Pseudo-Bartter Syndrome in Chinese Children with Cystic Fibrosis: Clinical Features and Genotypic Findings

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Abstract

Objectives: To characterize the clinical and genotypic features of Cystic fibrosis-associated pseudo-Bartter syndrome (CF-PBS) in Chinese children. Methods: We recruited and characterized the clinical manifestations of 11 Chinese children with CF-PBS. Sweat test, blood and urinary analysis, sputum culture, chest and sinus computed tomography, abdominal ultrasonography were obtained. Whole-exome sequencing, bioinformatics analysis, and sanger sequencing validation was performed to define the genotypes. Results: CF-PBS was accompanied by recurrent and/or persistent pneumonia (100%), pancreatitis (81.8%), vomit and/or diarrhea (63.6%), failure to thrive (FTT) (63.6%) and liver disease (54.5%) among our patients. The predominant organisms found in the airways was Pseudomonas aeruginosa (90.9%) and Staphylococcus aureus (81.8%). The mean concentration of blood gas and electrolytes were: PH 7.58, bicarbonate 40.8 mmol/L, sodium 126.7 mmol/L, chloride 80.0 mmol/L, and potassium 2.7 mmol/L, respectively. A high recurrence rate (54.5%) of PBS was observed despite continued electrolyte supplementation during follow up. 17 different mutations of CFTR gene were identified, and 9 of them turned out to be novel observations (c.262_266delTTATA, c.579+2insACAT, c.1210-3C>G, c.1733T>C, c.2236_2246delGAGGCGATACTinsAAAAATC, c.3635delT, c.3859delG, c.3964-7A>G and ΔE23 [c.3718-?_3873+?del]). The c.2909G>A/p.G970D was the most common mutation, with an allele frequency of 18.2%. c.1521_1523delCTT/p.F508del was the first time found with homozygous genotype in patients of Chinese origin. Conclusions: In China, CF-PBS always occurs early and repeatedly in infancy, accompanied by the high frequency of multi-system co-morbidities. Recurring in school-age patients is rare but does exist. The c.2909G>A/p.G970D is the most frequent mutation in Chinese patients with CF-PBS, showing a significant ethnic tendency of Chinese origin.

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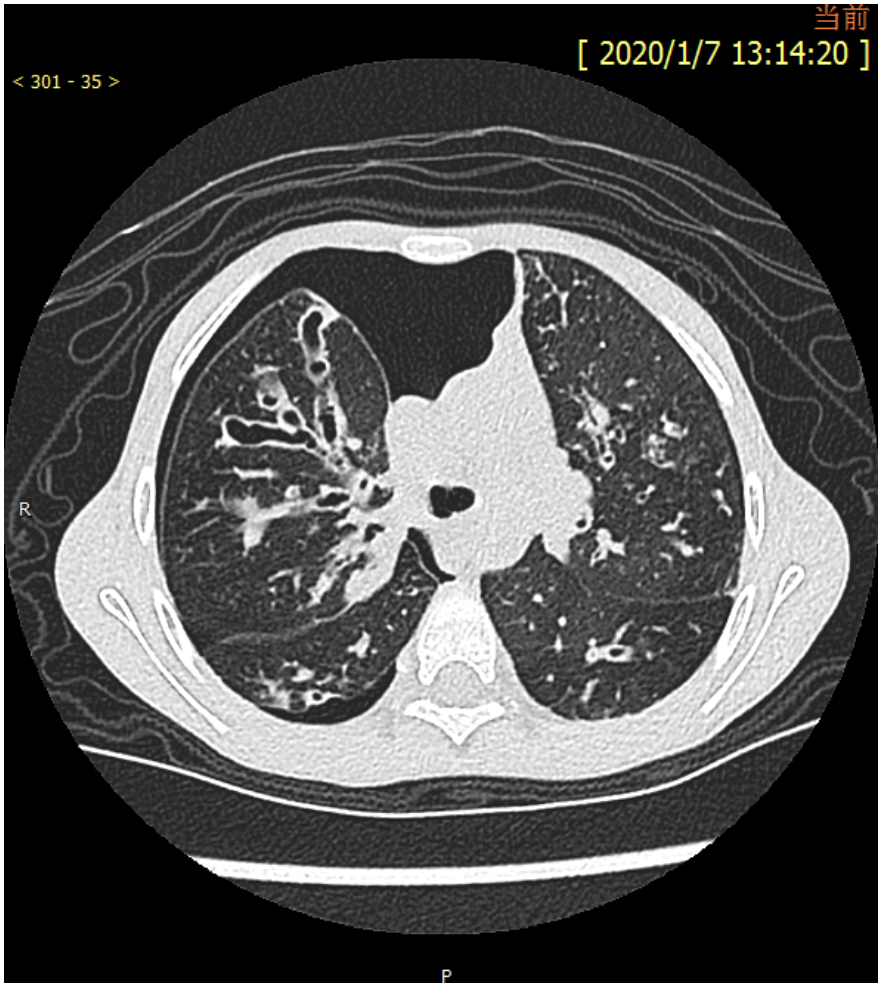

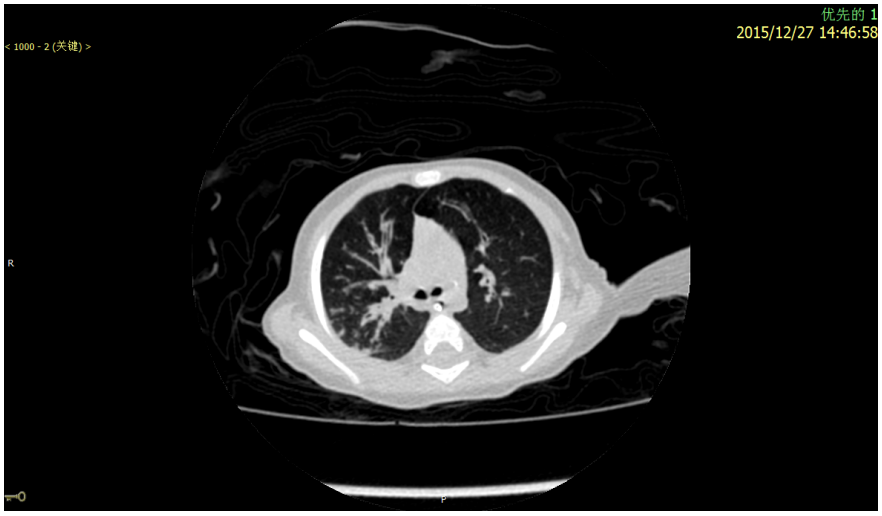

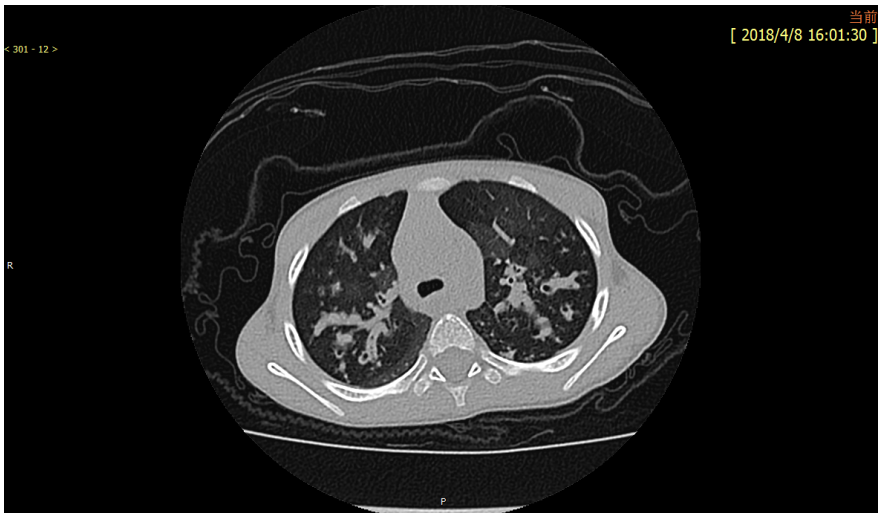

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