ABCA 3 mutation on a Portuguese female infant with respiratory distress syndrome (RDS): a case-report

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INTRODUCTION

- Genetic surfactant dysfunction disorders are caused by mutations in genes encoding proteins critical for the production and function of pulmonary surfactant.
- Pulmonary surfactant lowers alveolar surface tension and prevents alveolar collapse at the end of expiration. It is synthesized by alveolar type-II cells, stored in lamellar bodies and secreted by exocytosis[1].
- Surfactant is a complex mixture of 90% lipids (mostly phospholipids) and 10% surfactant-specific proteins (SP)-A, -B,-C and -D[2].
- Mutations in the genes encoding SP-B, SP-C and ATP--binding cassette transporter 3 *(ABCA3)* have been associated with surfactant dysfunction and respiratory disease in full-term infants with neonatal respiratory failure and interstitial lung disease in older children and adults[3].

CLINICAL HISTORY

- A 2,41 kg term female infant, born at 37 weeks gestation, was hospitalized four hours after birth with tachypnea and cyanosis.
- She was a first child without any prenatal or familiar relevant diseases.
- X-ray revealed bilateral reticulonodular infiltrates (Fig.1) and CT scan showed areas of condensation predominantly in left lung (Fig.2).

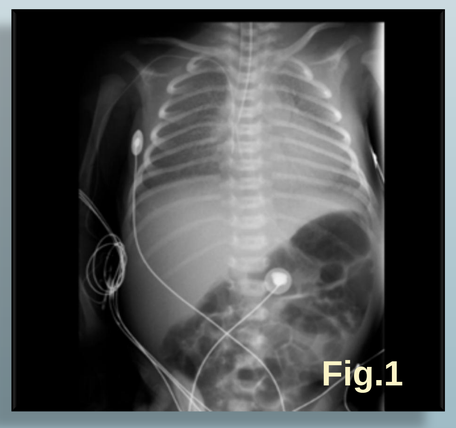


Fig.1

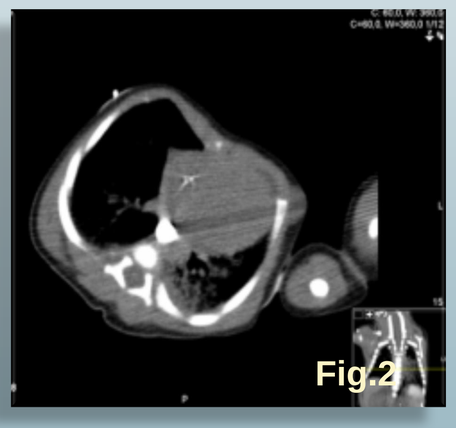
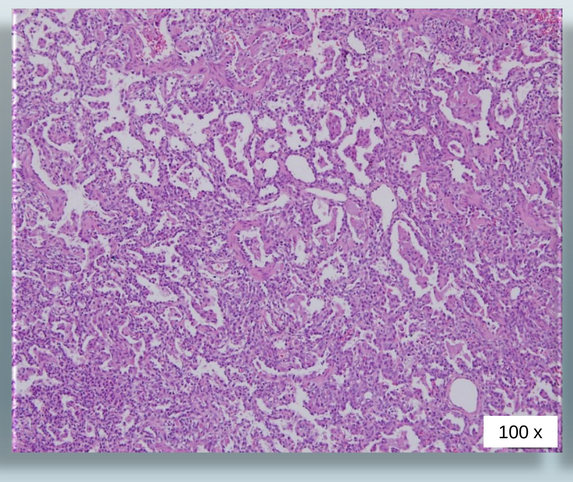


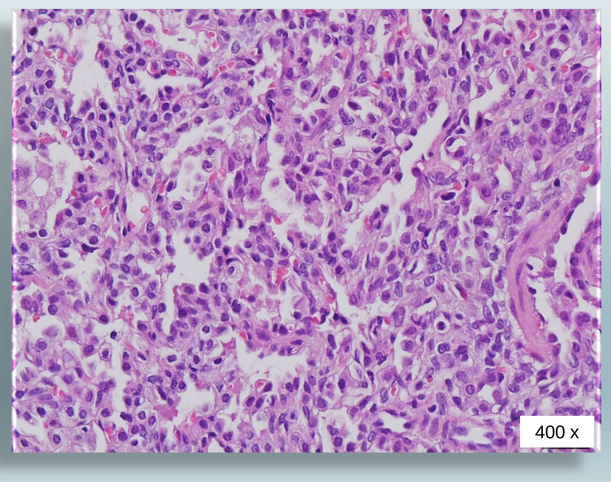
Fig.2

- She underwent several courses of exogenous surfactant and mechanical ventilation during the time she was hospitalized.
- A lung biopsy was performed because congenital alveolar proteinosis was suspected.
- The infant died three months after birth.

MICROSCOPIC FINDINGS

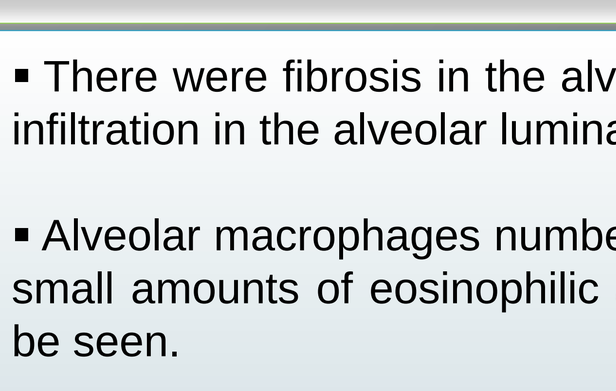
- Pulmonary parenchyma with preserved and collapsed areas.

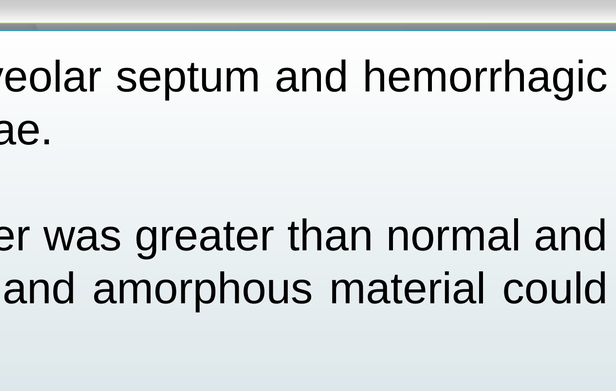




MICROSCOPIC FINDINGS

- There were fibrosis in the alveolar septum and hemorrhagic infiltration in the alveolar luminae.
- Alveolar macrophages number was greater than normal and small amounts of eosinophilic and amorphous material could be seen.





- No extensive inflammatory reaction was observed.

DISCUSSION

- Our final diagnosis was chronic pneumonitis of infancy (CPI).
- CPI is caused, among others, by surfactant protein deficiency.
- On routine histopathology the reported findings may suggest one of the surfactant disorders but it´s impossible to distinguish among the different genetic causes[4].
- Peripheral blood was sent for genetic study and no mutations were detected in the genes for SP-B and SP-C. *ABCA3* gene analysis revealed a previously undescribed mutation: a compound heterozygote carrier of a leucine$_{798}$ (CTT)→proline (CCT)/p.Leu798Prol/L798P exchange and arginine$_{1612}$ (CGG)→proline (CCG)/p.Arg1612Pro/R1612P substitution encoded by exons 18 and 31 of the *ABCA3* gene. Both parents were tested for the mutation and they are heterozygotes.
- *ABCA3* gene deficiency was first described in 2004 and more than 150 disease-associated mutations have been described[5].

REFERENCES

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