

Renal Abscess in Hyper-IgE Syndrome

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Kidney disease due to *Aspergillus fumigatus* is a rare finding in hyper-IgE syndrome. We report a patient with autosomal dominant hyper-IgE syndrome, recurrent pneumonia, and acute necrosuppurative pyelonephritis caused by *Aspergillus fumigatus* with a fatal outcome. We emphasize the severity and the difficulties in the management of renal complications that could be limiting the survival of these patients. UROLOGY 81: 414–416, 2013. © 2013 Elsevier Inc.

Hyper-IgE syndrome (HlgES) is a rare primary immunodeficiency caused by mutations of the STAT-3 gene (autosomal dominant inheritance) involving deficiency of multiple cytokine transduction, reduction of Th-17 cell differentiation, and insufficient interleukin-17 production.¹ Patients can present with chronic eczema, skin abscesses, recurrent respiratory infections, and high serum levels of IgE (≥ 2000 IU/mL).² The main causes of infections are *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*, with possible progression to bronchiectasis and pneumatoceles, usually due to disorders of lung remodeling.^{2,3} However, kidney disease due to *Aspergillus fumigatus* is not a frequent finding in those with HlgES.²⁻⁵

We report on a patient with autosomal dominant HlgES, recurrent pneumonia, acute necrosuppurative pyelonephritis caused by *Aspergillus fumigatus*, and a fatal outcome.

We emphasize the severity and the difficulties in the management of renal complications that could be limiting the survival of these patients.

CASE REPORT

The patient was a 16-year-old boy who presented with chronic eczema and severe recurrent infections that had been occurring since 2 months of age and affected the skin, ears, sinuses, lungs, and liver. Most were caused by *S. aureus*. He was referred to our primary immunodeficiency clinic at 3 years of age. The physical examination findings were remarkable for scaly facial eczema, rales, and

splenomegaly. He presented with cranial dysmorphisms, including a prominent forehead, macrocephaly, a broadened nasal bridge, and mild prognathism. His family history was unremarkable. The serum immunoglobulin levels were normal, except for IgE, which was very high (9080 IU/mL). The pneumococcal antibodies were normal. Human immunodeficiency virus serology was negative, and the sweat chloride concentration was normal. When the patient was 13 years old, a radiograph of the teeth showed retention of the primary teeth. Computed tomography of the lungs showed multiple pneumatoceles and bronchiectasis.

After HlgES was diagnosed, the patient started therapy with prophylactic sulfamethoxazole-trimethoprim at 40 mg/kg/d and intravenous gammaglobulin at 400 mg/kg/d every 21 days.

The patient developed various infections during clinical follow-up. At 12 years of age he had undergone pulmonary lobectomy because of functional exclusion and pneumatoceles of the middle lobe of the right lung. At 15 years of age, he developed new signs and symptoms of pneumonia and a left perirenal abscess. On that occasion, it was necessary to perform clinical drainage by lumbar puncture, because the volume of the perirenal abscess was very large and had extended to the pelvis. After surgery, the patient showed good recovery from the infection.

At age 16, the patient was admitted with abdominal pain and microscopic hematuria. Ultrasonography revealed a heterogeneous collection in the subcapsular retroperitoneal region of the left kidney measuring $14 \times 8 \times 7$ cm. Urinalysis revealed leukocyturia and hematuria; the urea and creatinine levels were normal. Percutaneous puncture of the collection revealed growth of *Morganella morganii*. Treatment with amikacin (15 mg/kg/d) and oxacillin (200 mg/kg/d) was started and continued for 14 days, with a good clinical response. After 1 month, the patient again began to have lumbar pain, with vomiting and dyspnea. Computed tomography of the abdomen revealed a collection close to the upper pole of the left kidney and extending to the spleen. An echocardiogram revealed pleural effusion on the left, and urine culture showed

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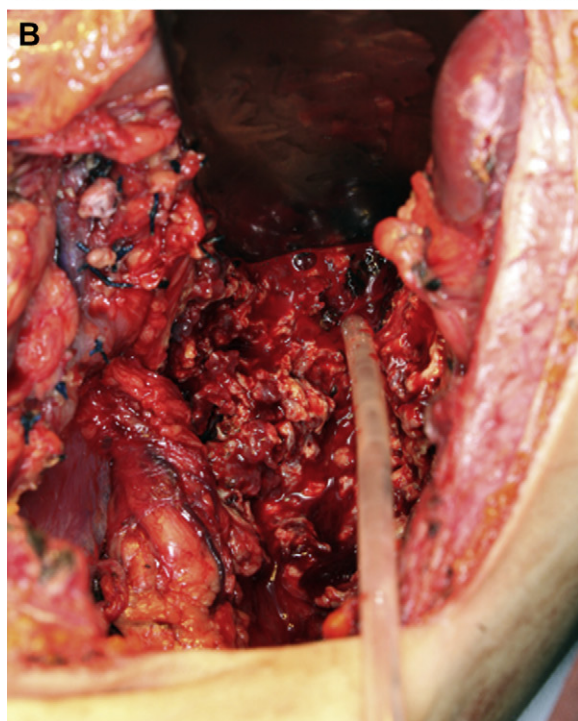
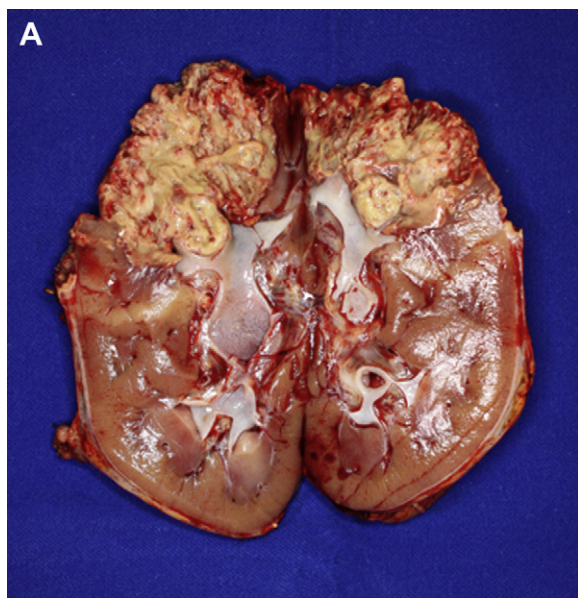


Figure 1. (A) Severe involvement of upper pole of left kidney. **(B)** Presence of perforations of left diaphragm with release of bubbles during respiratory movement. (Color version available online.)

the growth of *S. aureus* (>100,000 colonies/mL). Treatment with vancomycin (40 mg/kg/d) and cefepime (120 mg/kg/d) was started and continued for 30 days.

On that occasion, the retroperitoneal abscess was drained, and total left nephrectomy was performed, with ipsilateral pleural drainage. The upper pole of the left kidney was fully destroyed and had no cleavage plane with the left diaphragm because of the infection (Fig. 1A). Perforations of the left diaphragm were observed, with the release of bubbles during respiratory movement (Fig. 1B).

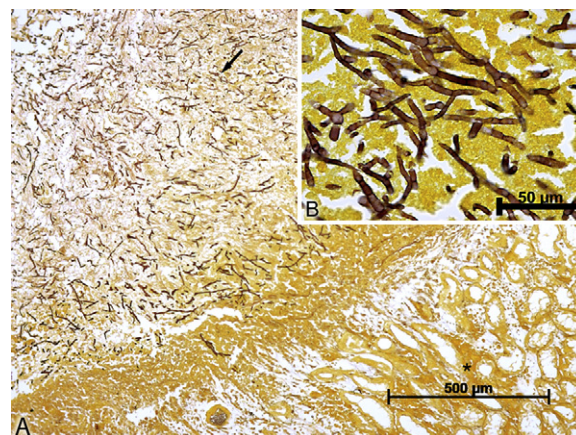


Figure 2. Gomori methenamine silver (GMS) stain showing interface between normal kidney parenchyma (asterisk) and infected area with septate hyphae with acute angle branching (arrow) compatible with *Aspergillus fumigatus*. (Color version available online.)

The patient developed persistent lumbar pain, dyspnea, and hemoptysis. The abdominal drain was kept under a water seal because of the pneumoperitoneum resulting from the diaphragmatic perforations. Cultures of the surgical wound, pleural fluid, and sputum revealed the growth of *Aspergillus fumigatus*, and voriconazole (6 mg/kg/crisis, with a maintenance dose of 4 mg/kg/d) was given for 30 days. The anatomic pathologic findings of the kidney were compatible with acute necrosuppurative pyelonephritis and showed *Aspergillus fumigatus* (Fig. 2). Liposomal amphotericin B was administered in combination (3 mg/kg/d). After 30 days, the abscess in the left renal pelvis had recurred and was again drained surgically. A large pleural-abdominal fistula was detected with active escape of air during respiratory movements, as well as a large amount of purulent secretions. An abdominal drain was again placed under a water seal, with progressive improvement of the escaping air. However, during the subsequent 3 weeks, the patient developed progressive clinical worsening, dyspnea, hemoptysis, and refractory septic shock and finally died.

COMMENT

HlgES is a multisystemic disease characterized by serum levels of IgE usually >2000 IU/mL, chronic eczema, abnormalities of the musculoskeletal system, joint hypermobility, prominent forehead, macrocephaly, broad nasal bridge, retention of primary teeth, and recurrent infections, especially of the skin and lungs.^{1,2,4,5} Pulmonary involvement is 1 of the main causes of a fatal outcome, and the limitation of life for these patients results from both infection and subsequent pulmonary destruction.^{6,7} Sulfamethoxazole-trimethoprim should be used prophylactically to prevent infections by *S. aureus*, and intravenous gammaglobulin can reduce the number of infections. However, the use of other immunomodulating agents is controversial.⁷ The main pathogens involved in the

infections are *S. aureus*, *Streptococcus pneumoniae*, and *H. influenzae*. Infections due to *Pseudomonas aeruginosa* and *Aspergillus fumigatus* occur less frequently.

However, despite the complexity of the signs and symptoms and a large number of studies involving genes, cytokines, interleukins, and lymphocyte differentiation, little is known or has been reported about kidney involvement in these patients. Kidney disease due to *Aspergillus fumigatus* is a rare finding in HlgES,³⁻⁵ but it can occur in other clinical situation such as human immunodeficiency virus infection, systemic long-standing steroid treatment, after transplantation, and other primary immunodeficiency diseases.^{4,8-13} This information could be of help in the treatment and prognostic evaluation. Our patient presented with very severe renal involvement concomitant with involvement of the left diaphragm and a pleural abdominal fistula that was treated appropriately with a satisfactory clinical response, although he rapidly progressed to a fatal outcome.

According to our data search, no reports have been published of patients with HlgES and renal abscess. From the present findings and the scarcity of published data, we emphasize that patients with HlgES and recurrent respiratory infections should be monitored early. *Aspergillus fumigatus* has angioinvasive properties and is able to disseminate by the hematogenic route to other organs such as the kidneys. Renal involvement is rare and is generally associated with the formation of abscesses.^{8,9} The diagnosis of invasive aspergillosis continues to be a challenge and is determined by the clinical findings in patients with risk factors, isolation of the microorganism, the serologic detection of antibodies or antigens, the radiologic findings, or histopathologic evidence of invasion. Invasive aspergillosis causes pulmonary involvement in 90% of cases, with a mortality rate of about 60%. Thus, a detailed clinical history and physical examination and laboratory and imaging examinations are important for the early detection of infectious processes and for the immediate institution of appropriate treatment.¹¹⁻¹⁵

Thus, additional studies of kidney involvement in HlgES are needed to estimate the response to treatment and the limiting factors regarding the quality of life of these patients.

The present study is apparently the first case report of kidney involvement in a patient with such primary immunodeficiency. It should attract the attention of urologists and serve as a warning.

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