CASE REPORT

Acute Kidney Injury Following Plastic Bronchitis Associated with Influenza B Virus in a Child with Nephrotic Syndrome

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Background: Plastic bronchitis is a rare but life-threatening disorder and is usually associated with congenital heart disease or pulmonary disease. **Case characteristics:** A 5-year-old boy with minimal change nephrotic syndrome who developed a relapse along with cough, fever and dyspnea. **Observation**: Chest *X*-ray showed atelectasis of right upper lobe of lung, and nasal swab was positive for influenza B virus. His respiratory condition worsened, and required ventilation; bronchoscopy revealed bronchial casts. This was followed by acute kidney injury which was successfully managed with hemodialysis. **Message:** Children with nephrotic syndrome on immunosuppressive agents can develop plastic bronchitis and acute kidney injury, following influenza virus infection.

Keywords: *Acute kidney injury, Influenza B virus, Minimal change nephrotic syndrome.*

Acute kidney injury (AKI), requiring dialysis, is an uncommon complication of childhood idiopathic nephrotic syndrome. Plastic bronchitis is an extremely rare and life-threatening disorder characterized by formation of large gelatinous branching airway casts, and is usually associated with congenital heart disease and pulmonary disease [1]. Plastic bronchitis has also been reported with pandemic 2009 influenza A virus infection [2-4]. We report a child with initial steroid-resistant minimal change nephrotic syndrome who developed relapse and AKI requiring dialysis, following plastic bronchitis associated with seasonal influenza B virus infection.

CASE REPORT

A 5-year-old boy with refractory nephrotic syndrome was admitted to our hospital because of the 5th relapse of nephrotic syndrome and dyspnea. On admission, his regular medication consisted of mizoribine and alternate-day prednisolone (10 mg/day). The patient had not been vaccinated against influenza. At the age of 2 years, the patient was diagnosed with initial steroid-resistant NS, and thus we performed first renal biopsy with histology showing minimal change disease (MCD). Thereafter, complete remission of NS was achieved with three courses of intravenous methylprednisolone pulses (20 mg/kg/day, total 9pulses) and cyclosporine A (6-7 mg/kg/day). However, after reduction in dose of steroids, frequent relapses of nephrotic syndrome occurred and single infusion of rituximab (375 mg/m^2) was given, resulting in withdrawal of steroids. The B-cell depletion period (defined by the time from rituximab treatment until the detection of CD19+ cells count >1% of total lymphocytes) was 5 months and the B cell count had recovered at the time of influenza B virus infection. A protocol renal biopsy 2 years after cyclosporine A treatment showed MCD and cyclosporine A-associated arteriolopathy, which prompted us to switch from cyclosporine A to mizoribine.

The patient had no history of congenital heart disease or chronic pulmonary disease. The day before admission, he had cough, fever, and wheeze. On arrival in our

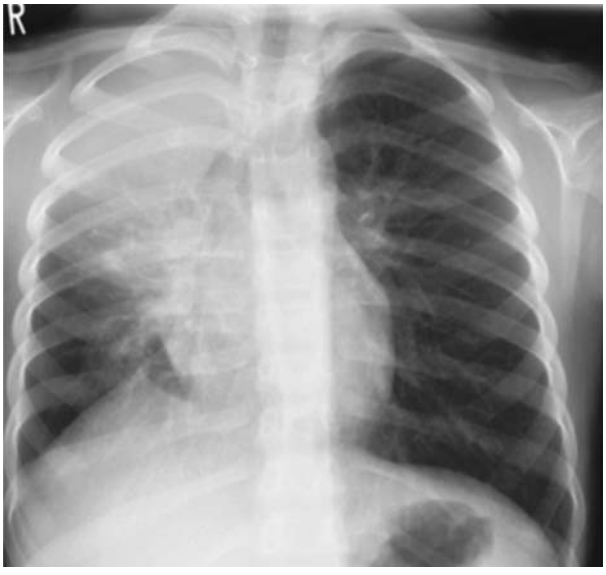

FIG. 1 *Chest radiograph on admission, showing atelectasis of the upper right lung with a mediastinal shift to the right.*

emergency room, he had fever, tachypnea and reduced breath sounds in the right hemithorax. A chest *X*-ray showed atelectasis of the right upper lung (***Fig***. **1**). Laboratory investigations were as follows: white blood cell count, 11,200/mm^3 (neutrophils, 81.1%; lymphocytes, 10.8%, monocytes, 7.0%; eosinophils, 1.1%); hemoglobin, 12.6 g/dL; platelet count, 329,000/mm^3; and C-reactive protein level, 5.16 mg/dL. Urinalysis showed 3+ protein by dipstick. The rapid nasal swab influenza antigen test was positive for influenza B virus.

Based on these findings, a presumptive diagnosis of relapse of nephrotic syndrome following pneumonia associated with both influenza B virus was made. The patient was treated with intravenous peramivir, antibiotics, steroids, and continuous inhalation of isoproterenol with supplemental oxygen. However, he responded poorly to treatment and his general condition deteriorated. On day 5 of hospitalization, generalized edema developed and blood examinations showed hypoproteinemia (total protein, 4.1 g/dL; albumin, 1.2 g/dL) and hemoconcentration (hemoglobin, 15.3 g/dL; hematocrit, 44.9%), whereas his renal function was normal at that time (serum creatinine concentration 0.24 mg/dL). The patient received infusion of 25% albumin because of decreased radiographic cardiothoracic ratio (38%) and poor peripheral perfusion (capillary refilling time >2 seconds) suggested presence of hypovolemia. Although respiratory support by mechanical ventilation was initiated, breath sounds in the right lung were not audible and chest *X*-ray showed mediastinal emphysema and subcutaneous pneumatosis, in addition to atelectasis. Therefore, a flexible bronchoscopy at the bedside was performed and bronchial casts were extracted from the right bronchus, leading to the diagnosis of plastic bronchitis. A second bronchial aspiration was performed the following day with further removal of the mucus plugging. After bronchial aspiration, oxygen saturation increased and chest radiography revealed marked improvement. On day 7 of hospitalization, the patient had raised blood urea nitrogen (57 mg/dL) and serum creatinine concentration (0.67 mg/dL). Oliguria (<0.5 mL/kg/h) continued for more than 12 hours despite the presence of hypervolemia (hypertension and increased radiographic cardiothoracic ratio 55%) after infusion of albumin, which prompted us to initiate continuous venovenous hemodialysis at bedsides using pediatric devices (TR-55X, Toray Co., Tokyo, Japan) and hemofilter (EXCELFRO AEF-03, Asahi medical Co., Tokyo, Japan). On day 11 of hospitalization, dialysis was discontinued because urine output increased, and extubation was performed the following day. Complete remission of NS was achieved with prednisolone (2 mg/kg/day), and he was discharged three weeks after admission.

DISCUSSION

Plastic bronchitis is an unusual cause of acute respiratory failure in children that can mimic status asthmaticus. In our patient, the ineffectiveness of inhaled β-agonists and steroids made us suspect this disorder. Recent studies indicate that a novel influenza A (H1N1), in which mucociliary clearance is more severely disturbed than in seasonal influenza virus may cause plastic bronchitis, irrespective of presence or absence of underling cardiopulmonary disease [2-4]. However, in our patient, seasonal influenza B virus induced severe plastic bronchitis. Ding, *et al*. [5], recently reported influenza B virus in three of nine Chinese children with plastic bronchitis; two of their patients developed renal failure. The reason why a simple seasonal influenza virus infection can cause plastic bronchitis is unclear. Plastic bronchitis has been reported in patients with Fontan physiology that is often accompanied by protein-losing enteropathy [6,7]. Hypoalbuminemia seen in our patient might have altered lymphatic flow leading to development of airway casts. Bronchial casts could be inflammatory (which occur in patients with cyanotic heart disease) or acellular (which occur during or following pneumonia and asthma) [8]. Histologic examination of bronchial casts was not performed in our patient. Intravascular volume depletion secondary to low serum albumin concentration and aggressive diuretic therapy during severe relapse of nephrotic syndrome may promote the formation of sticky bronchial casts. Narrowing of bronchi with mucosal edema in association with hypoalbuminemia might have led to the development of plastic bronchitis.

We speculate that influenza B infection under the aggressive immunosuppression (mizoribine and prednisolone) was associated with severe relapse of nephrotic syndrome leading to reversible idiopathic AKI in our case. However, exact pathogenesis of AKI remains unclear because renal biopsy at that time was not performed in our patient. Influenza virus has been associated with exacerbations and relapse of nephrotic syndrome, especially in unstable patients [10]. Our case demonstrates that the risk of plastic bronchitis and AKI should be kept in mind when children with nephrotic syndrome on immunosuppressive agents suffer from seasonal influenza virus infection.

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