

Clinical problems in rare interstitial lung diseases

Rare ILD/DPLD

PA-67873 - Phenotype-genotype correlations of pediatric patients with biallelic mutations in ABCA3 and SFTPB surfactant-related genes

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Background : Among childhood interstitial lung diseases (chILD) etiologies, the main genetic causes are surfactant metabolism disorders. Mutations in the ATP-binding-cassette transporter A3 (ABCA3) and in SFTPB genes lead to ABCA3 and SP-B deficiencies. Both recessive diseases, they are the most severe causes of chILD. More than 200 different pathogenic mutations of ABCA3 were described since 2004. A classification of ABCA3 mutations according to their predicted functional effect was proposed in 2014. More than 40 recessive loss-of function mutations in SFTPB were identified. The main goal of this study is to describe the initial clinical presentation and evolution of patients with ABCA3 and SP-B deficiency in the French RespiRare cohort and to establish phenotype-genotype correlations that could guide management and genetic counseling.

Methods : This is an observational, descriptive, retrospective, multicenter study. Data were collected between 2000 and 2023.

Results : Among the 623 patients followed in the 41 RespiRare pediatric centers for ILD, 40 patients had bi-allelic mutations in ABCA3 and 12 patients carried bi-allelic mutations in SFTPB. Their phenotypic characteristics are being analyzed.

Conclusion : Whereas the presentation and evolution of chILD due to ABCA3 mutations are variable, allowing to establish phenotype-genotype correlations, this is not the case for SFTPB mutations whose phenotype is always very severe.

Keywords: Children, Genetics, Mutations