de las células sanguíneas: estudiaron los cambios existentes en la concentración de pO_2 de agua oxigenada, evitando de esta manera la sangre *per se*, obteniendo similares resultados.

Es importante destacar que en aquellos trabajos con pO_2 inicial superior a la pO_2 ambiental el gradiente de difusión de los gases se invierte y la pO_2 desciende con el tiempo[12,14], lo que no hace más que reforzar la hipótesis de difusión simple de los gases.

Nuestros resultados también apoyan claramente esta teoría de la difusión física, ya que la variabilidad de la pO_2 se incrementa en función de la presión atmosférica de forma estadísticamente significativa, algo que nunca se había analizado previamente.

En resumen, parece evidente que con el paso del tiempo el pO_2 de la gasometría tiende a aumentar y que esta variación podría estar directamente relacionada con las jeringas de plástico y la difusión de los gases a través de su material poroso. Nuestro estudio apoya esta teoría, objetivando una relación directa de estas variaciones con la presión atmosférica.

A pesar de que las determinaciones de los gases sanguíneos varían significativamente con el tiempo, lo hacen en una cuantía poco relevante para la práctica clínica. En un futuro, sería planteable ampliar el estudio a diferentes tiempos.

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Pulmonary Emphysema in a Child With Alpha-1 Antitrypsin Deficiency: Evaluation of 2 Years of Intravenous Augmentation Therapy

Enfisema pulmonar en un niño con deficiencia de alfa 1 antitripsina: evaluación tras dos años con terapia de aumento

Dear Editor:

Alpha-1 antitrypsin deficiency (AATD) is an autosomal codominant condition, known to predispose to early onset pulmonary emphysema and chronic obstructive pulmonary disease. Generally, lung manifestations of the disease affect smokers at the third or fourth decade of life and so far, intravenous injections of purified alpha-1 antitrypsin are the single target therapy for AATD. Given that lung function in children is typically normal, augmentation therapy has never been systematically studied in pediatric population.

We report a case of a male neonate born at 40 weeks of gestation, weighing 2750 g, with an uneventful postnatal period. His first year of life was marked by downward crossing of weight percentile, recurrent suppurative otitis media and two hospitalizations due to respiratory infections. At 9 months of age, routine laboratory investigation revealed anemia (11.8 g/dL) and elevated liver enzymes (aspartate transaminase 596 U/L, alanine transaminase 722 U/L, alkaline phosphatase 239 U/L and gamma-glutamyl transpeptidase 75 U/L). Due to decreased alpha-1 antitrypsin (AAT) serum concentration (50 mg/dL) gene sequencing (*SERPINA1*) was performed and revealed a ZPlowell genotype. There was no ultrasound evidence of liver impairment. The child's follow-up was interrupted due to a problematic social situation. His family medical history was unremarkable. However, a significant passive smoke exposure due to paternal smoking was reported. He returned to our observation at age 10 years, complaining of recurrent productive coughing, wheezing as well as dyspnea on exertion. On physical examination the patient presented with pale skin, weak appearance and low weight for his age (10th percentile). The chest auscultation revealed diffuse expiratory wheezing and bilateral basal crackles. Pulmonary function tests indicated a non-reversible mild airflow obstruction (FEV1 71.3% pred, FEV1/FVC 74% pred). Laboratory studies showed aggravated anemia, peripheral eosinophilia, elevated total IgE and sensitization to common inhalant allergens (RAST positive). At this time serum level of AAT was 36.7 mg/dL. Chest computed tomography (CT) imaging showed lower lobe predominant panlobular emphysema and cystic bronchiectasis (Fig. 1).

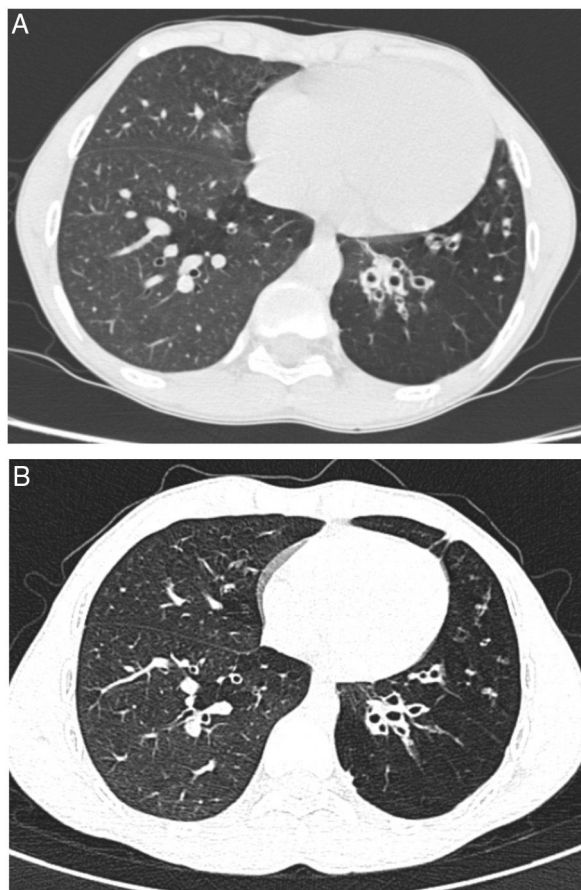He started inhaled therapy with medium-dose corticosteroid (budesonide 160 mcg) plus long-acting β-agonist (formoterol

Fig. 1. Computed tomography of the chest, before (A) and after 19 months of treatment (B), showing no progression of the emphysema or bronchiectasis.

4.5 mcg) and leukotriene receptor antagonist (montelukast 10 mg). Despite optimized anti-inflammatory and bronchodilator therapy associated with lifestyle preventive measures, the child remained symptomatic with recurrent use of antibiotic therapy owing to respiratory infections. Spirometric monitoring over 1 year demonstrated persistent mild airflow obstruction (FEV1 77.8% pred) and air trapping (RV 181.8% pred). At age 14 years, given the severity of emphysema and the risk of disease progression, and in the absence of therapeutic alternatives, it was decided to start AAT augmentation therapy. Up till now, he has been receiving weekly intravenous injections with 60 mg/kg of AAT (Prolastin, Bayer Corporation). So far, 132 infusions have been administered without complications. Regular treatment with inhaled corticosteroids and bronchodilators was left unchanged. Clinically, in the first two years of treatment, the patient has experienced a significant improvement in his overall condition (weight gain up to the 25th percentile) and respiratory symptoms. He had no emergency department admissions nor hospitalizations in the last two years. Functional reassessment at 18 months of treatment showed stable FEV1 and improvement of air trapping (FEV1 77.8% pred; RV 168.9% pred). Stability of pulmonary emphysema and bronchiectasis was observed on high resolution chest CT (Fig. 1).

Studies on the natural history of AATD indicated that emphysema usually begins in the third or fourth decade of life in those exposed to cigarette smoking.[1] Although there is paucity of data in the pediatric age group, children and adolescents with AATD have not been shown to have significant lung function abnormalities.[2] However, Hird et al. have suggested a tendency to hyperinflation in affected children with liver disease.[3] Our patient suffers from severe deficiency due to ZPlowell genotype. Plowell (rs121912714; p.Asp256Val) is a rare *SERPINA1* variant that has been associated with exaggerated intracellular degradation of newly synthetized protein and to 24% of normal serum levels. Compound heterozygotes with severe deficient Z allele were reported to have an increased risk of emphysema in adulthood.[4] In this case, it is possible that tobacco smoke exposure, coexisting inflammatory disease (atopic asthma), frequent low respiratory tract infections and poor nutritional status have contributed to pulmonary function deterioration and emphysema development at such early age. This case highlights the importance of family-based smoking intervention to attain a nonsmoking lifestyle in children with AATD. It is worth noting that determination of AAT serum concentration should be considered in the panel of tests for investigation of adolescents with respiratory symptoms unresponsive to usual asthma treatment interventions.[5,6] In case of AATD, the evaluation must be completed with genotyping and, eventually *SERPINA1* sequencing to exclude rare deficiency alleles.

Intravenous administration of AAT is currently the only specific treatment for AATD Evidence from randomized placebo-controlled clinical trials showing that augmentation therapy in adult patients with severe AATD is safe and effective at reducing the progression of emphysema as assessed by CT densitometry,[7,8] have supported its recommendation in international guidelines.[9] In addition, a large observational study reported decreased mortality and slower FEV1 decline in subjects receiving augmentation therapy as compared with those not receiving therapy.[10]

We report the second case described in the literature on augmentation therapy for AATD at pediatric age.[11] On both cases, a good safety profile and significant clinical benefit were observed. Based on these favorable outcomes, we believe that in selected children with AATD related-lung disease, augmentation therapy may provide the same benefits demonstrated in adults. Therefore, we encourage research groups to include children and adolescents in large AATD clinical trials.

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