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Case Report

Life-Threatening, Giant Pneumatoceles in the Course of Surfactant Protein C Deficiency

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Summary. Chronic interstitial lung diseases are rare in childhood and can present with a wide spectrum of histological abnormalities and radiological-clinical phenotypes. A 17-month-old female infant with malnutrition, recurrent lower respiratory tract infections, and failure to thrive since 3 months of age was diagnosed as surfactant protein C deficiency. Diffuse, giant, and life-threatening pneumatoceles developed during the course. They were treated with empiric drug treatment and oxygen support, and resolved rapidly. Substantial clinical and radiological improvement was observed 1 year after treatment initiation. Large-giant pneumatoceles can develop in the course of surfactant protein C deficiency and may be associated with biopsy. They can resolve with medical treatment. If available, genetic testing should be attempted as a first step for diagnosis. **Pediatr Pulmonol. 2015;50:E25–E28.** © 2015 Wiley Periodicals, Inc.

Key words: interstitial lung disease (ILD); surfactant protein C deficiency; children; pneumatocel.

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INTRODUCTION

Interstitial lung disease in children represents a diverse group of diseases with respect to its etiology and pathogenesis. Some rare causes of interstitial lung disease in children include hereditary disorders of surfactant homeostasis due to defects in proteins B and C and the adenosine triphosphate-binding cassette A3 transporter. These disorders have been reported in association with diverse clinical, radiological, and histological manifestations.[1] We report, herein, a 17-month-old female infant diagnosed as surfactant protein C deficiency together with her clinical follow-up. Diffuse, giant, and life-threatening pneumatoceles were observed in the right lung, which resolved rapidly with conservative treatment, without necessitating invasive procedures.

CASE PRESENTATION

A 17-month-old female infant was admitted to the pediatric pulmonology department for recurrent lower respiratory tract infections, failure to thrive and cyanosis. She had chronic cough and had been hospitalized three times for pneumonia. The physical examination revealed pectus excavatum, intercostal and subcostal retractions, crepitant crackles in the right lung, and hepatomegaly. Sweat chloride test was normal, and tuberculosis skin test was anergic. Diffuse interstitial infiltrates were detected on her chest radiograph and computerized tomography demonstrated common ground-glass opacities in both lung parenchyma and multiple, millimeter-sized subpleural cysts (Fig. 1). With 2 L of oxygen/minute, oxygen saturation was monitored around 95%. Total lymphocyte

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Conflict of interest: None.

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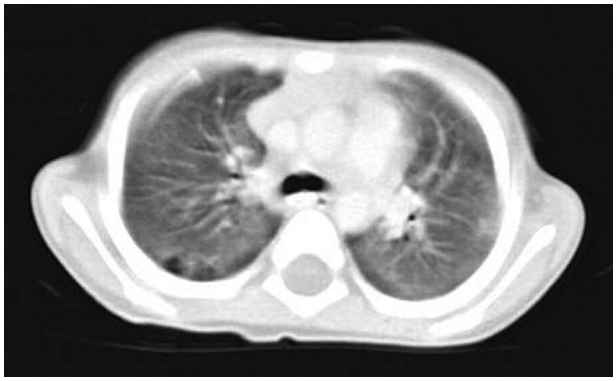

Fig. 1. Common ground-glass opacities in both lung parenchyma and multiple, millimeter-sized subpleural cysts, particularly on the right side, were detected on CT.

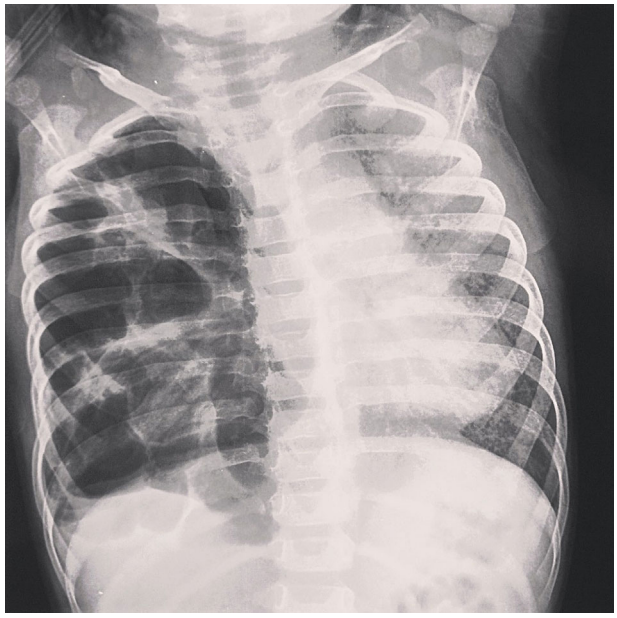

Fig. 2. Diffuse multilocalized giant pneumatoceles in the right lung were seen 42 days after biopsy procedure.

and neutrophil counts were within normal limits. Serum C3, C4, and immunoglobulin (Ig) G, M, A, D, and E levels were in normal ranges according to age, and CH50 and isohemagglutinin titer were positive. Peripheral blood lymphocyte subsets and in vitro T cell functions were within normal limits. No primary humoral or cellular immunodeficiency was detected. Pulmonary hypertension (pulmonary artery pressure of 33 mmHg, enlarged right heart chambers) was detected on echocardiography, and sildenafil treatment (1 mg/kg/dose, 3 doses/day) was started. Bronchoscopy was performed, and bronchoalveolar lavage cultures were negative.

For the diagnosis of interstitial lung disease, open lung biopsy was performed, and the pathology was reported as chronic pneumonitis of infancy. Genetic sequence analysis for surfactant metabolic disorders was performed and the heterozygous, disease-causing SFTPC mutation I73T was found.

Postoperative course was uneventful, the infant ventilated 3 hr in perioperative process with 16 cm H_2O maximal positive pressure, FiO_2 0,25, and there was no need for thoracic drain. She was discharged to the ward on day 2, having tachypnea, respiratory frequency of around 40/min, and saturation was around 95% with 2 L/min oxygen.

Following uneventful 6 weeks tachypnea, respiratory distress and oxygen demand increased (5 L/min). A chest x-ray on day 42 showed diffuse multilocalized, giant, pneumatoceles in the right lung, where the biopsy was taken (Fig. 2), and also on Thorax CT (Fig. 3). Due to her severe respiratory distress, she was transferred to the pediatric intensive care unit. She had no fever, and her acute phase reactants, blood cultures, and polymerase chain reaction for cytomegalovirus, herpes simplex virus, Epstein–Barr virus, mycobacteria in blood, and also *Pneumocystis jirovecii* in tracheal secretions were negative. Two days after pneumatoceles occurred, minimal pneumothorax was noted, but no invasive procedures were performed. Treatments with methylprednisolone (2 mg/kg/day), hydroxychloroquine (5 mg/kg/day), and azithromycin (10 mg/kg/day, 3 days/week) were started. Pneumatoceles had resorbed on the 10th day of treatment. Oxygen demand decreased to 2 L/min. She was discharged on oxygen 1 L/min and followed closely. Steroid treatment was tapered starting at the 4th month of the treatment, and was stopped at the 11th month. Azithromycin and hydroxychloroquine treatment was continued. The need for oxygen had disappeared, pulmonary hypertension had recovered, and sildenafil treatment was discontinued. Further radiological improvement was observed 1 year after treatment initiation (Fig. 4).

Written consent was obtained from the parents.

DISCUSSION

Chronic interstitial lung disease, which is rare in children, can present with a wide spectrum of histological abnormalities and radiological-clinical phenotypes.[1] We report, herein, a female infant with surfactant protein C deficiency due to I73T mutation. This mutation represents the most common mutation, responsible for up to 50% of the cases.[2] Surfactant protein C deficiency is an autosomal dominant disease, characterized by variable clinical presentation.[3] In detail, the age of onset, disease severity, and natural progression of the disorder can show differences even within the same family in the presence of the same mutation.[3] On chest imaging, commonly SP-C deficiency initially presents with ground glass opacities or crazy paving pattern, slowly developing into intraparenchymal and subpleural cysts and honeycombing, during the natural course of the disease.

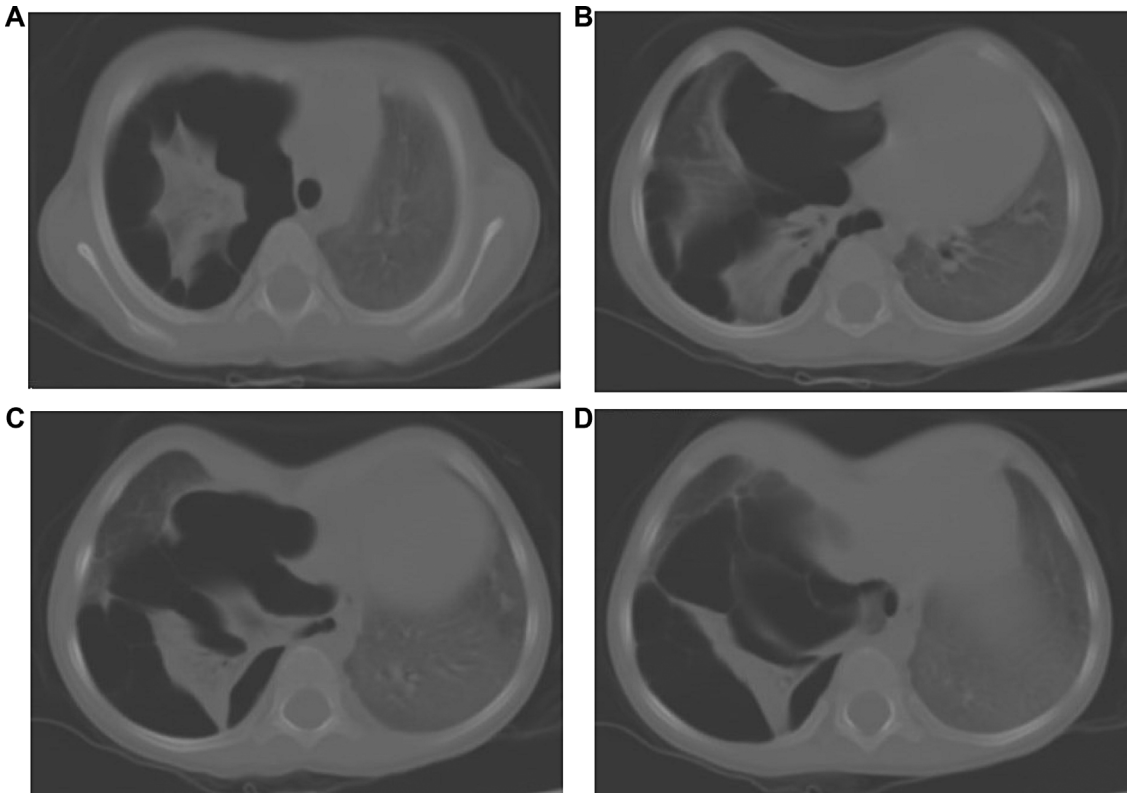

Fig. 3. (A–D) Appearence of pneumatoceles on Thorax CT.

Our patient developed diffuse and life-threatening giant pneumatoceles very early. It is possible that few already locally present cyst-like areas (Fig. 1), may have extended rapidly due to increased or changed transpulmonary pressures following the biopsy procedure. In addition, intrapulmonary air leak from the procedure may have contributed to the occurrence of the pneumatoceles. There is another another possibility; is pneumatoceles were resulted from localised persistent interstitial pulmonary emphysema due to invasive ventilation and positive pressure ventilation in this patient. We selected conservative treatment, that is, initiated empirical drug treatment for the interstitial lung disease and avoided drainage of the chest as may be associated with the risk of intubation and mechanical ventilation. Fortunately, the giant pneumatoceles were rapidly reversible with this treatment. To our knowledge, rapid development of such large and reversible pneumatoceles has not been reported with SP-C deficiency. Knowledge of this complication and empiric treatment may be helpful for future cases. Genetic diagnosis, which only became available during the course of disease in this patient, should be attempted as a first step if available, to avoid biopsy if possible.

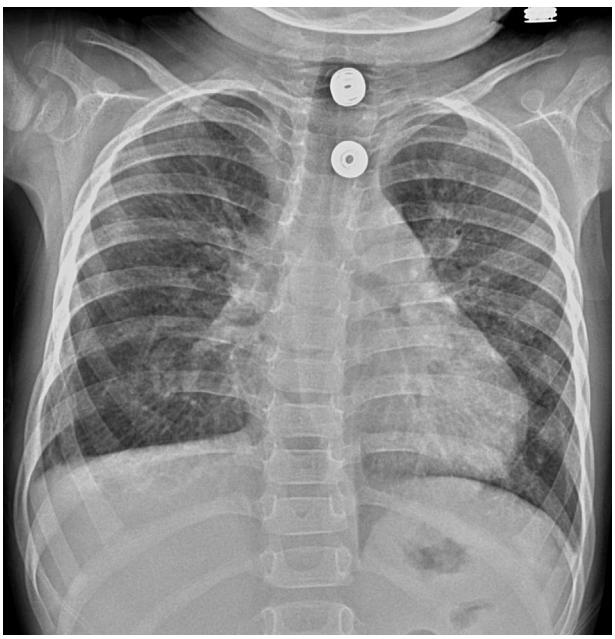

Fig. 4. Chest X-Ray in the first year of the treatment.

There are no randomized placebo-controlled studies regarding the treatments used empirically in SP-C deficiency. In this case, the combination of steroids, hydroxychloroquine, and azithromycin seemed to be effective. After the initiation of treatment, the patient improved clinically, oxygen demand disappeared. However, duration, dosage, route of application of the drugs, usage in combination or alone, and other details are currently undetermined. In a recent publication, it has been reported that the duration of hydroxychloroquine

treatment may be important for the long-term prognosis of the disease.[4] Taken together, randomized and controlled trials on these drugs are urgently needed and currently prepared (http://www.klinikum.uni-muenchen.de/Child-EU/en/index.html).

Pulmonary hypertension was reported as an additional major risk factor for mortality in children with interstitial lung disease.[5] Thus, we treated symptomatically with sildenafil, and together with the other treatments, significant improvement was observed clinically. Pulmonary hypertension was recovered, sildenafil treatment was discontinued.

In conclusion, in early life, interstitial lung disease should be considered in patients presenting with respiratory complaints, recurrent lower respiratory tract infections, gastrointestinal symptoms, and growth retardation. Large-giant pneumatoceles may develop during the course of surfactant protein C deficiency and associated diagnostic procedures. Medical treatment and oxygen support may not only be helpful in treating the underlying condition, but also complications like pneumatoceles, eliminating the need for invasive procedures.

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