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CASE REPORT

Mixed Pulmonary Infection, Asthma, and Nephrotic Syndrome in a Patient Diagnosed with Selective IgA Deficiency: A Case Report

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Abstract: Patients with selective IgA deficiency could have various clinical presentations ranging from asymptomatic to severe respiratory or gastrointestinal tract infection, as well as autoimmune disease and allergic reactions. Selective IgA deficiency is relatively common in Caucasians, but it is rare in the Asian population, meaning it could be easily missed in the clinic. In this study, we report a 26-year-old man with a history of asthma and nephrotic syndrome. He presented with symptoms of pulmonary infection, and his condition quickly deteriorated to respiratory failure that required endotracheal intubation and mechanical ventilation. Sputum smear; sputum, blood, and bronchoalveolar lavage fluid culture; and metagenomic sequencing examination identified multiple mixed pathogens, including *Mycobacterium chelonae-abscessus, Pseudomonas aeruginosa, Candida parapsilosis, Acinetobacter baumannii*, and *Klebsiella cepacia*. Finally, he was diagnosed with selective IgA deficiency after a laboratory test detected an extremely low serum IgA level (<0.06 g/L). The patient died of septic shock and multiorgan failure despite aggressive management with a combination of antibiotics and supportive care. We report this case to remind clinicians about this rare disease in the Asian population. Patients with multisystem illnesses that are related to immune dysregulation, such as asthma or nephrotic syndrome, should be tested for immune system disorder. Rare and mixed pathogens should be considered during antibiotic selection in patients with selective IgA deficiency.

Keywords: selective IgA deficiency, asthma, nephrotic syndrome, pulmonary infection

Introduction

Selective IgA deficiency (sIgAD) is the most common type of primary immunodeficiency.[1] The disease is characterized by an undetectable level of IgA, whereas the levels of other immunoglobulin remain in the normal ranges. IgA is the predominant antibody found in the mucous membranes lining the respiratory and gastrointestinal tracts. It plays a significant role in mucosal immunity and defends the mucosal surfaces against toxins and pathogens.[2] IgA deficiency (IgAD) can result in allergic disorders and an increased risk for infections, particularly in the respiratory and gastrointestinal tracts.[3] sIgAD is relatively common in Caucasians, with an incidence up to 1 in 150 individuals.[4] However, sIgAD is rare in the Asian population. In China, studies identified an incidence of only 1 in 4000 individuals, and the incidence is even lower at 1 in 18,000 individuals in Japan.[5,6] Studies from two other research groups also reported a low prevalence of sIgAD in Kazakhstan (Central Asia) and India (South Asia).[7,8] In this study, we described a Chinese man with a medical history of asthma and nephrotic syndrome who presented with pulmonary infection from multiple mixed pathogens. He was finally diagnosed with sIgAD. We report this case here to remind clinicians about this rare disease in Asian population.

Case Presentation

A 26-year-old man was admitted to the Zhejiang Provincial Hospital of Integrated Traditional Chinese and Western Medicine (Zhejiang, China) because of intermittent cough and shortness of breath for 10 months and exacerbation with

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fever for 1 month (Figure 1). He visited a local hospital several times because of the intermittent cough and shortness of breath and received bronchodilator, antitussive, and antibiotic therapy, which provided temporary relief. Then, 1 month before presentation, the patient exhibited sudden-onset shortness of breath after passing stool. An ambulance was called, and his oxygen saturation was low. He received endotracheal intubation, and he was admitted into the intensive care unit (ICU) at a local hospital. After treatment with biapenem, linezolid, and voriconazole, his condition improved, and he was extubated. However, 1 week before presentation, the patient experienced worsening cough and shortness of breath with low-grade fever (37.6–37.9°C) and night sweats. Chest computed tomography (CT) revealed bilateral multiple bronchiectasis with scatted patchy consolidation. The patient was transferred to our hospital for further management.

The patient's past medical history included asthma for 8 years and nephrotic syndrome for 14 years, with his symptoms including intermittent proteinuria, severe edema, hyperlipidemia, and hypoproteinemia. His routine medications were albuterol and budesonide/formoterol inhalers when necessary and long-term methylprednisolone. He had an allergy to moxifloxacin.

Upon admission to our hospital, his vital signs were as follows: blood pressure, 123/61 mmHg; respiratory rate, 25 breaths/min; heart rate, 97 beats/min; and temperature, 38.6°C. He was awake but slightly lethargic. Physical examination revealed a moon face with few skin abrasions around the lips. He had barrel chest with a few crackles on lung auscultation. The laboratory test results are presented in Table 1. In addition, the sputum Xpert tuberculosis test was negative, but the sputum acid-fast bacillus smear was positive. Repeat chest CT identified bilateral upper lobe consolidations (Figure 2). He was diagnosed with secondary bilateral upper-lobe pulmonary tuberculosis, asthma, and nephrotic syndrome. Anti-tuberculosis treatment was initiated with isoniazid, rifampicin, pyrazinamide, and ethambutol. In addition, a bronchodilator was given to relieve his symptoms.

Several days after hospital admission, sputum culture revealed the presence of nontuberculous mycobacteria, which were identified as *Mycobacterium chelonae-abscessus*. The minimum inhibitory concentrations were 4.0 μg/mL for streptomycin, 0.2 μg/mL for isoniazid, 40 μg/mL for rifampicin, and 2.0 μg/mL for ethambutol. In the clinic, the patient reported worsening of his cough and shortness of breath, and his oxygen saturation dropped to 70%. He was intubated and transferred to the ICU. Bronchoscopy was performed, revealing a large amount of necrotic granulation tissues in the trachea and right main bronchus. The pathological examination identified small pieces of parakeratotic atypical squamous epithelium in the degenerated mucoid tissue. Acid-fast, periodic acid-Schiff, periodic acid methenamine silver, and Giemsa staining were all negative. His antibiotics were switched to meropenem (1 g every 8 h), linezolid (0.6 g every 12 h), azithromycin (0.5 g daily), and cefoxitin (4 g every 8 h). However, the patient had a persistent high fever with a temperature of 39–40°C and a high

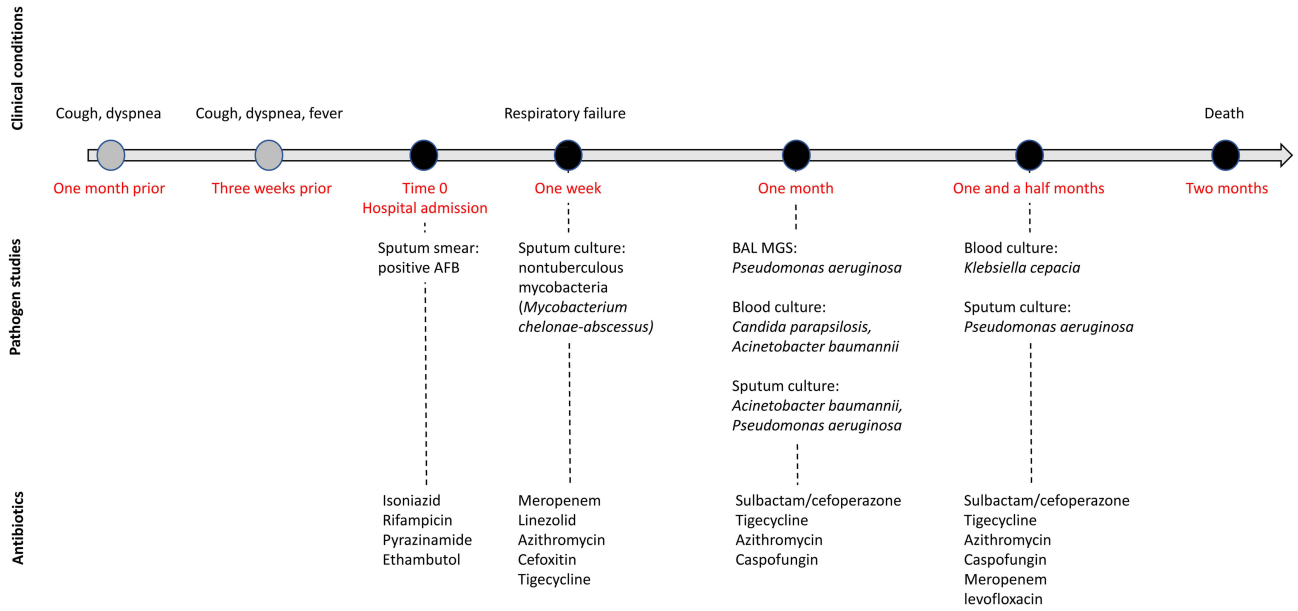

Figure 1 Disease course timeline.
Abbreviations: AFB, acid-fast bacillus; BAL, bronchoalveolar lavage; MGS, metagenomic sequencing.

Table 1 Dynamic Changes of Laboratory Test Results

Laboratory Test Results (Normal Range)	Time 0	1 week	1 Month	1.5 Months
Blood tests				
White blood cells, × 10^9/L (4.0–11.0)	16.5	11.7	12.6	39.5
Hemoglobin, g/dL (13.5–17)	11.8	10.9	7.3	5.8
Platelets, × 10^9/L (150–400)	311	296	270	187
Albumin, g/dL (3.5–5.5)	3.19	2.92	2.6	2.84
Cholesterol, mg/dL (<200)	36.54	32.94	13.68	22.8
Triglyceride, mg/dL (<150)	30.96	18.18	18.18	28.26
Blood urea nitrogen, mmol/L (2–8)	5.13	7.27	4.96	12.52
Creatinine, μmol/L (62–115)	55.4	45.6	37.1	63.6
Lactate, mmol/L (<2)	0.7	0.7	1.2	2.1
Immunoglobulins				
IgA, g/L (0.8–3.0)				<0.06
IgM, g/L (0.63–2.77)				0.14
IgG, g/L (6.9–16.2)				8.4
Complement C4 (0.16–0.36)				0.21
Complement C3 (0.66–1.30)				0.57
Lymphocyte subsets				
Total T lymphocyte CD3 (60.0–85.0%)				96.5
Cytotoxic cells CD8 (18.5–42.0%)				49.56
CD4/CD8 (0.71–2.87)				0.82
Total CD19 B lymphocytes (7.0–23.0%)				0.10
CD4 helper T cells (24.5–48.5%)				40.56
CD16+56 natural killer cells (8.0–20.0%)				3.3
Urine tests				
pH (4.5–8)	7.5	7.45	7.53	7.51
Protein (−)	−	−	+	++

white blood cell count. Tigecycline (50 mg every 12 h) was added because of its activity against *M. chelonae-abscessus*. In addition, methylprednisolone (40 mg daily) was added, but the drug was tapered and stopped because of evidence of gastrointestinal hemorrhage. One month after hospital admission, metagenomic sequencing of the bronchoalveolar lavage fluid disclosed *Pseudomonas aeruginosa*. The blood culture identified *Candida parapsilosis* and *Acinetobacter baumannii* (moderately sensitive to sulbactam/cefoperazone and sensitive to tigecycline). Sputum culture revealed *A. baumannii* and *Pseudomonas aeruginosa*. Repeat chest CT demonstrated bilateral scattered patchy infiltrations, cavities, and ground-glass shadows, mainly in the lower lobes, which were significantly increased compared with the findings of the first scan. The antibiotic regimen was changed to sulbactam/cefoperazone (2 g every 6 h), tigecycline (100 mg every 12 h), azithromycin (0.5 g daily), and caspofungin (50 mg daily). One and a half months after hospital admission, 2023, repeat blood culture identified *Klebsiella cepacia*, and sputum culture identified *P. aeruginosa* with moderate sensitivity to meropenem and levofloxacin. Therefore, meropenem (1 g every 6 h) and levofloxacin (0.5 g daily) were started. The immunoglobulin test results included an extremely low IgA level (<0.06 g/L; normal range, 0.8–3.0 g/L) and normal levels of IgM (0.14 g/L) and IgG (8.4 g/L). The lymphocyte subsets and flow cytometry analysis are presented in Tables 1 and 2. Bone marrow biopsy was also performed, identifying a chromosome 9 translation. However, the patient's clinical conditions continued to deteriorate, including persistent fever, low oxygen saturation even after tracheostomy, septic shock, and acute renal failure. Almost 2 months after the hospital admission, the family elected to discontinue treatment, with the patient quickly succumbing to the illness.

Discussion

sIgAD is the most common type of primary immunodeficiency. It is rare in the Asian population.[5,6] Most affected patients have no clinical symptoms, but some patients carry a high risk of recurrent infections in the respiratory and

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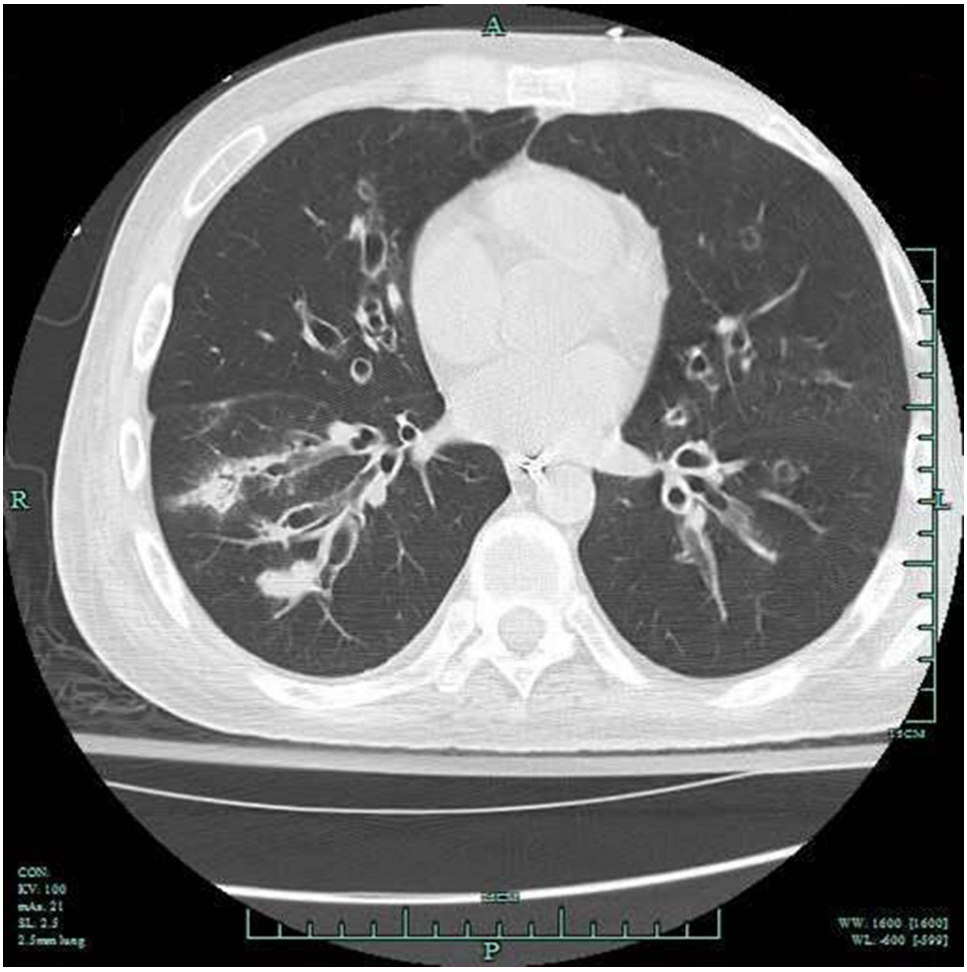

Figure 2 Chest computed tomography revealed bilateral upper lobe consolidations.

gastrointestinal tracts. In this study, we examined a Chinese patient with sIgAD with severe pulmonary infection from multiple pathogens. Antibiotics were given, but patient died of respiratory failure and septic shock.

The diagnostic criteria for sIgAD are as follows: 1) age ≥ 4 years; 2) serum IgA level < 0.07 g/L; 3) normal or elevated IgG and IgM levels; and 4) intact cellular immune function.[1] The pathogenesis of sIgAD is unclear, but it might may be related to immunoglobulin class switch recombination, effector or memory B cell defects, and chromosome 18q deletion syndrome.[9,10] We identified a translocation of chromosome 9 in our patient. Its relationship with sIgAD requires further study.

Table 2 Flow Cytometric Immunoassay Results

Cell Population	Percentage (%)	Cell Types/Phenotype Analysis
Lymphocytes	4.1	T cells accounted for 97.4% of lymphocytes. CD4/CD8 = 0.69, without obvious abnormality. Natural killer cells accounted for 1.3% of lymphocytes without obvious abnormality.
Granulocytes	92.0	Significant increase in the relative percentage.
Monocytes	2.3	Predominantly mature monocytes.
CD45 weakly positive cells	0.3	A small number of myeloid blasts were present.
CD45 negative cells	1.3	Mainly nucleated red blood cells and cell fragments.

The clinical presentation of patients with sIgAD can vary significantly,[11] but the disease is typically asymptomatic. Approximately 60% of patients with sIgAD have no symptoms, likely due to redundant immune mechanisms to compensate for individual type of immunoglobulin defect. The second presentation type is autoimmune disease, such as systemic lupus erythematosus, rheumatic arthritis, or Hashimoto disease. Our patient had nephrotic syndrome, which could be the result of immune dysregulation related to sIgAD. The third presentation type is allergic reaction. Many patients with sIgAD can have IgE-mediated allergic reactions, such as eczema or asthma. In addition, allergic or even anaphylactic reactions could occur after blood transfusion in these patients. In addition, sIgAD can present as infections with different severities. Most of these infections arise in the upper or lower respiratory tract or gastrointestinal system, which normally has abundant IgA levels. Finally, in the long-term course of the disease, IgAD can progress to common variable immunodeficiency or even malignancies in some patients. Previous case reports found that patients with sIgAD presented with various symptoms, such as anogenital tumor, persistent ulcerative gingivitis, endophthalmitis, and disseminated drug-resistant tuberculosis.[12–15] Clinical vigilance regarding sIgAD should be encouraged to avoid missed diagnosis of this rare illness.

There is no cure for IgAD. Patients with clinical symptoms can receive anti-allergic or antibiotic medications. Prophylactic antibiotics can also be considered in patients with recurrent infection. Nosocomial infection by multiple drug-resistant pathogens should be considered when selecting appropriate antibiotics. Treatments should consider bacterial sources as well as viral and fungal pathogens.[16] Immunoglobulin infusion was reported, but it should be applied cautiously because it can cause anaphylactic reaction.[1]

Our patient had a history of asthma and nephrotic syndrome. IgA plays a role in regulating immune responses at mucosal surfaces, including airways. The absence of IgA can cause immune dysregulation, leading to chronic inflammation in the lungs and airways and contributing to the development of asthma. The immune system in individuals with sIgAD is often compensated by increased levels of other antibodies, such as IgE. Higher IgE levels are associated with allergic responses, which can trigger or worsen asthma symptoms.[5] Patients with sIgAD have a higher risk of autoimmune diseases, which can affect the kidneys. Recurrent infections in sIgAD can lead to immune complex formation, in which clusters of antigens and antibodies accumulate and deposit in the kidneys, causing inflammation and contributing to nephrotic syndrome.[17] Meanwhile, both asthma and nephrotic syndrome could be attributable to immune dysregulation and exacerbate the clinical conditions of patients with sIgAD.[18]

In the current case presentation, the patient presented with respiratory infection. Sputum smear; sputum, blood, and bronchoalveolar lavage fluid culture; and metagenomic sequencing detected infections by multiple mixed pathogens, including *M. chelonae-abscessus, P. aeruginosa, C. parapsilosis, A. baumannii*, and *K. cepacia*. These pathogens are commonly observed in immunocompromised patients, and they commonly cause nosocomial infections.[19] In addition, the results of laboratory tests included a low level of serum IgA (<0.06 g/L). Despite multiple anti-bacterial and anti-fungal treatments, as well as respiratory supportive care, the patient died of septic shock, acute renal insufficiency, and respiratory failure.

In conclusion, patients with sIgAD could present with allergic diseases such as asthma and types of immune dysregulation such as nephrotic syndrome, in addition to respiratory or gastrointestinal infections. Appropriate immune screening tests might be considered as a routine examination in these patients with multisystem disorders. Their infections could be caused by multiple mixed pathogens, necessitating a combination of several antibiotic treatments.

Consent to Participate

The written informed consent to participate was obtained from the patient. The study also received ethical approval to publish case details from ethics committee of Zhejiang Provincial Hospital of Integrated Traditional Chinese and Western Medicine.

Consent for Publication

Written informed consent was obtained from the patient's father for publication of this case report and any accompanying images, as the patient has deceased.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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