cultured skin fibroblasts and the identification of two disease causing ASM mutations.

Pulmonary involvement is a common manifestation of the disease in patients of all ages. Lipid-laden macrophages accumulate in the alveolar septa, bronchial walls, and pleura, leading to a progressively worsening restrictive pattern on pulmonary function testing.

In some cases, progressive pulmonary disease can lead to oxygen dependence and/or reduced exercise tolerance. Nonetheless radiologic findings did not show strong correlation with the results of pulmonary function tests. As previously reported 94% of patients are commonly able to successfully complete spirometry with a mean percentage of predicted values for FVC, FEV1, and DLCO are 82.4%, 79.8%, and 60.4%, respectively. Mean FEV1/FVC ratio value reported is 0.84. At the end, an abnormal DLCO is observed in about 70% patients with a 70% of predicted value. The lack of correlation between functional pulmonary impairment and the findings at radiography and high-resolution CT may be due to the pathologic basis of the lung abnormalities in type B Niemann-Pick disease (see Fig. 1 on page 2, and Fig. 2 on page 3). Histopathological features include diffuse infiltration of the lymphatic interlobular space, subpleural spaces, alveolar walls and alveoli with lipid-storing foamy macrophages, without granuloma formation. Pulmonary architecture is usually preserved without fibrotic proliferation.

At our knowledge just few articles report chest x-ray and high-resolution CT interstitial lung conditions Niemann-Pick type B related.

Images for this section:
Fig. 1: Figure 1. Development of lung pathology in NPD: schematic view. Build-up of sphingomyelin in macrophages results in increased chemokine production leading to inflammatory cell recruitment and slow macrophage turnover. Reduced macrophage function also leaves the affected individuals immunologically compromised, and increased airspace sphingomyelin levels may give rise to pulmonary surfactant abnormalities.
Fig. 2: Figure 2. A: Cells obtained after bronchoalveolar lavage are very large, often bi- or multinucleated macrophages (red arrows) with foamy cytoplasm and increased numbers of neutrophils compared with normal. B: At low magnification histological specimens demonstrate interlobular thickening. Variable numbers of foamy macrophages are also seen in the interstitium as well as mild interstitial fibrosis.
It is possible to establish a correlation between the histopathological and imaging findings: histiocytes in the interstitial spaces may account for the smooth thickening of the interlobular septa on HRCT, while ground-glass opacities may be due to partial filling of the alveolar spaces with foamy cells.

Chest radiography usually shows diffuse nodular infiltrates involving both lungs with linear strands. These aspects can be well identify at high-resolution CT in which morphologic changes include thickened inter- and intralobular septa, and ground-glass opacities also occasionally intermixed in crazy paving areas. Although this is not the predominant CT pattern. This 4 cases serie shows progressive Niemann-Pick type B pulmonary involvement from a normal/minimal-changes condition to diffuse, bilateral crazy paving involvement.

**Case 1:** 59 yo, man. He never showed pulmonary dysfunction resulting therefore always asymptomatic. In Fig. 3 on page 6 and Fig. 4 on page 7 are presented chest x-ray and axial CT images that doesn't show any interstitial or nodular abnormalities. Pulmonary function test result in a absolute normal condition with expecially preserved DLCO.

**Case 2:** 32 yo, female. As reported in Fig. 5 on page 7 in a chest x-ray examination conducted during an acute episode of respiratory fail condition with fever, diffuse well defined interstitial thickening is shown. This was confirmed at high-resolution CT imaging (Fig. 6 on page 8) in which *arrows* indicate septal thickening without any other signs of pulmonary abnormalities. This patient required admission to department of internal medicine at our hospital. After 2 weeks subjected to corticosteroid and antibiotic therapy, but without need of intubation, she was discharged. As expected, the 1 month follow-up CT examination showed no significant changes. Subsequently the bronchoalveolar lavage led to the diagnosis of Niemann-Pick through the identification of macrophages with typical aspects. Diagnosis was then confirmed by genetical analysis.

**Case 3:** 43 yo, man. At the age of 17 he underwent aortic valve replacement for failure. Histological examination of the surgical specimen showed the presence of accumulation of sphingomyelin. Diagnosis was then confirmed by genetical analysis. This was a very rare onset. Chest x-ray and high resolution CT images shows diffuse pulmonary involvement. Septal smooth thickening (*arrows*) and patchy low attenuation ground-glass opacities (*arrowheads*) are reported in Fig. 7 on page 8 and Fig. 8 on page 9. Images belong to the last follow-up study but do not show significant changes with respect to the prior investigation (two years ago). Pulmonary function tests show restrictive moderate alteration and reduced DLCO.

**Case 4:** 25 yo, female. Some of the pulmonary symptoms may be secondary to restrictive changes caused by the marked hepatosplenomegaly noted in some patients.
In fact, despite to a very important diffuse pulmonary involvement with septal thickening, ground-glass consolidation, and intermixed crazy-paving pattern (Fig. 9 on page 10, Fig. 10 on page 10), this young woman did not show significant abnormalities at respiratory function tests. Instead, appear impossible to remain in clinostatic condition, due to dyspnea related to right hepatic lobe 25 cm in longitudinal diameter, and severe splenomegaly (longitudinal diameter about 22 cm).

In **Case 2** and **Case 4**, CT examination shown also some nodules (from 5 millimeters to 1.5 centimeters in diameter) (see Fig. 11 on page 10). Sometimes these nodules presented very low density (ground-glass opacities), well defined centrilobular distribution and close relationship with small arterial branches. Otherwise they presented more elevated density (# 5 Hounsfield Units) but with similar distribution. Rare intranodular calcification were identified.

In **Case 2** have also been identified rare cystic lesions (Fig. 12 on page 11). They have well round thickened walls, and may occur in clusters. A possible pathogenetic mechanism for the development of cysts is the migration of storage cells into the bronchiolar lumen, leading to air-trapping and airspace enlargement.

Further analysis of the CT scans revealed a significant difference between lesions observed in the lower and upper lung zones. In Fig. 10 on page 10 most severe abnormalities are represented at the lung lower lobes.

Finally, as previous discussed, according with previous Authors, we confirm the lack of correlation between radiologic findings, clinical respiratory manifestations, and pulmonary function tests decline.

**Images for this section:**

![Image A](image1.png) ![Image B](image2.png)
**Fig. 3:** Figure 3. 59 yo male without any imaging abnormalities at chest x-ray examination (A and B).

![Chest X-ray Image](image)

**Fig. 4:** Figure 4. 59 yo male without any imaging abnormalities at high-resolution CT examination.

![High-resolution CT Image](image)
**Fig. 5:** Figure 5. 32 yo female. Chest x-ray conducted in suspected infectious pneumonia. Arrows indicates diffuse septal thickening.

**Fig. 6:** Figure 6. CT examination conducted in a 32 yo female to well define septal thickening during episode of acute respiratory fail condition with fever. As shown no other significant pulmonary abnormalities were demonstrated. No significant changes were identified at 1 month follow-up CT.
**Fig. 7:** Figure 7. Circular shapes and magnified images show progressive diffuse pulmonary involvement identified by septal thickening (arrows) and peripheral airspaces replacement (arrowheads) in a 43 yo man subjected to aortic valve replacement at the age of 17.
**Fig. 8:** Figure 8. Coexistence of diffuse septal thickening and slight opacity (ground-glass type) in a 43 yo male with aortic valve replacement at the age of 17.

**Fig. 9:** Figure 9. To refer to Case 4, diffuse lung involvement with significant low attenuated pulmonary consolidation coexisting with reticular pattern.

**Fig. 10:** Figure 10. Chest high-resolution CT scans from Case 4 shows patchy intermixed crazy-paving pattern. Base-to-apical gradient of abnormalities is also shown.
**Fig. 11**: Figure 11. Chest CT scan showing ground-glass opacities with small central calcification (arrow), and dense nodule (arrowhead). We observed similar distribution and dimensions of these nodules.
**Fig. 12:** Figure 12. Chest CT scan showing septal thickening and focal areas of low attenuation consistent with well round thickened walls cysts. A possible pathogenetic mechanism is the migration of foam cells into the bronchiolar lumen, leading to air-trapping and airspace enlargement, similar to bronchiolar disease.
Conclusion

Although Niemann-Pick type B is a rare condition, radiologic imaging can supply diagnosis of pulmonary involvement. Radiologist could know these conditions leading to a differential diagnosis in clinical practice.

References

- Ozkurt H et al. Radiological Findings of Pulmonary Involvement of Type B Niemann-Pick Disease. Letters to the Editor / Arch Bronconeumol. 2010; 46(4):206-212
- Gonzalez-Reimers E et al. Pulmonary involvement in an adult male affected by type B Niemann-Pick disease. BJR 2003; 76:838-840
- Simpson WL et al. Imaging Manifestations of Niemann-Pick Disease Type B. AJR 2010; 194:W12-W19